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Original Article

Investigating Information, Attitudes and Behaviors about Breast Cancer Screening Methods of Women Aged 20-69 in Giresun

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Abstract

Aim: To evaluate the knowledge, attitudes and behaviors of women about knowing breast cancer screening methods and applying them at the right time and frequency.
Materials and Methods: A total of 206 women between the ages of 20-69 years who applied to the Family Medicine and General Surgery outpatient clinics of the Training and Research Hospital between July 2022 and February 2023 participated in the study. A 59-question questionnaire including the 'Breast Cancer Risk Assessment Forum' accepted by the Ministry of Health, which evaluates sociodemographic characteristics and breast cancer risk level, was applied face-to-face to the participants.
Results: The mean age of the participants was 40.57±14.25 and the median value was 38. According to the breast cancer risk assessment form, 81.1% (n=167) of the participants were in the low risk group, 13.6% (n=28) in the medium risk group, 1.5% (n=3) in the high risk group and 3.9% (n=8) in the highest risk group. 68% (n=119) of the participants had learned to perform CHCMM from healthcare professionals. The prevalence of those who practiced MMR was 43.2% (n=89).
Conclusion: Although the women who participated in our study were informed about breast cancer screening methods, the rate of application of these methods was low. For this reason, the role of healthcare professionals, especially family physicians, in identifying patients at high risk of breast cancer, examining them, applying screening methods and referring them to the necessary places is very important.

Keywords: Breast cancer screening, breast cancer risk, breast cancer awareness

CITATION
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INTRODUCTION

Cancer incidence and mortality are increasing rapidly worldwide due to the aging and growth of the population, as well as the increase in risk factors associated with many socioeconomic developments (1). In 2020, there were 19.3 million cancer diagnoses and approximately 10 million cancer-related deaths worldwide (1).

The risk of developing cancer in a person's lifetime (up to the age of 75) is around 20% and the risk of dying from cancer is around 10%, which means that 1 in 5 people will develop cancer in their lifetime and 1 in 10 people will die from cancer (2). With an estimated 2.3 million new cases in 2020, female breast cancer is the most commonly diagnosed cancer (1,2). Current data suggest that by 2030, the number of breast cancer cases diagnosed worldwide will reach 2.7 million per year and mortality will reach 870 000 (3). In low- and middle-income countries, the number of breast cancer diagnoses is projected to increase with the transition to a western lifestyle (late pregnancies, reduced breastfeeding, early menarche, decreased physical activity and unhealthy dietary practices) and with the further development of cancer screening and innovations in diagnostic facilities over the years (4).

When compared with the Global Cancer Observatory (GLOBOCAN: The Global Cancer Observatory) data, Turkey's cancer incidence is slightly higher than the world incidence.

Cancer incidences in the West Asia region, including Turkey, are lower than those in Turkey. The cancer incidences of countries with a high level of development such as the USA and Eastern and Central Europe are higher than those of Turkey (5).

Clinical breast examination (CBE) is a screening method with a lower budget; if studies on this subject can provide sufficient evidence, it can be introduced into routine practice (6). In women over 20 years of age, breast self-examination is performed once a month to increase breast cancer awareness and to provide information about early diagnosis of breast cancer; clinical breast examination is performed routinely once a year in women aged 20-40 years with a history of breast cancer in first-degree relatives and once every two years in women without a history of breast cancer; mammography is performed routinely in all women aged 40-69 years. It is performed every two years in addition to the annual clinical breast examination in women (7).

The Breast Cancer Risk Assessment Form, which was first adopted by the Ministry of Health in 2000 in Turkey, is recommended for use in the National Family Planning Service Guide. It questions age, body structure, age at first menarche, age at first birth, familial history of breast cancer, and personal history of breast cancer.

We aimed to determine the breast cancer risk levels of women aged 20-69 years who applied to the Family Medicine and General Surgery outpatient clinics of the Training and Research Hospital and to determine whether early diagnosis of breast cancer is possible and the positive results of early diagnosis, as well as to determine how well they recognize the symptoms of breast cancer by evaluating their knowledge of screening methods and their application at the right time and frequency.

MATERIALS AND METHODS

The study was conducted in Giresun Training and Research Hospital Family Medicine and General Surgery outpatient clinics. The population of the study consisted of women aged 20-69 years living in Giresun province. As of 01.07.2022, 147,662 women aged 20-69 years living in Giresun were randomly sampled from the study population (8).

The minimum sample size was previously determined by Kutlu and Biçer in a similar study conducted in Konya in 2017, in which the rate of CHCMM was found to be 24.5% (9). G*Power version 3.1.7 application was used to determine the sample size. In the study, using simple random sampling method, it was calculated that at least 51 participants could provide the representativeness of the population with 5% acceptable type 2 margin of error (with 95% power) and 95% confidence level.

The verbal consent of the women who applied to the Family Medicine and General Surgery Polyclinic of the Training and Research Hospital was obtained and they were informed about the study. The data were collected by the researcher by applying a sociodemographic data form and Breast Cancer Risk Assessment Form, and a questionnaire by face-to-face interview.

At the end of the questionnaire, the participating women were informed about their breast cancer risk status. Women who had not undergone screening were advised to undergo screening.

The Breast Cancer Risk Assessment Form, which was first adopted by the Ministry of Health in 2000 in Turkey, was recommended for use in the National Family Planning Service Guide. It questions age, body structure, age at first menarche, age at first birth, familial history of breast cancer, and personal history of breast cancer (10). According to the answers of the breast cancer risk assessment form, the participants received scores ranging from 10 to 300 and their risk levels were calculated according to the total score of the answers.

Statistical Analysis

Statistical analysis IBM SPSS 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) was used. Descriptive measures were presented as mean, standard deviation and percentage distribution. The conformity of the data to normal distribution was checked by Kolmogorov-Smirnov test. Chi-square (Fisher's Exact test when necessary) was used to compare the distributions of categorical variables, student t test was used to compare the means between 2 groups when parametric conditions were met, One-way ANOVA analysis was used to compare more than 2 groups, Mann-Whitney U test was used to compare the medians between 2 groups when parametric conditions were not met, Kruskall-Wallis analysis was used to compare continuous variables between more than 2 groups. Statistical significance level was taken as $p<0.05$.

RESULTS

The study included 206 women aged 20-69 years who applied to the Family Medicine and General Surgery Outpatient Clinic. The mean age of the participants was 40.57±14.25 and the median value was 38 (min:20-max:70). While 69.4% (n=143) of the participants were married, 30.6% (n=63) were single. Of the participants, 51.5% (n=106) were university graduates and 35.9% (n=74) were health workers or 35.0% (n=72) were housewives. Other sociodemographic characteristics of the participants are given in Table 1.

The mean breast cancer risk score of the women who participated in the study was 162.7±81.9 in the low risk range with a median value of 150 (min:60 - max:640). Risk scores were categorized 81.1% (n=167) of the participants were in the low risk group, 13.6% (n=28) in the medium risk group, 1.5% (n=3) in the high risk group and 3.9% (n=8) in the highest risk group (Table 2).

88.3% (n=182) of the women who participated in the study answered yes to the question "Do you think it is possible to recognize breast cancer at an early stage?" and 10.2% (n=21) did not know.

When the women who participated in the study were asked which early diagnosis methods can be used for early diagnosis of breast cancer, 59.2% (n=122) said yes to "breast self-examination",

48.1% (n=99) said yes to "physician examination", 52.9% (n=109) said yes to "mammography", 41.3% (n=85) said yes to "breast USG", and 13.6% (n=28) did not know the answer.

Table 1. Sociodemographic characteristics of the participants

		n	%
Age Groups	30	71	34.5
	31-40	40	19.4
	41-50	32	15.5
	51-60	43	20.9
	60-70	20	9.7
Marital status	Married	143	69.4
	Single	63	30.6
Income level	Low	30	14.6
	Middle	167	81.1
	High	9	4.4
Education level	Illiterate	11	5.3
	Literate	10	4.9
	Primary school graduate	41	19.9
	Secondary school graduate	7	3.4
	High school graduate	31	15.0
	University graduate	106	51.5
Profession	Housewife	72	35.0
	Health worker	74	35.9
	Retired	11	5.3
	Worker	16	7.8
	Officer	22	10.7
	Tradesmen/Private sector	11	5.3

Table 2. Mean breast cancer risk scores and grouped distribution of participants

		n	%
Risk Score (categorized)	Low risk (≤200 points)	167	81.1
	Medium risk (201-300 points)	28	13.6
	High risk (301-400 points)	3	1.5
	Highest risk (>400 points)	8	3.9

The rate of those who answered yes to the question "Can breast cancer be cured if diagnosed early?" was 94.2% (n=194).

To the question "Who do you think should perform breast self-examination?", 54.6% (n=112) of the respondents answered "all women after the age of 20" and 9.3% (n=19) had no opinion.

While 27.5% (n=19) of those with an education level of middle school and below knew that self-examination was an early diagnosis method, this rate was 75.2% (n=103) in those with an education level of high school and above. As a result of the statistical analysis, it was found that the rate of knowing that self-examination is an early diagnosis method in those with high school and above education level was statistically significant compared to those with middle school and below education level ($p<0.001$). While 30.4% (n=21) of those with an education level of middle school and below knew that physician's examination was an early diagnosis method, this rate was 56.9% (n=78) in those with an education level of high school and above. As a result of the statistical analysis, it was found that the rate of knowing that physician's examination is an early diagnosis method in those with high school and above education level was statistically significant compared to those with middle school and below education level ($p<0.001$).

While 40.6% (n=28) of those with an education level of middle school and below knew that mammography was an early diagnosis method, this rate was 59.1% (n=81) in those with an education level of high school and above. As a result of the statistical analysis, it was found that the rate of knowing that mammography is an early diagnosis method in those with high school and above education level was statistically significant compared to those with secondary school and below education level ($p<0.001$).

While 14.5% (n=10) of those with an education level of middle school and below knew that breast USG was an early diagnosis method, this rate was 54.7% (n=75) in those with an education level of high school and above. As a result of the statistical analysis, it was found that the rate of knowing that breast USG is an early diagnosis method in those with high school and higher education level was statistically significant compared to those with secondary school and lower education level ($p<0.001$).

Table 3. Examination of the relationship between level of education and level of knowledge about breast cancer screening methods

		Education Level			
		Secondary school and below		High school and above	
		n	%	n	%
Self-examination	Yes	19	27.5	103	75.2
	No	50	72.5	34	24.8
Physician's examination	Yes	21	30.4	78	56.9
	No	48	69.6	59	43.1
Mammography	Yes	28	40.6	81	59.1
	No	41	59.4	56	40.9
Breast USG	Yes	10	14.5	75	54.7
	No	59	85.5	62	45.3

To the question "Is a palpable swelling or lump in the breast one of the early symptoms of breast cancer?", the highest percentage of correct answers was 91.5% (n=65) in the 20-30 age group. It was found that 83.2% (n=119) of married women gave the correct answer, while 90.5% (n=57) of single women gave the correct answer. While 73.9% (n=51) of those with secondary school education and below gave the correct answer, this rate was 91.2% (n=125) in those with high school education and

above. While all of those with high income levels gave the correct answer, the lowest rate of correct answers was 73.3% (n=22) among those with low income levels. While all retired people gave the correct answer, the lowest rate of correct answers was found in housewives with 72.2% (n=52). The rate of self-examiners in the 20-30 age group was found to be statistically significantly higher than the other age groups ($p<0.001$).

It was found that 63.1% (n=77) of the self-examiners were married and 36.9% (n=45) were single, while 78.6% (n=66) of the non-self-examiners were married and 21.4% (n=18) were single, and this difference was statistically significant ($p=0.018$).

While 84.4% (n=103) of those who performed self-examination had high school education or higher, this rate was 40.5% (n=34) among those who did not ($p<0.001$).

There was no statistically significant difference between those who performed self-examination and those who did not in terms of income level ($p>0.05$)

It was found that 53.3% (n=65) of those who performed self-examination were in the health worker group, while 58.3% (n=49) of those who did not were in the housewife group ($p<0.001$).

DISCUSSION

Breast cancer is the most common cancer in women in our country and in the world and its incidence continues to increase. Identifying women at high risk of breast cancer and implementing screening methods reduces the mortality and morbidity rates due to breast cancer. In this sense, the practice of CHCMM, CMM and mammography is of great importance.

The average age at diagnosis of breast cancer in Turkey is 53 years (11). Advanced age is the biggest risk factor for breast cancer. Life expectancy in Turkey is increasing day by day and our population is aging. This situation has increased the importance of aging in terms of breast cancer risk. In a study covering 21 countries in Europe, the cumulative incidence of breast cancer in women was 2.7% at age 55, 5.0% at age 65 and 7.7% at age 75 (12). In Turkey, 44.5% of women diagnosed with breast cancer are between the ages of 50 and 69, while 40.4% are between the ages of 25 and 49 (13). In a case-control study conducted by Tan et al. in Malaysia, 70.6% of the 3683 breast cancer cases were aged 45 years and older (14). In a study conducted by Eroğlu et al. in 5000 women, it was observed that the highest mean risk score (189.49) was found in cases over 60 years of age (15). In this study, the age range of 60-70 years had the highest risk score with 250.8, and the mean risk score of breast cancer increased with age, giving a similar significant result to the studies in the literature.

In a case-control study on breast cancer risk factors in which 7,663 women participated, the education level of the control group was found to be significantly higher (14). In the study of Mermer and Esen, no statistically significant relationship was found between educational level and breast cancer risk score (16,17). In accordance with the literature, in this study, it was found that the breast risk score increased statistically significantly as the level of education decreased. It was thought that the older age of the participants with an educational level below high school contributed to this situation.

In the study conducted by Keten et al. in 2014, 17.7% of the participants knew that monthly MMM should be performed and 25% knew that mammography should be performed every 2 years (18). In a study conducted in Diyarbakır in 2018, it was reported that 34.9% of the participants were aware that the ideal day is after the end of menstruation, 26.9% were aware that it should be performed after the age of 20, and 35.4% were aware that it should be performed regularly once a month (19). In this study, it was pleasing to see that the data related to CHCMM were higher than the data in our country.

Although CHCMM is not a definitive diagnostic method for breast cancer, it is important in terms of increasing women's awareness of their own bodies and making them more sensitive about breast cancer, and it is also emphasized that the mass in breast cancer cases is mostly detected by the woman herself (20). In the study, we questioned the participants about their status and frequency of performing CHCMM. 28.3% of the participants performed regular CHCMM every month, 66.5% sometimes performed CHCMM, and 14.6% had never performed CHCMM. In the study by Alpteker et al. 28% of women performed regular CHCMM, and in the study by Türk et al. 25.6% of women performed regular CHCMM (20,21). In our study, the rates of regular practice of CHCMM were higher than the rates in the study of Türk and Alpteker, albeit with a slight difference.

CONCLUSION

As breast cancer screening methods have improved, the possibility of early detection has increased, leading to early intervention and reducing morbidity and mortality. As promising as this is, it has not prevented breast cancer from threatening the lives of women worldwide. The most important part of early diagnosis and increasing survival is that women know and apply screening methods. The role of family medicine is very important in identifying patients at high risk of breast cancer, examining them, applying screening methods and directing them to the necessary places.

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Ethical approval: This study was approved by Ondokuz Mayıs University Clinical Research Ethics Committee on 08.06.2022 according to the directive of the clinical research ethics committee with decision number 2022/290. Giresun Provincial Health Directorate gave approval on 16.11.2022 with decision number E-4154435352-799. The study was conducted in accordance with the Declaration of Helsinki.

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Original Article

Effects of Multiple Peripheral Nerve Blockade on Headache Parameters in Episodic and Chronic Migraine

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Abstract

Aim: Peripheral nerve blockades are effective in the acute and preventive treatment of many headache disorders. The combined use of multiple occipital and trigeminal nerve branch blockades has not been adequately investigated. In this study, we aimed to investigate the efficacy of multiple cranial nerve blockade (MCNB) in the treatment of episodic and chronic migraine.

Materials and Methods: Between 2020 and 2022, local anesthetic 0.5% Bupivacaine (1 ml=0.5 mg) 40-45 mg in a single session was administered to the bilateral greater occipital nerve (GON), lesser occipital nerve (LON), supraorbital nerve (SON), supratrochlear nerve (STC) and auricotemporal nerve (ATN) with a 26 G 13 mm syringe to 32 patients (24 episodic migraine and 8 chronic migraine patients) who failed to respond to preventive medication and/or developed drug intolerance. A total of 5 sessions were repeated at 1st week, 2nd week, 4th week, 2nd month and 3rd month. After each session, information was collected on visual analog scale (VAS) for pain to assess pain intensity, number of attacks, analgesic consumption, cumulative pain duration and MIDAS (baseline-3rd month).

Results: In the Episodic migraine (EM) and Chronic migraine (CM) group pre-procedure; VAS score was median (min-max) 8(5-9),7.5(5-8), number of attacks/months 6.5(3-12),15.5(15-18), analgesic consumption/month 5(2-9),8(2-9), cumulative pain duration/h 15(10-48),13(12-48). At the end of the 3rd month, VAS score was 4(3-7) in EM, 4.5(3-6) in CM, number of attacks 4(1-9),6(3-8), analgesic consumption 5(2-13),5.5(4-12), cumulative pain duration 15.5(5-33),21(10-31), respectively. The variability in headache assessment parameters after multiple cranial nerve blockade (MCNB) was similar in both groups and the difference between the groups was not significant.

Conclusion: In both migraine groups, MCNB containing local anesthetic is effective in pain intensity, number of attacks, analgesic consumption and cumulative pain duration for at least 2 weeks. The prophylactic effect decreases as the interval of local anesthetic application is prolonged and time progresses. MCNB can be used in both episodic migraine and chronic migraine to produce an analgesic effect in the acute phase of refractory pain.

Keywords: Episodic migraine, chronic migraine, pericranial nerve blockade, local anesthetic, bupivacaine

CITATION

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INTRODUCTION

Migraine is a primary headache disorder with clearly defined diagnostic features in the International Classification of Headache Disorders, third edition (1). Chronic migraine (CM) can be diagnosed in patients with migraine with or without aura who meet ICDH criteria and have 15 or more headache days at least 8 days a month (1). Although there is no specific diagnostic criteria for episodic migraine (EM) in ICHD-3, it refers to individuals with headache less than 15 days per month (2). Individuals with CM may be a migraine group with more severe and prolonged migraine, more difficult to treat and more functional impairment than individuals with EM (2). Migraine is one of the most common neurologic disorders with a lifetime incidence of 43% and 18% in women and men, respectively (3). Despite numerous recent advances in pharmacologic and

neuromodulatory options for the treatment of migraine, these therapies may not be the best available option in conditions such as cardiovascular and/or cerebrovascular disease, renal or hepatic impairment, pregnancy, psychiatric comorbidities or drug interactions, and current therapeutic modalities (lifestyle and dietary recommendations, symptomatic and preventive treatment) may not provide satisfactory pain management in some patients. For many of these patients, peripheral nerve blockades (PNBs) can be dramatically effective and should be considered.

PNB are commonly used procedures. They are generally considered to be safe and well-tolerated procedures that can provide relief within minutes not only of headache but also of allodynia and photophobia symptoms in an outpatient setting (4). The pain-modulating effects of PNBs can last up to several months in some patients, much longer than the pharmacokinetic profile of the type of local anesthetic used in the procedure (5). The analgesic effects of PNBs are not fully understood, but the pain suppression is due to selective blockade of sensory fibers while preserving motor function and then producing central pain modulating effects via second-order neurons in the trigeminocervical complex. PNBs are most commonly performed in the anatomical distribution of the pain experienced by the patient, but there may also be analgesic effects outside the distribution of the anesthetized nerve due to the convergence of multiple nociceptive systems centrally (6).

The common target for peripheral nerve blockades is the greater occipital nerve (GON). However, other nerves that innervate the scalp can also be targeted, including multiple branches of the trigeminal nerve, such as the lesser occipital nerve (LON), supratrochlear (STN), supraorbital (SON) and auriculotemporal (ATN) nerves.

The use of blockades of multiple occipital and trigeminal nerve branches has not been adequately investigated in migraine subgroups. Our aim in this study is to evaluate the efficacy and safety of multiple cranial nerve blockade in both EM and CM patients over a three-month period.

MATERIALS AND METHODS

Study population

After obtaining Siirt University Ethics Committee approval (63355number/2023/01/02), this retrospective observational analytical study was conducted between 2020 and 2022 in 32 migraine patients, including 24 episodic migraine and 8 chronic migraine patients, who did not respond to preventive drug treatment and developed drug intolerance in Siirt Training and Research Hospital Neurology Polyclinic Headache Unit. The diagnostic criteria and classification of migraine were made according to 'The International Classification of Headache Disorders, 3rd edition (ICHD-3 beta version)' updated by the IHS in 2013 (1).

Our inclusion criteria were that the patients had not received any prophylactic treatment in the last month, had not been diagnosed with analgesic/triptan use headache, had not received botulinum toxin injection in the past, had not described aura, had 3 or more attacks per month, and had a VAS score of 5 or higher.

Our exclusion criteria included hypertension, diabetes mellitus, ischemic chronic heart disease, congestive heart failure, chronic renal failure, chronic liver disease, presence of tumor and/or vascular disease, chronic inflammatory diseases, active psychiatric disease, prior peripheral nerve blockade, botulinum toxin injection, occipital nerve stimulation or occipital surgery or active infection, local anesthetic allergy and/or intolerance, anticoagulant use, lack of follow-up data. Complete blood count, routine biochemistry and thyroid function tests were performed and vitamin B-12, folate and ferritin levels were measured in each patient to exclude possible secondary causes of headache. Computed tomography (CT) or magnetic resonance imaging (MRI) was performed when deemed necessary.

Age, gender, duration of migraine headache/month, number of attacks/month, pain intensity, cumulative pain duration/hour, analgesic and/or triptan use/month were recorded for all migraine patients to be treated in our unit. Headache severity was recorded using a visual analog scale (VAS). Migraineurs were informed about the VAS numbered from 0 (no pain) to 10 (worst pain) and asked to indicate the severity of pain. In the headache unit, large occipital nerve (GON), small occipital nerve (LON), supraorbital nerve (SON), supratrochlear nerve (STN) and auriculotemporal nerve (ATN) nerve blockades were performed by the same specialist for a total of 5 sessions repeated at the 1st week, 2nd week, 4th week, 2nd month and 3rd month. After each procedure, pain intensity, number of attacks, cumulative pain duration, analgesic consumption was recorded on the headache follow-up form.

The multiple pericranial nerve blockade (MCNB) protocol and application

Tenderness along the GON (over the occipital protuberance) and LON (approximately 3 cm superomedial from the tip of the mastoid process) was detected by palpation with light pressure on the nerve. The origin of the GON is located 3 cm below the occipital process and 1.5 cm lateral to the midline. GON blockade was performed radially with a 26G 13mm needle and 3 ml of 0.5% bupivacaine (1ml=5mg) bilaterally 2 cm lateral and 2 cm below the protuberantia occipitalis externa, LON blockade was performed by injecting 3 ml of 0.5% bupivacaine (1ml=5mg) bilaterally 4-6 cm caudal to the line connecting the lowest points of the external auditory canals and approximately 6-7 cm lateral to the midline.

The SON blockade was performed after palpation of the corrugator muscle at the midline of the pupil at the upper edge of the orbit, a 26G 13mm needle was advanced laterally and 0.5 ml of 0.5% bupivacaine was injected bilaterally at a slight angle to avoid entering the foramen.

STN was performed by inserting the needle at the border of the medial line just above the eyebrow and injecting 0.5 ml 0.5% bupivacaine bilaterally.

At the point just anterior to the auriculotemporal (ATN) nerve tragus, after gentle aspiration to exclude any arterial return with a 26 G 13mm needle to a depth of approximately 4-6mm into the subcutaneous tissue, 0.5ml of 0.5% bupivacaine was injected bilaterally.

The maximum safe dose for bupivacaine infiltration or subcutaneous injection is 175 mg per dose. In this study, a total dose of 45 mg of bupivacaine was injected. The procedure took approximately 20 minutes to complete.

Following the informed consent process, patients were asked to lie on their back on the examination bed or sit in a chair, depending on the superficial nerve injected. Patients were also advised to eat and drink before participating in the procedure to reduce the possibility of syncopal episodes. Patients were kept under observation for 30 minutes post-injection to observe possible immediate side effects.

Following Patient Data

Patients were evaluated by the same neurologist at the first and follow-up visits in terms of pain intensity, cumulative attack duration, number of attacks, analgesic/triptan consumption at 1st week, 2nd week, 4th week, 2nd month and 3rd month after each session. Patients were given a headache diary in the form of a chart and were asked to fill in the parameters in the chart each time they had a headache attack. These findings were recorded on the patient headache form in the data system at control visits. At the end of the 3rd month, follow-up was terminated. In addition, MIDAS (Migraine Disability Assessment Scale) was documented for all migraine patients pre-procedure (baseline) and at the end of the 3rd month. The MIDAS test is the most widely used test to measure migraine disability since 2001 (7).

Statistical Analysis

Statistical analysis of the study was performed using Statistical Package for Social Sciences version 28.0 software for Windows (IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp., USA). Descriptive statistics of the variables were given as Mean±Standard Deviation, Median (Min-Max), and frequencies as n (%). The normality assumption for quantitative variables was tested with Kolmogorov-Smirnov and Shapiro-Wilk tests. Homogeneity of variances was tested with Levene homogeneity test. Statistical analyses of qualitative variables were performed using Fisher Exact Test and Fisher Freeman Halton Exact Test, taking into account expected values and rowxcolumn dimensions. Quantitative variables were analyzed using Independent t test, Mann-Whitney U and Friedman tests. When a significant difference was detected between the groups as a result of the Friedman test, pairwise comparisons were made with the Wilcoxon Signed Rank Test to determine the group that caused the difference. As a result of the Wilcoxon Signed Rank Test, group averages that were not significantly different were shown with the same letter.

RESULTS

A total of 32 migraine patients, 24(75%) episodic migraine patients and 8(25.0%) chronic migraine patients, completed the study. 81.3% of the patients were female and 18.3% were male. The relationship between gender and migraine type was not statistically significant (p=0.296). The proportion of patients with headache duration <12 months was 42.8%. The relationship between headache duration and migraine type is statistically significant (p=0.004). Chronic migraine was not detected in the group with a headache duration of <12 months, whereas chronic migraine was detected in 8 (100.0%) patients in the ≥12 group. Patients have a minimum of 3 episodes and a maximum of 18 episodes. The mean number of attacks was 8/month. The difference between the groups in terms of the number of attacks is statistically significant (p=0.000). The difference between the groups in terms of cumulative pain duration was not statistically significant (p=0.848). The difference between the groups in terms of frequency of analgesic/triptan use was not statistically significant (p=0.070). The relationship between MIDAS baseline scores and migraine groups is statistically significant (p=0.016). While 29.2% of patients in the episodic migraine group were in MIDAS 3 and 66.7% in MIDAS 2 at baseline, 87.5% of patients in the chronic migraine group were in MIDAS 3. When MIDAS was evaluated at the 3rd month, 87.5% of EM patients were in MIDAS 1 and 75.0% of CM patients were in MIDAS 2. Although there was an improvement in MIDAS scores at 3 months, the relationship between migraine types was not statistically significant (p=0.578). Mean±Standard Deviation, Median (Min-Max), frequency and % values of headache parameters are given in Table 1.

The change in VAS score according to group and time is given in Table 2. According to these results, the temporal difference between VAS scores in the EM group was statistically significant (p=0.000). The median (min-max) VAS score pre-procedure was 8 (5-9), and the VAS score at 15 min post-procedure was 0 (0-2) significantly decreased. It was 1(0-3) at the 2nd week. However, the VAS values of the patients increased again as the duration of the procedure interval increased and time progressed. This change over time was statistically significant (p=0.000). A similar situation was found in the CM group. In CM, the median (min-max) VAS score pre-procedure was 7.5(5-8), and the VAS score at 15 min post-procedure was 0(0-1), which decreased significantly. At the 2nd week, the VAS score was 0.5(0-2). However, VAS pain scores of the patients increased again as time progressed. This change in VAS scores over time was statistically significant (p=0.000). The difference in VAS scores between EM and CM groups at pre-procedure, post-procedure 1st week, 2nd week, 4th week, 2nd month and 3rd month was not statistically significant (p>0.05) (Figure 1).

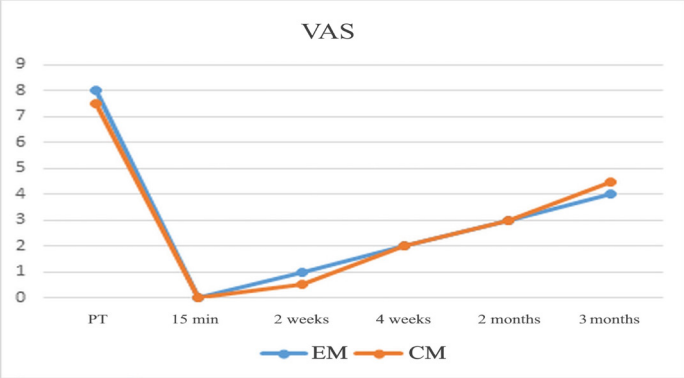

Figure 1. Variability of VAS score pre-procedure and post-procedure according to time and groups

The variation of the number of attacks according to group and time is given in Table 3. The temporal variation of the number of attacks in the EM group was statistically significant (p=0.000). In the 1st week, the median (min-max) number of attacks was 0 (0-1), in the 2nd week the number of attacks was 1 (0-4), and at the 3rd month the number of attacks was 4 (1-9). Temporal change in the number of attacks in the chronic migraine group was statistically significant (p=0.000). In the 1st week, the median (min-max) number of attacks was 2 (0-1), while in the 2nd week the number of attacks decreased to 0.5 (0-1). The number of attacks in 4th week, 2nd month and 3rd month were significantly different from each other (p=0.000). There is a statistically significant difference between EM and CM groups in terms of the number of attacks pre-procedure (p=0.000). The number of attacks was higher in the chronic group. There is no difference between EM and CM groups in terms of the number of attacks in the 1st week, 2nd week, 4th week, 2nd month and 3rd month (p>0.05) (Figure 2).

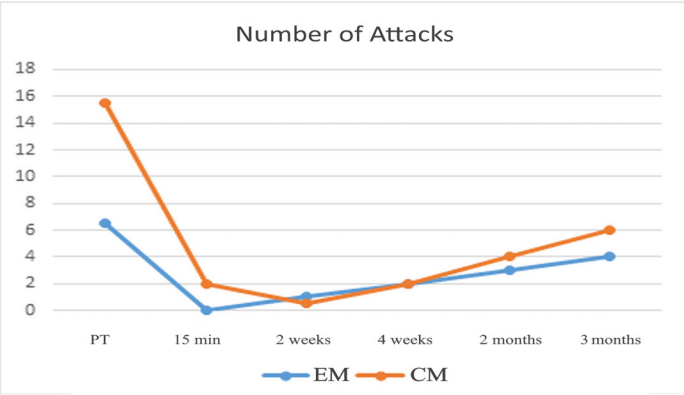

Figure 2. Number of attacks pre-procedure and post-procedure according to time and groups

The distribution of analgesic/triptan consumption/day values according to time and groups is given in Table 4. The change in the number of analgesic/triptan consumption/day in the EM group over time is statistically significant (p=0.000). 1st week median (min-max) 0(0-1), significantly decreased by 5(2-9) in the 2nd week 0.5(0-3), compared to pre-procedure, but increased over time. Analgesic/triptan consumption in the CM group decreased median (min-max) 0.5(0-3) in the first 2 weeks, 8(2-9) compared to pre-procedure, but increased over time. This increase was statistically significant (p=0.000). There was no difference between episodic and chronic migraine groups in terms of analgesic consumption in the 1st week, 2nd week, 4th week, 2nd month and 3rd month pre-procedure and post-procedure (p>0.05) (Figure 3).

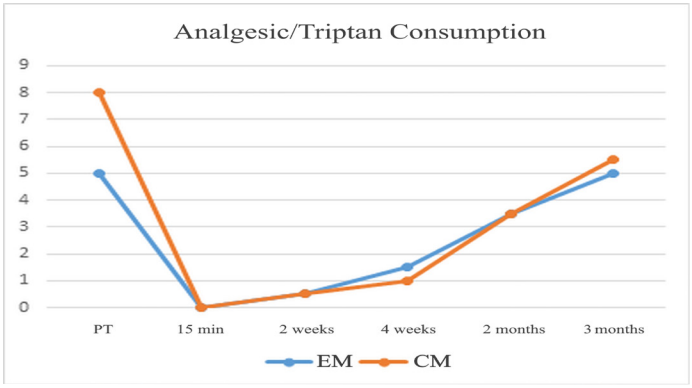

Figure 3. Variability of analgesic/triptan consumption pre-procedure and post-procedure according to time and groups

The values of cumulative pain duration according to time and groups are given in Table 5. According to these results, the change in cumulative pain duration in the EM group over time was statistically significant (p=0.000). The median (min-max) cumulative pain duration was 0(0-5) at the 1st week and 2(0-8) at the 2nd week, which decreased significantly compared to the pre-procedure period, but started to increase again as time progressed. In the CM group, the temporal difference in cumulative pain duration was statistically significant (p=0.000). In the CM group, cumulative pain durations decreased significantly with a median (min-max) of 0(0-4) at the 1st week and 2(0-8) at the 2nd week and then increased at the 2nd and 3rd month according to time. There was no difference between EM and CM groups in terms of cumulative pain duration at 1st week, 2nd week, 4th week, 2nd month and 3rd month (p>0.05) (Figure 4).

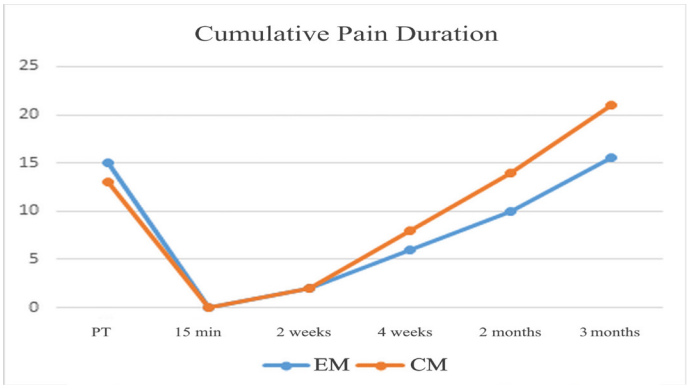

Figure 4. Cumulative pain duration variability pre-procedure and post-procedure to time and groups

Table 1. Descriptive statistics of variables and group comparisons

		Total n=32	Episodic Migraine n=24 (75.0%)	Chronic Migraine n=8 (25.0%)	*p*
Age, Mean±SD		32.34±11.83	32.25±12.23	32.63±11.28	*0.940#*
Sex	Female	26(81.3%)	18(75.0%)	8(100.0%)	*0.296**
	Male	6(18.3%)	6(25.0%)	0(0.0%)	
Headache duration	<12/month	14(43.8%)	14(58.3%)	0(0.0%)	*0.004**
	≥12	18(56.3%)	10(41.7%)	8(100.0%)	
Number of attacks/months, Median (Min-Max)		8(3-18)	6.5(3-12)	15.5(15-18)	*0.000$*
Cumulative pain duration/h, Median (Min-Max)		15(10-48)	15(10-48)	13(12-48)	*0.848$*
Frequency of analgesic/triptan consumption/month,Median (Min-Max)		5.5(2-9)	5(2-9)	8(2-9)	*0.070$*
MIDAS Basal	1	1(3.1%)	1(4.2%)	0(0.0%)	*0.016&*
	2	17(53.1%)	16(66.7%)	1(12.5%)	
	3	14(43.8%)	7(29.2%)	7(87.5%)	
MIDAS 3rd month	1	27(84.4%)	21(87.5%)	6(75.0%)	*0.578**
	2	5(15.6%)	3(12.5%)	2(25.0%)	

#: Independent t test, *: Fisher Exact Test, &: Fisher Freeman Halton Exact test, $: Mann-Whitney U

Table 2. Comparison of VAS score by time and groups

	VAS (pre-procedure)	VAS (post-procedure) 15. min	VAS 2nd week	VAS 4th week	VAS 2nd month	VAS 3rd month	$p^{\&}$
Episodic	8(5-9)a	0(0-2)b	1(0-3)c	2(0-4)d	3(1-5)e	4(3-7)f	*0.000*
Chronic	7.5(5-8)a	0(0-1)b	0.5(0-2)bc	2(1-3)cd	3(2-4)d	4.5(3-6)d	*0.000*
*p**	*0.761*	*0.789*	*0.944*	*0.272*	*0.873*	*0.800*	

*: Mann-Whitney U, &: Friedman Test, the difference between the means in the same row was performed with Wilcoxon Signed Rank Test. The difference between the values in the same row with the same letter is not statistically significant (p>0.05).

Table 3. Comparison of the number of attacks by time and groups

	Pre-procedure	Post-procedure 1st week	2nd week	4th week	2nd month	3rd month	$p^{\&}$
Episodic	6.5(3-12)f	0(0-1)a	1(0-4)b	2(0-5)c	3(1-7)d	4(1-9)e	*0.000*
Chronic	15.5(15-18)	2(0-1)a	0.5(0-1)b	2(1-4)a	4(1-4)c	6(3-8)d	*0.000*
*p**	*0.000*	*0.224*	*0.566*	*0.658*	*0.309*	*0.151*	

*: Mann-Whitney U, &: Friedman Test, the difference between the means in the same row was performed with Wilcoxon Signed Rank Test. The difference between the values in the same row with the same letter is not statistically significant (p>0.05).

Table 4. Comparison of analgesic/triptan consumption by time and groups

	Pre-procedure	Post-procedure 1st week	2nd week	4th week	2nd month	3rd month	$p^{\&}$
Episodic	5(2-9)e	0(0-1)a	0.5(0-3)b	1.5(0-6)c	3.5(0-8)d	5(2-13)e	*0.000*
Chronic	8(2-9)	0(0-1)a	0.5(0-3)a	1(1-5)b	3.5(2-10)c	5.5(4-12)d	*0.000*
*p**	*0.070*	*0.123*	*0.813*	*0.964*	*0.724*	*0.692*	

*: Mann-Whitney U, &: Friedman Test, the difference between the means in the same row was performed with Wilcoxon Signed Rank Test. The difference between the values in the same row with the same letter is not statistically significant (p>0.05).

Table 5. Comparison of analgesic/triptan consumption by time and groups

	Pre-procedure	Post-procedure 1st week	2nd week	4th week	2nd month	3rd month	p&
Episodic	15(10-48)e	0(0-5)a	2(0-8)b	6(0-24)c	10(2-26)d	15,5(5-33)e	*0.000*
Chronic	13(12-48)c	0(0-4)a	2(0-8)a	8(3-18)b	14(3-20)c	21(10-31)d	*0.000*
*p**	*0.848*	*0.166*	*0.504*	*0.119*	*0.120*	*0.190*	

*: Mann-Whitney U, &: Friedman Test, the difference between the means in the same row was performed with Wilcoxon Signed Rank Test. The difference between the values in the same row with the same letter is not statistically significant (p>0.05).

DISCUSSION

Some studies support peripheral nerve blockades (PNBs) as an effective and safe technique in patients with primary headache disorders such as migraine (8). This intervention is therefore considered as a treatment (6).

Pain in migraine and other primary headaches appears to be associated with activation of nociceptors in the duramater and intracranial blood vessels innervated by fibers from the first branch of the trigeminal nerve. Many studies also support the convergence of trigeminal afferents with the upper cervical roots at the level of the trigeminal nucleus caudalis in the brainstem (9).

For effective nerve blockade, it is important to know the superficial branches of the trigeminal nerve and the anatomical signs of the occipital region (10). Pain is usually defined in the forehead, behind the eyes, temporal, occipital and upper cervical regions. The forehead and upper periocular regions are innervated by the peripheral branches of the first division of the trigeminal nerve (V1), especially the supraorbital and supratrochlear nerves. The temporal regions are largely innervated by the branch of the auriculotemporal nerve that leaves from the mandibular division (V3) of the trigeminal nerve. The upper cervical and occipital region is innervated by the C2/C3 posterior cervical branches, especially the greater, lesser and third occipital nerves (10). PNBs targets include the greater occipital nerve, lesser occipital nerve, auriculotemporal nerve, supratrochlear and supraorbital nerves, sphenopalatine ganglion, and cervical spinal roots (8). It is usually performed using small subcutaneous injections of local anesthetics such as bupivacaine, lidocaine, mepivacaine and prilocaine, all of which have been used to treat headache (8). Local anesthetics reversibly inhibit voltage-gated sodium channels. When used in low doses, these drugs act selectively on sensory nerve fibers. However, the point that the drug effect lasts for several hours while the benefits may last up to several months is not fully understood. One explanation for this may be a break in the pain cycle, which is thought to be present in central sensitization in migraine (8). Moreover, the trigeminocervical complex is important in explaining the role of local anesthesia in reducing the frequency of migraine attacks, as this complex acts as a bridge between peripheral nociceptive stimuli and intracranial nociceptive receptors (11). Lidocaine, mepivacaine, and prilocaine (these three are about a quarter of the amount of bupivacaine) have a similar and mid-range duration of action.

Lidocaine in 1% solution is the most common choice, with onset of action about 4 to 8 minutes after injection and duration of action of about 1 to 2 hours. Bupivacaine in 0.25% or 0.50% solution has a longer duration of action, starting in approximately 8 to 12 minutes and lasting between 4 and 8 hours (8). Although these agents are thought to have similar effects, the different local anesthetics used make comparison between studies difficult. After bupivacaine (15,16), lidocaine is the second most commonly used drug for migraine (12-14,4,5); some studies used a combination of these two drugs (4). Ashkenazi et al. found no difference in the outcome of greater occipital nerve blockade for headache with lidocaine and bupivacaine alone or with the same agents with the addition of a steroid drug. Headache severity and related symptoms were not significantly different between the two groups. Long-term benefits were also similar between the two groups (17). M. Ruiz Pi ñero et al. decided to use an anesthetic agent with an intermediate duration of action (mepivacaine) versus an anesthetic with longer duration of action (bupivacaine). Their study shows that pericranial nerve blockade is a safe and effective preventive treatment for migraine (18). Corticosteroids are usually used only for GON blockades, but some headache centers also use them for infiltration into the LON. Lambru G et al. recommend that we avoid corticosteroids for any of the trigeminal nerve blockades, especially because of undesirable cosmetic side effects such as localized alopecia and lipoatrophy (19). The systemic effects of corticosteroids in PNB are not negligible and cases of iatrogenic Cushing's syndrome have been reported in the literature among headache centers (20). Repeated corticosteroid use may cause trophic changes in the occipital region that may be tolerated, but corticosteroid use in the facial region is not recommended (5). As discussed above, we decided not to use corticosteroids because our study design included the possibility of blocking the peripheral branches of the trigeminal nerve, SON, STN, ATN nerves. We decided to use bupivacaine alone, which has a long duration of action compared to other local anesthetics, because the procedure is multiple and involves the facial area.

Several recent randomized controlled trials and cohort studies have examined the efficacy of PNBs, particularly GON blockades. The level of evidence for the efficacy of PNBs in the treatment of different headache disorders varies in outcome depending on the pericranial nerve targeted and the measure used (21).

The only double-blind placebo-controlled clinical trial to evaluate

anesthetic blockade as a preventive treatment for migraine was published in 2001.In this crossover study, participants received two separate injections of 0.5% bupivacaine and a saline solution into the GON bilaterally, one month apart. Of the 63 patients included in the study, only 37 were included in the final analysis. No statistically significant difference was found in the duration or number of episodes (16). Blockade of GON with lidocaine was reported to stop migraine attacks in 88% of a patient group (22). 82% of another patient population experienced relief 15 minutes after GON and SON blockade with adrenaline and lidocaine (12). It was also reported to reduce pain in 90% of a patient group 20 minutes after lidocaine injection into the GON (13). To date, two placebo-controlled studies have been conducted entirely on CM patients. In 37 patients, there was no difference in the meantime without headache between local anesthetic (3.7 days) and local anesthetic and steroid injections (1.0 day) (17).

Caputi and Firetto applied a maximum of 10 blockades with 0.5% bupivacaine to the pressure-sensitive nerve exit points of both the GON and SON in 27 refractory migraine patients. Patients underwent 5 to 10 sessions on alternate days and experienced a decrease in total Pain Index (from 347.1 to 106.8 at one month and 60.9 at 6 months), monthly number of attacks (from 12.8 to 7.1 at one month and 5.1 at 6 months), and monthly analgesic consumption (from 12.4 at baseline to 5.6 at one month and 3.8 at 6 months) (15). In a recent study of 26 patients with migraine, lidocaine infiltration given in 3 doses 3 days apart in both SON and ION significantly reduced the number of attacks per month (from 9.9 to 2), pain intensity (from 9 to 3.5) and disability according to the MIDAS scale (from 3.2 to 1.4) at 6 months (14).

In a randomized, double-blind, placebo-controlled study by Malekian et al., 55 patients were treated with 4 different protocols: triamcinolone 0.5 ml + 2 ml saline, lidocaine 2% + 0.5 ml saline, lidocaine 2% + 0.5 ml 20 mg triamcinolone and 2.5 ml 0.9 saline solution in the last group. Patients were evaluated at baseline, one week, two weeks and four weeks after injection for severity and duration of headaches. GON blockade significantly reduced the number of attacks in episodic migraine for at least two weeks, while no group was superior to placebo for duration and severity of headaches (23).

In our study, in both migraine subgroups, the pain intensity evaluated by VAS score decreased from 7.5-8 pre-procedure to 0 (0-2) at 15 minutes in multiple cranial nerve blockade with 0.5% bupivacaine injection. With MNBs, pain intensity decreased in EM (1 in the first 2 weeks, 4 at the end of the 3rd month), in CM (0.5 in the first 2 weeks, 4.5 at the end of the 3rd month), number of attacks decreased in EM (1 in the first 2 weeks, 4 at the end of 3 months), in CM (0.5 in the first 2 weeks, 6 at the end of 3rd month), analgesic/triptan consumption decreased in EM (0.5 in the first 2 weeks, 5 at the end of 3rd month), in CM (0.5 in the first 2 weeks, 5.5 at the end of 3rd month). Cumulative pain duration was in EM (2/hour in the first 2 weeks, 6/h in the 4th week) compared to CM (2/h in the first 2 weeks, 8/h in the 4th week). From week 4 onwards, both groups showed a temporal increase. There was no significant difference between EM and CM in terms of pain intensity, number of attacks, duration of pain and analgesic consumption at 1st week, 2nd week, 4th week, 2nd month and 3rd month post-procedure. On the MIDAS scale, baseline decreased from 2(66.7%) to 1(87.5%) in EM and from 3(87.5%) to 2(25.0%)-1(75.0%) in CM. A positive correlation between the MIDAS score and the migraine did exist, however, that correlation did not reach statistical significance.

It is extremely difficult to compare our data with the data in the literature. First of all, the target nerves are not the same: options in the literature include SON and ION (14), bilateral GON (24,17) and GON and/or SON (15).

Although the American Headache Society made recommendations in 2013 about peripheral nerve blockades, frequency and amounts that can be performed in headache, there is still no clear consensus on this issue due to the lack of randomized controlled trials with a large number of patients. It is not known exactly whether single or multiple blockades can be used in clinical practice. However, as discussed above, studies from different centers have shown that peripheral nerve blockades are especially effective in primary headache patients. There are a limited number of studies investigating the long-term effects of such applications on pain.

To the best of our knowledge, our study is the first publication showing the temporal change in headache parameters with the combined use of multiple occipital (GON+LON) and trigeminal nerve branches (SON+STN+ATN) blockades in episodic and chronic migraine group.

Limits of the study

Due to the COVID-19 pandemic, we limited patient recruitment, considering patient and staff safety. While occipital nerve blockade was well tolerated, patients who could not tolerate the local anesthetic agent applied to the STC, ATC, SON nerves, especially those separated from the trigeminal nerve, and who had side effects had to be excluded from the study. Since the required sample size was not met equally in each group, the study tended to be inadequate in finding intergroup differences. However, it is noteworthy that despite the smaller sample size, the migraine groups experienced significant improvements over time. As we mentioned earlier, there were some challenges limiting the length of follow-up. We also did not examine the effect of MCNB on other symptoms, including nausea and vomiting.

CONCLUSION

Our own experience shows that MCNBs provide a safe and effective short-term preventive treatment for migraine and good analgesia in the acute phase. Typically, the duration of the therapeutic effect varies between patients, but for patients with migraine, injections with an interval of at least 2 weeks should be performed, as the benefits vary from weeks to months. MCNBs, especially at 2-week intervals, are more effective on pain intensity, number of attacks, analgesic/triptan consumption, and cumulative pain duration in both EM and CM groups. The

effect decreases as the interval of local anesthesia application increases and time progresses. In addition, the improvement of pain intensity at 15 minutes post-procedure in both groups supports that neurologists and algologists can also use it in acute treatment. Not only in prophylactic treatment but also as a daily procedure in the clinic or emergency room where rapid pain relief can provide a satisfactory result.

Given the heterogeneity of methods of using pericranial anesthetic blockade to prevent migraine and based on expert recommendations (6), placebo-controlled multicenter clinical trials need to be conducted with a high number of migraine groups to gather sufficient evidence to list MCNBs as a potential way to reduce migraine attack frequency and prevent pain severity.

Clinical implications

* The combined use of blockades of multiple occipital and trigeminal nerve branches is used to produce an analgesic effect in the acute phase of refractory pain in both episodic migraine and chronic migraine.

* In both episodic migraine without aura and chronic migraine, MCNBs containing local anesthetic are effective in pain intensity, number of attacks, analgesic consumption and cumulative pain duration for at least 2 weeks. The effect decreases as the interval of local anesthetic application is prolonged and time progresses.

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Original Article

Evaluation of Necessity for Intensive Care Stay, Mortality, and Morbidity in Poisoning Cases Admitted to the Emergency Department

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Abstract

Aim: Intoxications can occur as a result of the ingestion of the drugs or substances with a suicidal purpose or unintentional exposure to toxic substances. Patients are treated in emergency department, ward or intensive care unit.
Materials and Methods: We recorded demographic data of patients, including age, gender, coexisting medical conditions, and psychiatric history. The factors causing acute intoxication, the Glasgow Coma Scale (GCS) score at the time of admission, suicidal intent, the need for hospitalization (ward or intensive care unit), and mortality status were assessed.
Results: A total of 120 patients were included in the study. 67 patients (55.8%) were identified with suicidal intent. The ratio of suicidal intent among females was significantly higher compared to males (p=0.005). 35.8% of the patients were monitored in the emergency department, 9.2% in the general ward, and 55% in the intensive care unit.Among patients with a diagnosis of suicide, no mortality was observed. It was noted that 7 patients who were deceased had methanol intoxication, and 2 had mushroom-related intoxication. Among patients diagnosed with suicide, the most common causes of intoxication were analgesics (49.25%), antidepressants (25.37%), and antipsychotics (23.88%).
Conclusion: The ready availability and widespread and irregular use of antidepressants and analgesics contribute to frequent ingestion of these drugs for suicidal intent. In terms of public health, paying attention to regional mushroom consumption is crucial for reducing related fatalities.

Keywords: Intoxication, intensive care, suicidal intent

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INTRODUCTION

Acute intoxications constitute a significant portion of reasons for admissions to emergency departments. Studies evaluating intoxications indicate an annual incidence rate ranging from 0.002% to 0.93% in developed countries, while in our country, emergency department admissions are reported to be 0.46% to 1.57% due to intoxications (1,2). Intoxication can be defined as the impairment of hemodynamics resulting from exposure to a toxic substance or the consumption of a non-toxic substance in high doses. Intoxications can occur due to suicidal ingestion of drugs or substances, unintentional exposure to toxic substances, consumption of high doses of medication, or undesired drug reactions. Factors such as the type and quantity of the toxic substance, time of hospital admission, and duration of diagnosis and treatment influence the development of mortality and morbidity. While patients presenting to the emergency department due to acute intoxication require close hemodynamic monitoring and intensive care unit follow-up. Studies indicate that between 3% and 40% of these cases require intensive care monitoring (3).

In this study, our aim was to retrospectively evaluate the

demographic data of intoxication cases admitted to our hospital's emergency department over a two-year period, along with the reasons for intoxication and the necessity of intensive care admission.

MATERIALS AND METHODS

After obtaining ethical committee approval and institutional research permits (Giresun Training and Research Hospital Clinical Research Ethics Committee with number KAEK/145), patient records of individuals aged 18 and above who were admitted to the Giresun Training and Research Hospital Emergency Department with a diagnosis of intoxication between June 1, 2021, and June 1, 2023, were retrospectively reviewed.

Demographic data of patients, including age, gender, coexisting medical conditions, and psychiatric history, were recorded. In addition to the factors causing acute intoxication, the Glasgow Coma Scale (GCS) score at the time of emergency department admission, the nature of intoxication (suicidal intent), the need for hospitalization (ward or intensive care unit), and mortality status were assessed.

For patients admitted to the intensive care, the initial Acute Physiology and Chronic Health Evaluation (APACHE) scores upon admission, duration of hospital stay, requirement for mechanical ventilation, and organ damage conditions (such as acute kidney failure, liver failure, neurological sequelae) were also documented.

Statistical Analysis

We used Statistical Analysis IBM SPSS Statistics 23.0 (IBM SPSS, Chiago USA) software for statistical analysis of the data obtained in the study. We used the chi-square test while evaluating the categorical data. Categorical variables were presented as frequencies and percentages, while continuous variables were presented as mean ± standard deviation. A p-value lower than 0.05 was considered statistically significant.

RESULTS

A total of 120 patients were included in the study, with 67 (55.8%) being female and 53 (44.2%) male. The mean age of all patients was 41.03±17.29, with females having a mean age of 38.57±16.72 and males having a mean age of 44.13±17.65. Among the patients, 35.8% were monitored in the emergency department, 9.2% in the general ward, and 55% in the intensive care unit (Table 1). The average duration of stay for patients in the intensive care unit was 4.75±11.29, while the mean overall hospital stay was 5.27±12.41. Additionally, the initial Glasgow Coma Scale (GCS) score for patients admitted to the intensive care unit was 12.73±3.88, and the average APACHE II score was 7.68±7.74. Among the patients in intensive care, mechanical ventilation support was administered to 11 (16.7%) patients.

Of the patients presenting with intoxication to the emergency department, 55.8% (67 patients) were identified with suicidal intent. It was observed that the ratio of suicidal intent among females was significantly higher compared to males (p=0.005). Furthermore, patients diagnosed with a psychiatric disorder who had a history of treatment were found to have significantly higher rates of suicidal intent (p=0.031). Patients who presented with suicide-related reasons were found to have higher GKS (Glasgow Coma Scale) scores and lower APACHE scores compared to those who presented with other reasons. Mechanical ventilator support was required only in one patient. Intensive care unit stay durations were also significantly lower in suicide-related cases compared to those with other reasons for intoxication, as observed in Table 2. The mean age of patients with a suicidal diagnosis was 33.93±14.14, with females having a mean age of 33.38±13.05 and males having a mean age of 35.05±16.42. Among patients with a diagnosis of suicide, no mortality was observed, but 11 patients (16.4%) were referred to a specialized hospital for follow-up and treatment. For patients with intoxication due to other causes, the mean age was 50.00±16.83, and it was observed that 9 of them were deceased.

Table 1. Demographic data of the patients

		n	%
Sex	Female	67	55.8
	Male	53	44.2
Age	18-29 years	40	33.3
	30-39 years	23	19.2
	40-49 years	17	14.2
	50-59 years	19	15.8
	60 years and above	21	17.5
Psychiatric Treatment	Yes	54	45.0
	No	66	55.0
Suicidal intent	Yes	67	55.8
	No	53	44.2
Follow-up	ED	43	35.8
	Ward	11	9.2
	ICU	66	55.0
Mechanical ventilation support	No	109	90.8
	Yes	11	9.2

ED; Emergencydepartment, ICU; Intensivecareunit

The causes of intoxication for patients without a diagnosis of suicide are shown in Table 3, with the majority being related to mushrooms (45.28%) and methanol (32.07%). It was noted that 7 patients who were deceased had methanol intoxication, and 2 had mushroom-related intoxication. Among patients diagnosed with suicide, the most common causes of intoxication were analgesics (49.25%), antidepressants (25.37%), and antipsychotics (23.88%). Additionally, 38 patients (56.71%) experienced intoxication due to a single group of drugs, while 29 (43.28%) used drugs from multiple groups, resulting in intoxication.

Table 2. Evaluation of suicid-induced intoxications

		Suicidal intent		p
		No n (%)	Yes n (%)	
Sex	**Female**	22 (41.5)	45 (67.2)	**0.005**
	Male	31 (58.5)	22 (32.8)	
Psychiatric Treatment	**No**	35 (66.0)	31 (46.3)	**0.031**
	Yes	18 (34.0)	36 (53.7)	
Mortality	**No**	44 (83.0)	67 (100.0)	**0.000**
	Yes	9 (17.0)	0 (0.0)	
Mechanical Ventilation Support	**No**	43 (81.1)	66 (98.5)	**0.001**
	Yes	10 (18.9)	1 (1.5)	
		Mean±SD	**Mean±SD**	
Glasgow Coma Scale (GKS)		10.90±4.74	14.34±1.79	**0.000**
Acute Physiology and Chronic Health Evaluation (APACHE II) scores		12.97±8.34	3±2.30	**0.000**
Duration of stay in the intensive care units		6.94±14.72	2.06±1.13	**0.005**

Table 3. Causes of intoxication

	Agents	n	%
Causes of suicidal intoxications	**Analgesics**	33	49.25
	Antidepressants	17	25.37
	Antipsychotics	16	23.88
	Antiepileptic drugs	5	7.40
	Other groups	9	13.43
Causes of intoxication cases developed for other reasons	**Mushroom**	24	45.28
	Methanol	17	32.07
	Drugs	8	15.09
	Corrosive substance	2	3.77
	Thinner	1	1.88
	Pesticide	1	1.88

DISCUSSION

In our study, it was noted that the majority of patients presenting to the emergency department with intoxication were of suicidal intent. Particularly, a higher prevalence of suicide-related admissions among young females compared to males is evident in our country (4-6). Similarly, our study also found a higher proportion of suicide-related intoxications, consistent with the literature. Additionally, a significantly higher prevalence of suicide-related intoxications was observed among females.

The patients in our study were 18 years of age and older, and the majority of suicide-related intoxication cases were between the ages of 18-29, with an average age of 33.93. Similar studies have shown that the average age of suicide-related intoxication cases generally falls between 20-40 years (7,8). This phenomenon is influenced by various factors including social, cultural, and regional elements, with economic status playing a significant role.

It has been mentioned in similar studies that a significant portion of those attempting suicide have previously been diagnosed with a psychiatric disorder (7,9). Especially in cases of depressive disorders, a high occurrence of suicide attempts is noted, often involving medications used in their treatment. Similar studies indicate that approximately 50% of suicide attempt cases have a history of psychiatric diagnoses (7). In our study, 53.7% of suicide-related intoxication cases had a previous psychiatric diagnosis. This could be attributed to irregular follow-ups and medication usage, especially during the pandemic, as well as limited availability of closed psychiatric units in our region.

It is common in suicide-related intoxications for antidepressants to be the predominant class of drugs used. This is due to the widespread use and easy accessibility of antidepressants, the prevalence of psychiatric diagnoses like major depression in patient histories, and a higher incidence of suicidal thoughts in depressive patients (10,11). Additionally, suicide attempts often involve multiple drug classes, including a frequent combination of antidepressants and analgesics (3,12). In our study, the majority of suicide attempt cases (56.71%) reported using a single drug group, primarily analgesics (49.25%). The uncontrolled widespread use of analgesics in our society, many of which can be acquired without prescription, and their easy accessibility, are contributing factors.

The Black Sea region of Turkey, characterized by heavy rainfall and diverse vegetation, is prone to mushroom poisoning due to its rich fungal flora. Particularly in rural areas where mushrooms are commonly consumed as food, intoxications are encountered frequently. These can lead to gastrointestinal symptoms, fulminant liver failure, and even fatal complications. For example, a study evaluating 28 mushroom poisoning cases in an intensive care unit reported 6 fatalities (13). In our study, 24 patients were admitted to intensive care due to mushroom intoxication, and 2 of them died. Increased public awareness in mushroom-consuming regions is essential, emphasizing that toxic mushroom species cannot be reliably distinguished based on appearance alone and that consumption can lead to severe consequences including liver failure or death.

In our study, a significant portion (17 patients) of non-suicide-related intoxication cases were attributed to methanol poisoning, resulting in high mortality (7 patients). Methanol poisoning, often associated with illegal alcohol production, can lead to complications such as respiratory depression, metabolic acidosis, central nervous system symptoms, and even blindness, with a high mortality rate. In similar literature, mortality rates as high as 41.17% have been reported for methanol poisonings, as in our study. Increasing public awareness and taking preventive measures against illicit alcohol production are essential to prevent rising cases of methanol poisoning in our country.

CONCLUSION

In conclusion, our study revealed that the majority of emergency department admissions for intoxication were related to suicide attempts, particularly among young individuals and more frequently among females compared to males. The ready availability and widespread and irregular use of antidepressants and analgesics contribute to this phenomenon. In non-suicide-related attempts, mushroom and methanol poisonings were prevalent, with high morbidity and mortality rates. A significant portion of intensive care unit admissions were attributed to intoxication cases, highlighting the need for preventive measures against this public health threat.

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Original Article

Intolerance of Uncertainty in Patients with Alcohol Use Disorder

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Abstract

Aim: Alcohol is one of the most consumed substances worldwide, and the prevalence of alcohol use disorder is increasing. Intolerance of uncertainty has been proved to be one of the causes of alcohol intake. This study aimed to investigate whether the levels of uncertainty intolerance of people with alcohol use disorder differed from the healthy population.
Materials and Methods: 53 patients with alcohol use disorders and 55 healthy controls were included in the study. Sociodemographic data form and Intolerance of Uncertainty Scale were given to participants.
Results: Patients with alcohol use disorder were found to have a higher intolerance of uncertainty than healthy controls.
Conclusion: In Since alcohol use can play a role as a coping method in people with intolerance of uncertainty, this should be considered in treating alcohol use disorder.

Keywords: Alcohol use disorder, intolerance of uncertainty, anxiety

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INTRODUCTION

Alcohol is one of the most consumed substances worldwide and prevalence of alcohol use disorder is increasing. Alcohol consumption can cause significant problems in a person's health, psychology, family and social life, and economic-academic life (1). Alcohol intoxication and alcohol withdrawal can threaten people's lives (2). In the treatment of alcohol use disorder, detoxification is the first stage and to prevent craving and relapse is the second stage. As in all other substance addictions, personal factors play an important role in the success of treatment (3).

Intolerance of uncertainty (IU); it is defined as the inability in tolerating uncertainty, and experiencing distress in situations of uncertainty (4). The concept of intolerance of uncertainty, whose role in many mental illnesses was proved, has recently been the focus of attention in studies on addiction (4). It has been determined that intolerance of uncertainty may be an important factor related to more alcohol use (5).

In this study, it was planned to investigate the levels of intolerance to uncertainty in patients who applied to alcohol detoxification treatment and to contribute to the limited number of data in the literature in this field. The hypothesis of the study is that the level of intolerance of uncertainty is higher in patients with alcohol use disorder who apply to detoxification treatment than in the control group.

MATERIALS AND METHODS

The study was conducted between October-2022 and May-2023 at Ankara Training and Research Hospital, Alcohol and Substance Addiction Treatment Center (AMATEM). For the patient group, people who applied to our clinic for treatment due to alcohol use, and for the control group, patients' relatives and clinical staff were invited to the study, and 53 patients and 55 healthy controls who agreed to participate and met the conditions for inclusion were included in the study.

The inclusion criteria were being 18 years of age or older, being able to give informed consent, and not having severe mental illness (schizophrenia, schizoaffective disorder, bipolar affective disorder). The other criterion was to have been diagnosed with Alcohol Use Disorder according to DSM-5 for the patient group and not to have an alcohol-substance use disorder for the control group. Informed consent was obtained from all participants in the study. The study was carried out in accordance with the ethical standards in the 2013 Declaration of Helsinki. Ethical approval was obtained from the Clinical Research Ethics Committee of Ankara Training and Research Hospital for the study (date: 24.08.2022 - no: E-22-1033). The forms and scales used in the study are as follows:

1. Sociodemographic data form: In this form prepared by the researcher, the sociodemographic data of the participants such as age, gender, education level and employment status were asked. Additionally, the patient group was asked about clinical parameters such as first alcohol use age, average amount of alcohol they consumed per day, whether there were other substances they used, previous treatment histories, the longest periods without alcohol, and whether they had delirium tremens or epileptic seizures due to withdrawal.

2. Intolerance of Uncertainty Scale-12 (IU): It was developed by Carleton et al. in 2007, and its Turkish validity and reliability study was performed by Sarıçam et al. in 2014. In this 5-point Likert-type scale consisting of 12 questions, scores between 12-60 points can be obtained, and higher scores indicate intolerance of higher uncertainty. The first 7 questions consist of Prospective Anxiety (PA) subscale related to cognitions about future uncertain events, and the last 5 questions consist of the anxiety symptoms related to uncertainty and the inhibitory anxiety (IA) subscale related to behavioral symptoms (6).

Statistical Analysis

Research data were evaluated using SPSS (Statistical Package For Social Sciences for Windows v.22.0, SPSS Inc. Chicago, IL). The descriptive statistics were presented as mean±standard deviation, frequency distribution and percentage. The Kolmogorov-Smirnov test was used to determine whether the data set conformed to the normal distribution. In intergroup comparisons, Chi-square test was used for categorical variables, Independent sample t-test was used when normality assumptions were met for continuous variables, and Mann-Whitney U test was used when normality assumptions were not met. The relationship between variables was evaluated with Spearman correlation coefficient. Statistical significance level was accepted as $p<0.05$.

RESULTS

The study was carried out with 108 participants consisting of 53 patients and 55 healthy controls. It was observed that the patient and control groups were similar in terms of age, gender and marital status ($p>0.05$ for all three), and the education period of the control group was higher than the patients ($p=0.010$). Various sociodemographic data of the participants are shown in Table 1.

Table 1. Various sociodemographic data of the participants

	Patient (n=53)	Control (n=55)	p
Age (Mean±SD)	42.2±11.8	38.5±7.6	0.056[a]
Gender (male) n (%)	50 (94.3)	50 (90.9)	0.716
Marital Status (married) n (%)	28 (52.8)	37 (67.3)	0.169
Education period, years (Mean±SD)	9.7±3.2	12.6±6.1	**0.010**[b]
Being employed, n (%)	28 (52.8)	39 (70.9)	0.053
First alcohol consumption age (Mean±SD)	18.6±5.3		
Standard drink/day (Mean±SD)	11.9±4.0		
Longest withdrawal, month (Mean±SD)	8.4±15.4		
DT history+ n (%)	4 (7.5)		
Seizure history+ n (%)	9 (17.0)		
Judicial case+ n (%)	16 (30.2)		
Other substances+ n (%)	6 (11.3)		
Treatment History+ n (%)	37 (69.8)		

SD: Standard Deviation, n: Number, %: Percentage, DT: Delirium Tremens, [a]: Independent sample t test, [b]: Mann-Whitney U test

When the patient and control groups were compared in terms of the mean IU scores, it was observed that the mean IU scores of the patients were statistically significantly higher than the control group (IU-PA: $p<0.001$; IU-IA: $p<0.001$, IU $p<0.001$). The comparison of patients and control groups IU mean scores is shown in Table 2.

Table 2. Comparison of IUS score averages between patient and control groups

	Patient (n=53)	Control (n=55)	p
IU-PA, (Mean±SD)	24.9±5.7	18.8±6.3	**<0.001**[a]
IU-IA, (Mean±SD)	15.9±4.5	12.0±5.1	**<0.001**[b]
IU, (Mean±SD)	40.8±8.6	30.8±11.2	**<0.001**[a]

IU: Intolerance of Uncertainty Scale, PA: Prospective Anxiety, IA: Inhibitory Anxiety, [a]: Independent sample t test, [b]: Mann-Whitney U test

When various patient groups IU scores were compared, it was found that there was a significant difference between the groups of patients who used and did not use other substances, who suffered DT and who did not (p=0.020, p=0.007, respectively). The comparisons of IU and IU subscale scores between various patient groups are shown in Table 3.

Correlation analysis was applied to examine the relationship between the patients' IU and IU subscale scores and various clinical variables. As a result of the correlation analysis, a positive correlation was found between IU and IU-PA and first alcohol intake age. Moreover, a positive correlation was observed between the longest withdrawal period and education period. Correlation analyses are given in Table 4.

Table 3. Comparison of IU and IU subscale scores between various patient groups

n=53		IU-PA (Mean±SD)	p	IU-IA (Mean±SD)	p	IU (Mean±SD)	p
Sex (n)	Female (3)	26.3±5.0	0.714	15.0±1.7	0.923	41.3±6.5	0.985
	Male (50)	24.90±5.8		15.96±4.6		40.86±8.8	
Work (n)	Yes (28)	24.07±4.6	0.249	16.68±4.8	0.231	40.75±8.0	0.630
	No (25)	26.00±6.7		15.04±4.1		41.04±9.5	
Other substance (n)	Yes (6)	21.17±5.0	0.063	12.17±1.7	**0.021**	33.33±6.3	**0.020**
	No (47)	25.47±5.7		16.38±4.6		41.85±8.4	
Treatment History (n)	Yes (37)	24.11±5.7	0.168	15.95±4.9	0.869	40.05±9.4	0.332
	No (16)	27.00±5.4		15.81±4.8		42.81±6.3	
DT history+ (n)	Yes (4)	19.00±1.4	**0.012**	10.75±0.9	**0.007**	29.75±2.3	**0.007**
	No (49)	25.47±5.7		16.33±4.4		41.80±8.3	
Seizure history (n)	Yes (9)	25.67±5.3	0.803	13.22±1.7	0.050	38.89±5.7	0.400
	None (44)	24.84±5.8		16.45±4.7		41.30±9.1	
Judicial case (n)	Yes (16)	23.38±5.1	0.203	16.63±5.3	0.669	40.00±9.0	0.528
	None (37)	25.68±5.9		15.59±4.2		41.27±8.5	

IU:Intolerance of Uncertainty Scale, PA:Prospective Anxiety, IA:Inhibitory Anxiety, [a]: Independent sample t test, [b]:Mann-Whitney U test

Table 4. Correlations between IU and clinical variables in the patient group

		1	2	3	4	5	6	7
1. IU-PA	r	1						
2. IU-IA	r	0.417**	1					
3. IU	r	0.874**	0.782**	1				
4. Education period	r	0.023	0.008	-0.012	1			
5. First alcohol consumption age	r	0.423**	0.188	0.348**	0.106	1		
6. Std. drink/day	r	0.189	0.152	0.211	-0.215	0.550	1	
7. Longest withdrawal	r	-0.145	-0.230	-0.214	0.309*	-0.067	0.196	1

IU: Intolerance of Uncertainty Scale, PA: Prospective Anxiety, IA: Inhibitory anxiety, r: Spearman correlation coefficient, *: p<0.05, **: p<0.01

DISCUSSION

In this study, patients with alcohol use disorder were found to have higher intolerance of uncertainty compared to healthy controls. It was observed that patients who used substance other than alcohol had lower levels of intolerance of uncertainty than those who did not, and similarly, patients who had delirium tremens had lower intolerance levels of uncertainty than those who did not. Finally, it was found that there was a positive correlation between the first alcohol use age and levels of intolerance of uncertainty, and between the education duration and the longest sobriety period.

In our study, consistent with the literature data showing that alcohol consumption increases as the intolerance of uncertainty intensifies, the intolerance of uncertainty of patients with alcohol use was found to be higher than healthy individuals (4). People may be drinking alcohol to avoid anxiety and negative feelings caused by uncertainty.

There is no study in the literature showing the relationship between multiple substance use and intolerance of uncertainty, and the finding of intolerance to higher uncertainty in people who do not use substances in addition to alcohol in our study

may be related to the aspect of inhibitory anxiety, which is the behavioural inhibition sub-dimension of IU. Studies on IU have shown that both IU and anxiety decrease after some interventions (7). The fact that people who had DT have lower IU than those who did not, perhaps because delirium functions as in exposure therapies, may be related to the extinction of the person's anxiety response to possible dangerous situations after being exposed to a dangerous event such as DT.

In a nationwide study conducted in Australia, it was found that early-onset anxiety disorders were associated with starting alcohol at an earlier age (8). In our study, contrary to this result, it was found that as the age of the first alcohol use increased, intolerance of uncertainty also increased.

Another noteworthy result of our study is that the longer the education period, the longer the individuals were able to take a break from alcohol. The findings of our study are consistent with the literature data showing that higher education level and better socioeconomic conditions are protective against alcohol use disorder (9).

Limits of the study

The limitations of our study can be considered as the fact that our study was conducted in a single center, the data were not detailed on the day of treatment of the patients or what they received for treatment, and the anxiety levels were not examined since it may affect the IU results.

CONCLUSION

In summary, this study reveals a significant link between intolerance of uncertainty (IU) and alcohol use disorder, with patients in detoxification treatment displaying higher IU levels than healthy controls. The research also highlights differences within patient groups, indicating that individuals using additional substances or experiencing delirium tremens exhibit varying levels of IU. Furthermore, positive correlations were found between IU and the age of first alcohol intake, as well as education duration and sobriety period, emphasizing the multifaceted nature of the issue.

Competing interests: No conflict of interest was declared by the authors.

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Ethical approval: Ethical approval was obtained from the Clinical Research Ethics Committee of Ankara Training and Research Hospital for the study [Date: 24.08.2022 - No: E-22-1033].

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Original Article

Evaluation of the Knowledge Attitudes and Behaviors of Mothers with 0-6 Age Group Children on Domestic Accidents and Methods of Protection

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Abstract

Aim: Home accidents aged 0-6 are among the leading causes of global public health problems. Childhood and development processes vary according to age, gender, family structure, education and the economy and cultural values of the society. This situation increases the diversity and consequences of these accidents globally. In this study, it was aimed to evaluate the level of knowledge of mothers with 0-6 age group children about knowing their children's home accidents and ways to protect them from these accidents.
Materials and Methods: 127 volunteer mothers were included in our cross-sectional, descriptive study. In the study, mothers' sociodemographic data, information about home accidents, children's home accidents, gender, number, number of children, and type of home accident were evaluated. Local ethics committee approval was obtained for our study.
Results: The mean age of the mothers participating in the study was 31.3±6.054. While 80.3% (n=102) were nuclear families, 19.7% (n=25) were from extended families. 29.9% (n=38) of the mothers were university graduates and 23.6% (n=30) were secondary school graduates. When the income status of the family was questioned, 80 people (63%) stated that their income was equal to their expenses, while 34 people (26.8%) stated that their income was more than their expenses. 57 of the participants (44.9%) had two children at home. The number of mothers with one child and mothers with 3 or more children were equal (n=35, 27.6%). 68.5% of the children (n=87) did not have their own room at home. 31% (n:40) of the mothers had a home accident and the most common home accident was burns with 27.5% (n=11). As a security measure in the houses, there was a window lock with the highest rate of 23% (n=47). Home accidents were mostly encountered by boys. There was no significant difference between number of children at home, mother's education, employment, child care, separate nursery, mother's age and home accident, however, the status of taking safety precautions varied according to the status of having a home accident.
Conclusion: Preventive medicine practices of family physicians are among their primary duties. In the study, it was determined that mothers took more precautions with experience of home accidents due to lifelong learning. Rather than gaining from bad experiences, home accidents should be included in the counseling services during field medicine, starting from the pregnancy period of the mothers, and these services should continue periodically.

Keywords: Home accidents, preventive medicine, mother, family medicine

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INTRODUCTION

As a result of home accidents, which is a global public health problem, hundreds of thousands of children die every year after injuries, and millions of them struggle with the various consequences of non-fatal injuries. These results can sometimes even be life-long disabilities. For this reason, the report published by the World Health Organization (WHO) and the United Nations

Children's Fund (UNICEF) aimed to raise awareness about the extent, risks and effects of child injuries, to draw attention to the preventability of these accidents, and made recommendations that can be implemented by all countries. (1)

Childhood and development processes vary according to age, gender, family structure, education and the economy and cultural values of the society. This situation increases the diversity and consequences of these accidents globally. In the United States, half of the deaths of children under the age of 5 due to injury are due to accidents that occur in the home environment. (2) In home accidents, besides children, elderly individuals, individuals with mental or physical disabilities are also at risk. (3)

However, children are the individuals most at risk for home accidents because they are not aware of the seriousness of possible dangers, they are curious about learning-exploration, and they have not completed their neurological development while their development processes continue in all aspects. Home accidents have negative effects on the quality of life of both the child and the parents. Home accidents are preventable. Although this situation seems to be much easier today than it used to be with the developing technology and industrial designs, home accidents still cannot be completely prevented due to different reasons in the current world order. Considering that we live in the information age, it is very valuable to prevent accidents with great biopsychosocial effects.

In studies conducted in our country, it is seen that home accidents in children aged 0-6 range between 1.3% and 38%. (4,5) According to death and cause of death statistics, the highest number of child deaths in the 1-17 age group in our country in 2021 was due to external injuries and poisonings. (6) In a study conducted in Ireland, it was reported that 39.2% of all home accidents occur between the ages of 0-15 and 19.4% in children under the age of 5. (7) When the most common reasons for applying to the emergency service in Adana due to home accidents were examined, it was determined that 205 people (67.7%) applied due to crashes and falls, while 19 people (6.3%) applied due to drinking medical, pharmaceutical or chemical substances. Other causes include burns, incisions, and foreign body aspiration. (8)

Home accidents can be prevented with simple arrangements and regular training to the parent/caregiver who spends the most time with the children. (9) Parents are responsible for protecting children in the 0-6 age group from accidents, creating safe environments for this and controlling these environments. In this study, it was aimed to evaluate the knowledge and attitudes of mothers with 0-6 age group children about knowing their children's home accidents and ways to protect them from these accidents.

MATERIALS AND METHODS

Our study, which was planned as a cross-sectional, descriptive study, included 127 volunteers from mothers with 0-6-year-old children who applied to Ordu University Medical Faculty Family Medicine Polyclinic for any reason. In the study, mothers' sociodemographic data, information about home accidents, children's home accidents, gender, number, number of children, and type of home accident were evaluated. Refusal to participate in the study and not being a mother were the exclusion criteria from the study. Ethics committee approval for this study Ordu University Received from the Clinical Research Ethics Committee of the University Clinical Research Ethics Committee (Date and No: 31.12.2021, 282).

Statistical Analysis

In the study, chi-square analysis was used to determine whether the status of having a home accident changed according to safety measures, the number of children in the house, the education level of the mother, the working status, the care of the children, the status of a separate nursery room, and the age of the mother. The SPSS v21.0. statistical package program was used for all statistical calculations. It was considered that the research findings were significant at the $p<0.05$ level by expressing as n, percentage.

RESULTS

The mean age of the mothers participating in the study was 31.3±6.054. The sociodemographic characteristics of mother are shown in Table 1.

Table 1. Sociodemographic characteristics of mothers

		n	%
Family Structure	Nuclear family	102	80.3
	Extended family	25	19.7
Mother's Education Level	University and above	38	29.9
	High School	27	21.3
	Middle School	30	23.6
	Primary School	27	21.3
	Illiterate	5	3.9
Mother's Working Status	Working	43	33.9
	Not Working	84	66.1
Mother's Chronic Disease Status	Yes	12	9.4
	No	115	90.6

85% (n=108) of children were cared for by mothers. The sociodemographic characteristics of children are shown in Table 2.

Mothers had experienced the home accident story most often with their first child. (80%, n=32) Features of Home Accidents and Safety Precautions are shown in Table 3.

31% (n:40) of the mothers encountered home accidents and the most common home accident was burns with 27.5% (n=11), followed by falling on a slippery floor (n:10, 10%). The distribution of home accident types is given in Graph 1.

Table 2. Sociodemographic characteristics of children

		n	%
Number of Children at Home	One	35	27.6
	Two	57	44.9
	Three and more	35	27.6
The Person Caring for Children	Mother	108	85
	Grandmother	9	7.1
	Babysitter	10	7.9
Availability of a Room for Children	Yes	40	31.5
	No	87	68.5

Table 3. Features of Home Accidents and Safety Precautions

		n	%
Mother's Knowledge About Home Accidents	Yes	112	88.2
	No	15	11.8
Type of Home Accident	Injury with sharp piercing instrument	1	2.5
	Falling on slippery ground	10	25
	Falling from a height	8	20
	Poisoning	4	10
	Burning (with fire/iron/ hot subtances/water)	11	27.5
	Electric shock	1	2.5
	Drowning in water	2	5
	Strangulation with foreign objets	3	7.5
Security Measures at Home	Window lock	47	22.9
	Door holder	33	16.1
	Electric socket protector	45	22.0
	Cabinet lock	34	16.6
	Angular item protector	27	13.2
	Oven/stove button protector	19	9.3
History of Home Accident	Yes	40	31.5
	No	87	68.5
Child's Gender in Home Accidents	Boy	29	72.5
	Girl	11	27.5

There was no significant difference between the order and gender of the children who had an accident and the number of home accidents (p>0.05). There was no significant difference between mothers' age, number of children at home, mothers' education, child care, separate child room and home accident (p>0.05), however, the status of taking safety precautions varied according to the status of having a home accident (p=0.017) Accordingly, it was found that mothers of children who had home accidents took more safety precautions (Table 4, Table 5).

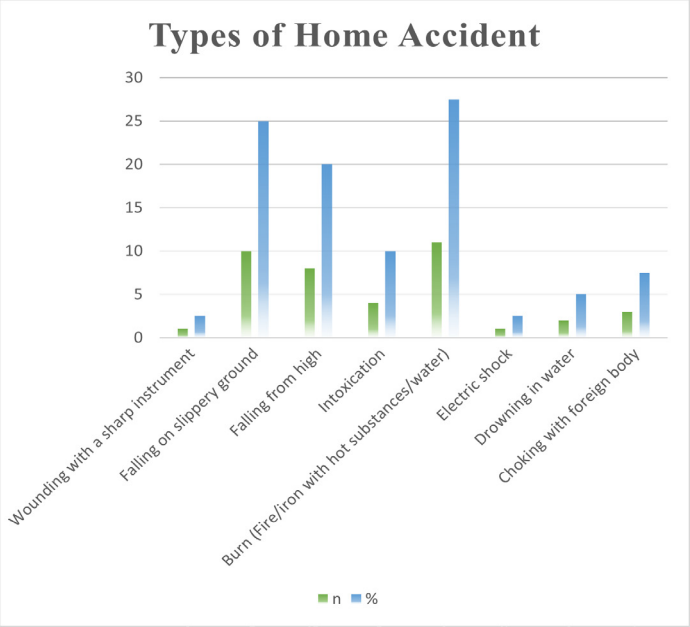

Figure 1. Distribution of Types of Home Accidents Encountered

Table 4. Age of the mother according to having a home accident

		n	Mean	SD	
History of Home Accident	Yes	40	30.9	5.57	0.544
	No	87	31.4	6.28	

Table 5. The relationship between home accidents and safety precautions, number of children, mother's education, caregivers, and the presence of a room for the child

		History of Home Accident				p
		Yes		No		
		n	%	n	%	
Security Measures at Home*	Yes	34	37.8	56	62.2	**0.017**
	No	6	16.2	31	83.8	
Number of Child at Home	1 child	10	28.6	25	71.4	0.734
	2 childs	20	35.1	37	64.9	
	3 childs and above	10	28.6	25	71.4	
Education Status of Mothers'	University and above	14	36.8	24	63.2	0.753
	High school	10	37.0	17	63.0	
	Middle school	8	26.7	22	73.3	
	Primary school	7	25.9	20	74.1	
	Illiterate	1	20.0	4	80.0	
The Person Caring for Children	Mother	33	30.8	74	69.2	0.329
	Grandmother	5	50.0	5	50.0	
	Caregiver	2	20.0	8	80.0	
Child Room	Yes	29	33.3	58	66.7	0.512
	No	11	27.5	29	72.5	

χ^2: 5.65

DISCUSSION

When classified according to age periods, most play period children are curious, inquisitive and unaware of the dangers that may arise. In a study conducted in the emergency department in Adana, the rate of admission due to home accidents was 0.66%. (8) The frequency of home accidents in various studies conducted in our country; It was determined as 15.5% (n=31), 19.65% (n=104), 27.5% (n=110), 58% (n=116) (10,11,12,13). In our study, this rate was found to be 31% (n=40). We think that these differences in the studies are due to the differences in the regions where the studies were conducted and the possible sociocultural and socioeconomic status differences.

As a requirement of our social culture, we have come to the conclusion that some problems will be seen more than expected in the face of the young age of the mother. Studies that are consistent with this opinion have been identified in the literature. (14,15) In our study, however, no significant difference was found between maternal age and home accident. In this determination made on the basis of the statements of the people, the differences between the studies may be that our participants did not interpret the accidents that can be described as very simple in the routine of life as home accidents.

In the study of Çiçek et al. (14), it was observed that mothers who graduated from primary school took more safety precautions for home accidents compared to mothers who graduated from secondary education and undergraduate education. In the study of Hazazi et al., there was statistical significance in the measures against home accidents of parents with high education level ($p<0.05$). (16) In the study of Üçüncü et al., it was determined that mothers with higher education levels were more aware of home accidents. ($p<0.001$) (13) In our study, however, no relationship was found between mothers' educational status and home accidents. This difference between the studies may be due to the sample difference and the different groupings in the comparison of the education relationship. According to the report published by WHO in 2011, while 2000 babies die due to accidents in a year, 10,000 children continue to live with disability due to accidents. (17) According to the results of the systemic meta-analysis published in 2017, the number of children seeking health care after injury in Brazil between 2013 and 2014 was 122000. (18)

In the report published by WHO to prevent accidents in children, it is stated that boys encounter more frequent and serious accidents than girls. (1) In the study of Erdem SS et al., this rate was found to be 86.7% in favor of boys. (7) In the study of Balibey M et al., in the study of home accidents, in which families compared home accidents according to rural, semi-urban and urban living areas, the accident rate of boys in rural areas was found to be high, but statistical significance was not determined. In the analyzes made according to these regions, it was stated that this may be due to the high number of boys in the rural region. (19) In most of the available sources, it was stated that home accidents are generally seen in boys. (10,11,20) In our study, the majority of children (n=29, 72.5%) who had an accident were male. According to these results, it can be said that our result is also compatible with the literature. These results may be due to the fact that boys prefer games that require more physical activity than girls.

It was determined that the most common type of home accident was falling (53.7%), and mostly the arms and legs (40.0%) were affected as a result of home accidents. In the study of Erdem SS et al., falling was reported as the most common home accident. (7) In our study, fall was the second most common accident after burns, and there was no significant difference between the two accident types in terms of numbers. It has been shown that when children's exposure to hazards at home can be reduced, injuries from home accidents requiring medical attention are reduced by 70 percent. (22) In our study, it was observed that mothers with experience of home accidents increased their safety measures more than two times proportionally. When the types of injuries that are detected in the first place in home accidents are analyzed, it is possible to prevent them with effective but practical safety measures, which are even easier to reach today, and training to be given to parents. Thus, health expenditures will be saved and the traumatic processes of both children and parents will be manageable and irreversible results will be protected.

When the income status of their families was questioned among the participants in our study, 80 people (63%) stated that their income was equal to their expenses, while 34 people (26.8%) stated that their income was more than their expenses. This indicates that the socioeconomic level of the participants in our study was high. This situation may be the common reason for the lack of similar results at some points with the available studies on this subject in our country. Among the limitations of our study are the low number of volunteer participants in our study, the fact that the studies were designed with mothers rather than parents, and the possibility that some questions were given emotional answers, except for 5 people, who filled the questionnaire themselves.

CONCLUSION

Preventive medicine practices of family physicians are among their primary duties. Comparison of home accidents according to sociodemographic characteristics can be interpreted differently by being affected by socioeconomic and sociocultural dimensions of societies. However, it may be possible to achieve a certain standardization with health education that is structured in accordance with the culture and economy, regardless of its structure. In the study, it was determined that mothers took more precautions with experience of home accidents due to lifelong learning. Rather than gaining from bad experiences, home accidents should be included in the counseling services during field medicine, starting from the pregnancy period of the mothers, and these services should continue periodically.

Competing interests: No conflict of interest was declared by

the authors.

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Ethical approval: Ethics committee approval for this study Ordu University Received from the Clinical Research Ethics Committee of the University Clinical Research Ethics Committee (Date and No: 31.12.2021, 282).

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Original Article

Evaluation of Nosocomial Infections Developing in the Tertiary Intensive Care Unit of a Training and Research Hospital

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Abstract

Aim: Nosocomial infections (NI) lead to negative consequences such as prolonged stay in the intensive care unit (ICU), increased morbidity and mortality. In this study, we aimed to develop infection control measures and strategies by evaluating the distribution of nosocomial infections in tertiary ICU according to the systems and causative microorganisms.
Materials and Methods: 388 patients monitored in the Anesthesia and Reanimation ICU (ARICU) between January 2022 and December 2022 were evaluated retrospectively for nosocomial infections.
Results: In the one-year monitoring period, in 5044 hospitalisation days of 388 patients, 40 NI episodes were detected in 33 patients in the ARICU. The hospital infection rate was 10.3, and the hospital infection incidence density was 7.9. The most common admission diagnosis was community-acquired pneumonia with 10 (25%), while the most common underlying disease was cardiovascular disease with 18 (26.1%). Among the catheter utilisation rates, urinary catheters presented the highest value with 1.00, while considering the infection rates, ventilator-associated pneumonia (VAP) reached the highest value with 2.63. The most common nosocomial infection, 'pneumonia with specific laboratory findings', was followed by 'laboratory-confirmed bloodstream infection' and 'lower respiratory tract infections other than pneumonia' (27.5%, 20.0%, 17.5%, respectively). Among gram-negative pathogens, *Acinetobacter* spp was the most common, with 11 (30.6%), while among gram-positive pathogens, S. aureus was the most common, with 2 (40%). While the incidence of multi-drug resistant pathogen was highest in VAP with 6 (85.7%), it was lowest in catheter-related urinary tract infection with 1 (50%). The prevalence of 30-day ICU mortality in patients who developed NI was found to be 18 (54.5%).
Conclusion: Surveillance studies and infection control practices are gaining importance in the prevention of nosocomial infections in the ICU. Appropriate treatment strategies should be developed, and rational antibiotic use should be ensured by the institutions evaluating their own data.

Keywords: Intensive care unit, mortality, multiple drug resistance, nosocomial infection, surveillance

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INTRODUCTION

Nosocomial infections (NI) lead to negative consequences such as prolonged stay in the intensive care unit (ICU) and increased morbidity and mortality. Despite infection control measures, critically ill patients are at higher risk of developing nosocomial infections. Early recognition and correct management of nosocomial infections are important in terms of providing ideal conditions in ICUs (1). The widespread use of broad-spectrum antibiotics in ICU patients due to the increase in infection frequency leads to drug resistance in causative microorganisms, increasing the frequency of infections caused by resistant strains (2). The pathogens in the ICU and their antimicrobial resistance status differ among institutions. For this reason, surveillance studies that determine the local flora of each institution gain importance in initiating appropriate empirical antimicrobial therapy (3).

In this study, we aimed to develop measures and strategies for infection control by evaluating the distribution of hospital-

acquired infections and causative microorganisms in the tertiary ICU.

MATERIALS AND METHODS

Study Design

In this study, 388 patients who were monitored in Ordu University Training and Research Hospital, Anesthesia and Reanimation ICU (ARICU) between January 2022 and December 2022 were evaluated retrospectively for nosocomial infections. This study, which was performed in accordance with the Declaration of Helsinki, was approved by the Ordu University Ethics Committee under the date 01.09.2023 and decision number 222. Due to the retrospective design, informed consent was not obtained.

Assessment Tests

Nosocomial infections were determined according to the diagnostic criteria of the Centers for Disease Control and Prevention (CDC) (4). The identification and antibiogram susceptibility tests of the isolated microorganisms were evaluated with the automated system Becton Dickinson Phoenix (USA). The antimicrobial resistance status was defined according to Magiorakos et al. (5). The minimal inhibitory concentration (MIC) levels were evaluated according to the breakpoints of the European Committee on Antimicrobial Susceptibility Testing (EUCAST 2022) (6). Pathogens with intermediate antimicrobial susceptibility were considered resistant.

Calculation Formulas

The following formulas were used: hospital infection rate = (number of developing infections/number of inpatients) x 100; nosocomial infection incidence density = (number of developing infections/patient days) x 1000; central venous catheter-associated bloodstream infection (CVCR-BI) rate = CVCR-BI number/CVC days x1,000; ventilator-associated pneumonia (VAP) rate = VAP number/ventilator days x 1,000; catheter-associated urinary tract infection (CR-UI) rate = CR-UI number/ urinary catheter day x 1,000; instrument utilisation rate = number of device days/patient days.

Statistical Analysis

In SPSS v.26.0 (IBM Inc., Chicago, IL, USA) package program was used for the statistical evaluation of the data. Normality of the data was tested using the Kolmogorov-Smirnov test. In descriptive statistical analysis, parametric data were presented as mean ± standard deviation and categorical data as %.

RESULTS

During the one-year monitoring period, 388 patients were followed up on 5044 hospitalisation days in the 14-bed Anesthesia and Reanimation ICU. During this period, a total of 40 nosocomial infections were detected in 33 patients. The hospital infection rate was 10.3 per cent, and the hospital infection incidence density was 7.9 per thousand. Of the patients with nosocomial infections, 21 (52.5%) were male and 19 (47.5%) were female. The mean age was 68.1±12.3 in men and 66.4±11.7 in women. The main diagnoses and underlying diseases of the patients admitted to the ICU are shown in Table 1. The most common admission diagnosis was community-acquired pneumonia with 10 (25.0%), while the most common underlying disease was cardiovascular disease with 18 (26.1%).

Table 1. Main causes of patients with nosocomial infections on admission and underlying conditions

		n	%
Diagnosis (n=40)	Community acquired pneumonia	10	25.0
	Sepsis	7	17.5
	Heart failure	6	15.0
	Renal failure	5	12.5
	COPD	4	10.0
	Cerebrovascular disease	3	7.5
	Trauma	3	7.5
	Others	2	5.0
Underlying conditions (n=69)	Cardiovascular	18	26.1
	Pulmonary	15	21.7
	Diabetes mellitus	13	18.8
	Neurological	10	14.5
	Renal	9	13.0
	Malignancy	4	5.8

COPD: Chronic obstructive pulmonary disease

The duration and rates of invasive instrument utilisation observed during the monitoring of the patients in the ICU are given in Table 2. Among the catheter utilisation rates, urinary catheter (UC) had the highest value with 1.00; while considering the infection rates, VAP reached the highest value with 2.63.

Table 2. Usage periods and rates of invasive devices

	Number of days	Rate of device usage
CVC	2609	0.52
UC	5042	1.00
MV	2285	0.45
	Number of infections	**Rate of infections**
CVCR-BI	6	2.30
CR-UI	2	0.40
VAP	6	2.63

CVC: central venous catheter, UC: urinary catheter, MV: Mechanical ventilator, CVCR-BI: central venous catheter-related bloodstream infections, CR-UI: catheter-related urinary tract infections, VAP: ventilator associated pneumonia

The distribution of the isolated agents according to the sites of infection is presented in Table 3. The most common nosocomial infection, 'pneumonia with specific laboratory findings', was followed by 'laboratory-confirmed bloodstream infection (LC-BI)' and 'lower respiratory tract infections other than pneumonia'

pneumonia' (LRTIOP) (27.5%, 20.0%, 17.5%, respectively). Of the 42 isolated organisms, 36 (85.7%) were gram-negative, 5 (11.9%) were gram-positive pathogens, and 1 (2.4%) was a fungal agent. Among the gram-negative pathogens, while *Acinetobacter* spp. 11 (30.6%) was the most common, and among the gram-positive pathogens, *S. aureus* was the most common with 2 (40%). When the antimicrobial resistance status of the agents in the infection areas was evaluated, multi-drug resistant (MDR) pathogen incidence was highest in VAP with 6 (85.7%) and lowest in catheter-related urinary tract infection (CR-UI) with 1 (50%).

Table 3. Distribution of isolated agents according to infection sites

Diagnoses	Agents	n	%
Pneumonia with specific laboratory findings	MDR pathogens	9	75.0
	K. pneumoniae	3	25.0
	Acinetobacter spp.	2	16.7
	P. aeruginosa	2	16.7
	S. aureus	2	16.7
	Others	3	25.0
LRTIOP	MDR pathogens	5	71.4
	Acinetobacter spp.	2	28.6
	K. pneumoniae	2	28.6
	P. aeruginosa	2	28.6
	P. mirabilis	1	14.3
VAP	MDR pathogens	6	85.7
	P. aeruginosa	3	42.9
	Acinetobacter spp.	2	28.6
	K. pneumoniae	1	14.3
	E. coli	1	14.3
LC-BI	MDR pathogens	6	75.0
	K. pneumoniae	3	37.5
	Acinetobacter spp.	2	25.0
	E. coli	2	25.0
	E. cloacae	1	12.5
CVCR-BI	MDR pathogens	4	66.7
	Acinetobacter spp.	3	50.0
	K. pneumoniae	1	16.7
	E. faecalis	1	16.7
	C. albicans	1	16.7
CR-UI	MDR pathogens	1	50.0
	P. aeruginosa	1	50.0
	E. coli	1	50.0

LRTIOP: lower respiratory tract infections other than pneumonia, VAP: ventilator associated pneumonia, LC-BI: laboratory-confirmed bloodstream infection, CVCR-BI: central venous catheter-related bloodstream infections, CR-UI: catheter-related urinary tract infection, MDR: multi-drug resistant

When the clinical outcomes of critically ill patients were evaluated, the prevalence of 30-day ICU mortality was found to be 18 (54.5%) in patients with nosocomial infections (data not shown).

DISCUSSION

The monitoring of risky patients and the prolongation of hospitalisations have increased the incidence of nosocomial infections in ICUs. In addition, these infections cause a prolongation of the length of stay and an increase in morbidity, mortality and hospital costs (7). In surveillance studies conducted in our country, infection rates in ICUs show significant differences both between institutions and in different units in the same hospital.

In the study of Karahocagil et al., in which they investigated nosocomial infections in different ICUs, the incidence of infection was found to be 18.3% for ARICU, 5.9% for pediatric ICU, and 5.6% for chest diseases ICU (8). Balin et al., in their study conducted in ARICU for two years, found the nosocomial infection rate to be 11.1% and the incidence density per 1000 patient days to be 23.6 (9). In another two-year study, Tarakcı et al. determined the infection rate in tertiary general ICU as 7.98% and the incidence density as 11.2 per thousand (10). In the study performed by Akın et al. in ARICU for five years, it was shown that the incidence of infection was 18%, and the incidence density was 58 per thousand (11). In our study covering the year 2022 in the ARICU, the hospital infection rate was found to be 10.3% and the incidence density was 7.9 per thousand. These differences observed in the results may be related to factors such as the studies being conducted in different periods, the inadequacies in surveillance practices and the evaluation of hospital infections in different units.

Due to critical illnesses and invasive procedures, the incidence of infection in ICUs is increasing (12). Tarakci et al. investigated invasive device-associated nosocomial infections in their study at a training and research hospital (TRH). It was found that the rates of ventilator utilisation and ventilator-associated pneumonia (VAP) were 0.5 and 2.32; the central venous catheter (CVC) utilisation and central venous catheter-related bloodstream infections (CVCR-BI) were 0.52 and 2.04; the UC utilisation and CR-UI were 0.95 and 0.37 (10). In the National Nosocomial Infections Surveillance Report (NNISR), the rates reported in ARICUs in training and research hospitals in 2022 were 0.54 and 5.70 for ventilator utilisation and VAP, 0.59 and 5.10 for CVC utilisation and CVCR-BI, 0.98 and 1.20 for UC utilisation and CR-UI (13). Similarly, in the study we conducted in the training and research hospital ARICU, the ventilator utilisation and VAP rates were 0.45 and 2.63, the CVC utilisation and CVCR-BI rates were 0.52 and 2.30, and the UC utilisation and CR-UI rates were 1.00 and 0.40. Although the rates of invasive instrument utilisation were consistent with NNISR in our study, the rates of invasive instrument-associated infections were generally lower. This may be due to the difference in conditions in the

ICU, including the number of beds and patient profile, and the meticulous adherence to infection control measures in catheter placement and monitoring.

Metabolic disorders, comorbid diseases, invasive interventions and the widespread use of antibiotics in critically ill patients increase the risk of resistant pathogens, which are more difficult to treat, in-hospital infections that develop in the ICU (14). In the study in which Inanç et al. evaluated the infection factors developed in mechanically ventilated patients in the neurology ICU, the most frequently detected microorganisms were *A. baumannii*, *P. aeruginosa*, and *K. pneumonia* (15). In another study in the neurology ICU, *A. baumannii* and *K. pneumonia* were the most frequently isolated agents in VAP (12). In our study, the fact that the most frequently observed agents were P. aeruginosa 42.9%, *Acinetobacter* spp. 28.6% and *K. pneumonia* 14.3% was consistent with previous studies. In addition, VAP was the nosocomial infection with the highest antimicrobial resistance rates. These results show that, due to the increase in antimicrobial resistance observed in nosocomial infections, empiric antimicrobial therapy should be planned to cover MDR pathogens. In addition, early diagnosis and appropriate antimicrobial therapy may be effective in reducing the length of stay in the ICU, mortality, development of resistant strains and hospital costs (15). Therefore, it is important to conduct surveillance studies to determine the ideal treatment (16).

In the EPIC II study, which evaluated the prevalence of infections in the ICU, it was shown that respiratory infections accounted for 64% of the ICU infections (17). In studies performed in different ICUs, pulmonary infections were defined as the most common nosocomial infections, with 80.9% and 53.8% (10, 12). In our study, respiratory tract infections were found to be the most common nosocomial infection with a rate of 60% (27.5%pneumonia with specific laboratory findings, 17.5% other non-pneumonia lower respiratory tract infections and 15% VAP), which was consistent with previous studies. This may be caused by underlying diseases, impaired consciousness and swallowing reflexes, as well as the increased rate of mechanical ventilation, which increases the risk of nosocomial pneumonia in critically ill patients.

In the EPIC II prevalence study in which infections in the ICU were investigated, microbiological culture positivity was observed in 70% of the infected patients, and 62% of the isolated organisms were gram (-), 47% gram (+) and 19% fungal agents (17). In the study performed by Gözütok et al. in the internal medicine ICU, 40.5% of the isolated agents consisted of gram (-) bacteria, 43.7% of gram (+) bacteria and 15.7% of yeast (18). In another study in our country, Göktaş et al. showed that 59.3% of the agents in the ARICU were gram (-) and 40.7 were gram (+) bacteria (19). In the studies of Balin et al. in ARICU, gram (-) bacteria were detected in 83% of the isolated agents and gram (+) bacteria in 17% (9). In our study, 85.7% of the causative microorganisms were gram (-), 11.9% were gram (+), and 2.4% were fungal agents, which was similar to previous studies performed in the ARICU. These results are consistent with the fact that the infectious agents in the ICU vary both between hospitals and between different units in the same hospital (20).

Microorganisms with increased antibiotic resistance often play a role in nosocomial infections in the ICU, increasing the risk of mortality (1,2). Vincent et al. examined the clinical consequences of infections in the ICU in the EPIC II study. It was shown that mortality in infected patients was significantly higher than in non-infected patients (25% vs. 11%, respectively) and that infection was an independent predictor of hospital mortality (17). Çevik et al., in a study evaluating the effect of nosocomial infections on mortality in the neurology ICU, found that the mortality in patients with infection was 68.9%. When nosocomial infections were analysed by regions, the mortality rate in patients who developed pneumonia reached 75.6, and nosocomial pneumonia was independently associated with mortality (21). In the study of Tarakcı et al., the mortality rate in patients with nosocomial infections in the general ICU was 51.1% (10). The high rate of 30-day ICU mortality (54.5%) in patients with nosocomial infections in our study was similar to previous studies showing an increased risk of mortality.

CONCLUSION

Preventing nosocomial infections in the ICU requires surveillance studies and infection control practices. Considering the increase of nosocomial infection incidence in all critical patients, especially patients with underlying heart disease, necessary invasive procedures should be conducted with correct indications and catheter use should be limited. Common agents and their antimicrobial resistance patterns should be determined in each unit, ensuring that appropriate treatment strategies are determined and that antibiotics are used rationally.

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Ethical approval: This study, which was performed in accordance with the Declaration of Helsinki, was approved by the Ordu University Ethics Committee under the date 01.09.2023 and decision number 222.

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Original Article

Ameliorative Effect of Exogenous Calcitriol Treatment Against Muscle Injury in Myositis-Induced Rats

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Abstract

Aim: Calcitriol (vitamin D3) is a metabolite of vitamin D. Vitamin D is an essential nutrient for human health and plays a role in various biological processes in the body. This study aimed to investigate the therapeutic effect of Calcitriol in rats with valproic acid-induced myositis.
Materials and Methods: A total of 24 Wistar Albino rats weighing 250-350 g and 20 weeks old were included in the study. The rats were divided into three groups: the Control group (n=8), the Valproic acid (Myositis) group (n=8), and the Myositis + Calcitriol 200 ng/kg/day group (n=8). Oral valproic acid (VPA) (500 mg/kg/day) was used for myositis induction for 14 days. On the 15th day, euthanasia was performed. The gastrocnemius muscle of each animal was dissected and histopathologically examined in the pathology laboratory. In addition, Caspase3 levels were obtained immunohistochemically, and apoptosis was evaluated. The results obtained were compared statistically.
Results: The study found a significant difference between the groups regarding congestion, degeneration, necrosis, inflammation, and disorganization ($p<0.01$). Additionally, there was a significant difference in Caspase3 levels ($p<0.01$). This difference was observed between the Valproic Acid and Vitamin D groups and the other groups ($p<0.01$).
Conclusion: In this study, we demonstrated the healing efficacy of Calcitriol in damaged muscle tissues in rats with myositis. Thus, Calcitriol may contribute positively to the healing of muscle damage by monitoring vitamin D levels and using appropriate supplements in case of deficiency.

Keywords: Calcitriol (Vitamin D3), myositis, apoptosis, valproic acid, muscle damage

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INTRODUCTION

Myositis is a condition characterized by inflammation of muscle tissue and may occur for different reasons (1). Muscle damage can negatively affect quality of life and physical performance. Inflammation of muscles is often caused by an immune system response (1-2). The body's immune system is usually designed to fight foreign microorganisms and prevent infections, but sometimes, it can be aggressive against its tissues. Myositis is an autoimmune disease where the immune system attacks the muscles, but the exact cause is unknown. It is believed to be a combination of genetic predisposition and environmental factors that trigger this response. Other factors, such as viral or bacterial infections and certain medications, can also contribute to the development of myositis (2-4). Treatment of myositis can vary depending on the type and severity of the disease. Generally, treatment includes the following elements: Corticosteroids and immunosuppressants may be used to reduce inflammation-physiotherapy and exercises to maintain muscle strength and support the muscles. Adequate rest and limiting activities are also crucial for the muscles to recover. In addition, a healthy diet may help recovery (3,4).

Vitamin D is an essential vitamin that plays a vital role in calcium and phosphorus metabolism and protects bone health (5,6). Calcium is a mineral that helps keep bones healthy and strong. Vitamin D helps regulate calcium levels by increasing calcium absorption from the intestines and decreasing calcium excretion

from the kidneys. Calcitriol (D3) is a vitamin D metabolite shown to increase angiogenesis, have anti-inflammatory properties, and inhibit oxidative stress (5-7).

Vitamin D deficiency may prevent adequate calcium absorption and lead to weak bones and bone diseases such as osteoporosis and muscle weakness. Vitamin D deficiency may lead to a decrease in muscle strength and performance (6,7). In addition, vitamin D deficiency can increase the sensation of pain and weakness in muscles. Adequate vitamin D levels can help muscles stay strong and function usually (6). Regarding the muscle protective effect of Calcitriol, positive results have been obtained in some studies. Vitamin D may positively affect muscle function and muscle mass maintenance. Vitamin D is vital in muscle contraction and strengthening processes (7). Many studies have shown that low vitamin D levels are associated with muscle weakness, loss of muscle mass, and poor physical performance. Vitamin D deficiency may increase the risk of falls in the elderly by negatively affecting muscle function and strength. Vitamin D also supports muscle recovery by reducing inflammation and helping regenerate muscle fibers. However, the data on the muscle-protective effects of vitamin D supplementation still need to be completely clear, and the topic must be investigated. It is also a complex issue that needs to be evaluated, taking into account various personal characteristics of individuals, such as age, gender, lifestyle, dietary habits, and genetic factors. Further research is needed better to understand this issue (7-10).

Valproic acid is an antiepileptic drug used to treat neurological disorders like epilepsy. It is also used to treat other conditions, such as bipolar disorder. Like any drug, valproic acid may have some side effects, including muscle damage (11). A rare side effect of valproic acid is valproic acid-related myopathy, which can cause muscle damage. This side effect can usually occur due to long-term high-dose use (12). Myopathy associated with valproic acid use may manifest with symptoms such as muscle pain, weakness, and twitching. In case of muscle pain, weakness, or other muscle problems while taking valproic acid, a supplement with known efficacy will be helpful in treatment (11-13). Treatment is usually a long-term process, and the course of the disease may vary individually. With early diagnosis and appropriate treatment, symptoms can be controlled, and disease progression can be slowed. Therefore, a supplementary nutrient or mineral to facilitate treatment would be necessary in people with myositis symptoms (12,13).

Vitamin D is a vital nutrient that has essential effects on human health. It plays a critical role in maintaining and promoting health by regulating various biological processes ranging from bone health to the immune system and cardiovascular health to gene expression (5-7). There is a need for research on the effectiveness of vitamin D supplements in treating myositis. However, recent studies have shown that vitamin D may also positively affect muscle health (14-16). In light of this information, our study aimed to investigate the healing effect of Calcitriol on muscle tissue in rats with valproic acid-induced myositis.

MATERIALS AND METHODS

This study, which is an experimental in vivo study, was conducted at Hüsnü Sakal Experimental and Clinical Application Center of Health Sciences University Ankara Training and Research Hospital. Approval (Protocol No: 725/2023) was obtained from the Local Animal Experiments Ethics Committee before starting the study.

Study Design

Before the study, the rats were kept in a climate-controlled environment for at least fourteen days for adaptation in the laboratory where the experiment would be conducted. All animals were physically examined daily by a veterinarian. There was no restriction on the amount of feed and water in the diet of the rats. During the study, rats were fed with standard feed and water ad libitum and kept in housing cages under standard laboratory conditions with a 12:12 h light-dark cycle, a controlled temperature of 21 ± 2 °C, and a humidity of 65-70%.

For this study, 24 adult Wistar Albino rats were included as subjects. A total of 24 rats weighing 250-350 g and 20 weeks of age were divided into three groups as control group (n=8), Valproic acid (Myositis) group (n=8) which was exposed to muscle damage to create myositis model with oral valproic acid (Convuleks® 500 capsules, Liba Co, İstanbul, Turkey) and Myositis + Calcitriol (Calderol® 1 mcg/ml, Pharmada Ilac Sanayi ve Ticaret AS, İstanbul, Turkey) 200 ng/kg/day group (n=8) (17).

Group 1 (Control): No procedure was performed; after 14 days, muscle tissue was removed.

Group 2 (Myositis): Myositis was induced with oral valproic acid (VPA) (500 mg/kg/day) for 14 days.

Group 3 (Myositis + vitamin D3 200 ng/kg): Oral VPA (500 mg/kg/day) and 200 ng/kg/day Calcitriol (1, 25-dihydroxyvitamin D3) in 0.5 ml for 14 days.

The doses of VPA and Calcitriol used in this study were determined by an unpublished preliminary study conducted by the requirements of the Local Ethics Committee for Experimental Animals. Valproic acid (VPA) was administered at 500 mg/kg/g for two weeks to induce myositis. On the 15th day, the animals were euthanized. Animals in all groups were given high-dose anesthetic Xylazinne (Rompun®, Bayer, İstanbul, Turkey) and sacrificed by cervical dislocation method. Immediately afterward, gastrocnemius muscle tissue samples were placed in a 10% formaldehyde solution for histopathologic and immunohistochemical examination, and the experiment was terminated.

Histopathologic Evaluation

Tissue samples were fixed in 10% neutral buffered formalin (pH 7.2-7.4) and taken for routine pathology protocol. The tissues were dehydrated in increasing degrees of alcohol in an

automatic tissue tracking device; xylol was applied to obtain transparency and embedded in paraffin blocks. The embedded tissues were frozen in paraffin blocks at room temperature and then cooled in the refrigerator. After the cooling process was completed, five µm thick serial sections were taken from these blocks with the help of a microtome and deparaffinized. The first three and every tenth section of the five µm sections taken with a Leica RM 2125 RT were mounted on slides. The preparations were passed through alcohol and xylol series and stained with a Hematoxylin and Eosin stain (H&E). A veterinary pathologist performed all stained section evaluations. Light microscopy (Olympus BX-50, Tokyo, Japan) examined and scored the specimens at X40-X400 magnification. Striated muscle tissue was evaluated histopathologically for degeneration of muscle fibers, vascular congestion, signs of necrosis in muscle fibers (irregular eosinophilia in fibers, loss of connections between fibers), disorganization of muscle fibers (loss of striations, increase in connective tissue between muscle fibers) and signs of inflammation (mononuclear cell infiltration). A semi-quantitative scoring system was used to evaluate the findings. 0: Normal (no structural changes), 1: Mild, 2: Moderate, 3: Severe structural changes were scored between 0-3 (Figure 1) (18).

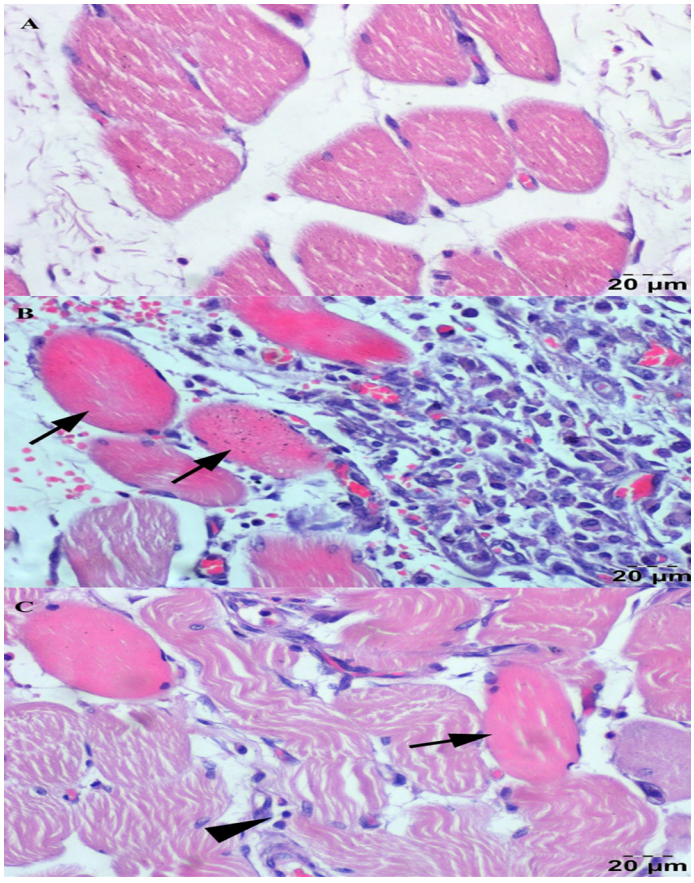

Figure 1. Histopathologic appearance of muscle tissues of all groups; **A.** Control group (H&E), **B.** Myositis group induced by VPA; arrows indicate severe degenerative muscle inflammation (H&E), **C.** Myositis+Calcitriol group; arrow shows single degenerative cells, and arrowhead shows mild inflammation (H&E)

Immunohistochemical Evaluation

Immunohistochemical methods in muscle sections determined Caspase3 receptor activity. For immunohistochemical examinations, five µm thick sections were obtained from paraffin blocks. The Avidin Biotin Complex (ABC) technique was applied after routine deparaffinization and rehydration. Antigen retrieval was performed in a microwave oven at 700 W and pH 6.0 citrate buffer solution in 10 minutes. Endogenous peroxidase activation in tissues was blocked with 0.3% hydrogen peroxide (H2O2) in 0.01 mol/l Phosphate Buffered Saline (PBS) in methanol for 15 minutes. Tissues were incubated with 5% normal goat serum for 20 minutes for protein blockage before primary antibody application. Sections were incubated with Caspase3 (1:50) primary antibodies for one hour. The tissues were then reacted with a biotinylated secondary antibody for 30 minutes after removing the unbound primary antibody. The tissues were then reacted with horseradish peroxidase conjugate for 30 minutes. After washing, the sections were incubated with DAB chromagen for 5 minutes. Finally, the background of the sections was stained with hematoxylin. All steps were performed at 37°C in a humidified room. PBS was used as a washing solution during all staining steps.

The immunoreactivity of histologic preparations was assessed by a semi-quantitative scale modified according to the degree of staining [(-): no immunostaining, (+): Weak staining, (++): Moderate staining, (++++): Intense staining]. The sections were visualized with an imaging-assisted light microscope (Olympus BX-50, Tokyo, Japan) (Figure 2).

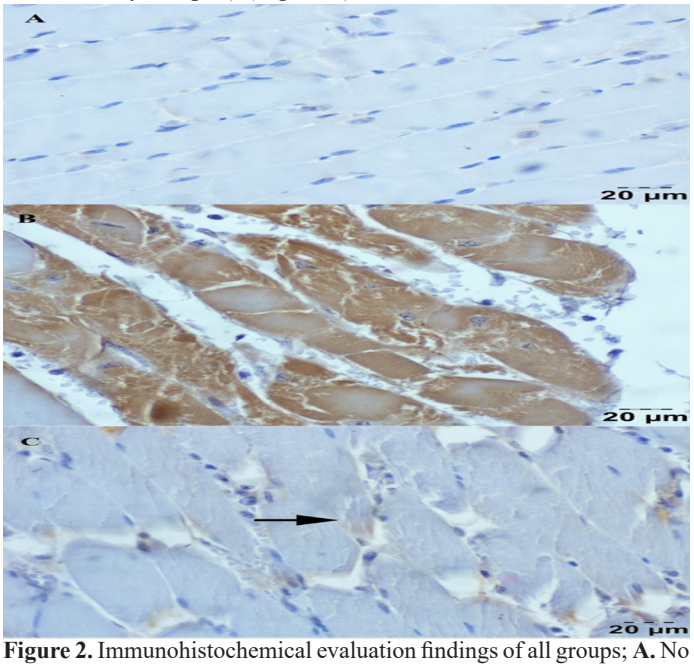

Figure 2. Immunohistochemical evaluation findings of all groups; **A.** No positivity was observed for Caspase3 immunoreactivity in the control group (immunonegative), **B.** In the myositis group, strong positivity for Caspase3 immunoreactivity was detected (strongly immunopositive); no Caspase3 immunoreactivity, **C.** Myositis+Calcitriol group; slightly positive (arrow) Caspase3 immunoreactivity

Statistical Analysis

The data obtained were statistically analyzed in a computer environment using the Statistical Package for Social Sciences for Windows (SPSS v24.0, IBM SPSS Inc., Chicago, IL The conformity of the numerical values of the data in the study to normal distribution was examined by the Shapiro-Wilks test. The median (minimum; maximum) was used to represent the descriptive statistics of the variables that did not show normal distribution. Mean±standard deviation values were given as additional information. The non-parametric Kruskal-Wallis test was used for histopathologic data to compare the differences in the measured parameters between the groups. The Mann-Whitney U test was used to compare the two groups. P values under 0.05 were considered statistically significant.

RESULTS

In the Hematoxylin-Eosin staining examination of the samples taken from the control group, it was observed that the gastrocnemius muscle sections had the standard muscle structure in the control group. Mononuclear cell infiltration, degeneration in myofibrils, disorganization showing increased connective tissue, necrosis, and vascular congestion findings were not detected. Muscle tissues of the myositis group showed mononuclear cell infiltration, hemorrhage, degeneration of myofibrils, disorganization, necrosis, and vascular congestion. When the muscle samples of group 3, which had myositis and received Calcitriol, were examined, a small amount of congestion, myofibrillar disorganization, necrosis, inflammation, and degeneration were detected compared to the myositis group. In the apoptosis evaluation with caspase3, no positivity was observed in the control group regarding Caspase3 immunoreactivity, and strong positivity was detected in the myositis group regarding Caspase3 immunoreactivity. Slightly positive Caspase3 immunoreactivity was observed in the Myositis+Calcitriol group.

As a result of the typical distribution analysis observed that all groups were not normally distributed in terms of congestion, degeneration, necrosis, inflammation, disorganization, and caspase3 (Shapiro-Wilks test; $p<0.05$). Therefore, the Kruskal-Wallis test was used to compare groups (Table 1).

The study found a significant difference in congestion between the groups ($p<0.01$). The difference was due to variations between the control group and the valproic acid group ($p<0.01$), the control group and the vitamin D group (0.01), and the valproic acid group and the vitamin D group ($p<0.05$).

The statistical analysis of degeneration showed a significant difference between the groups ($p<0.01$). The statistical comparison between all three groups revealed that the difference was between the control group and both the valproic acid group ($p<0.01$) and the vitamin D group ($p<0.05$). Additionally, there was a significant difference between the valproic acid and vitamin D groups ($p<0.01$).

Moreover, a statistically significant difference was found in the statistical evaluation of the groups in terms of inflammation, necrosis, and disorganization ($p<0.01$). These differences are due to the control and valproic acid ($p<0.01$) and valproic acid and vitamin D ($p<0.01$) groups.

Regarding Caspase 3, the difference was statistically significant between the groups ($p<0.01$). This difference resulted from the differences between control and valproic acid ($p<0.01$), control and vitamin D ($p<0.01$), and valproic acid and vitamin D ($p<0.01$) groups (Table 2).

Table 1. Statistical comparison of scores obtained from histomorphologic changes in gastrocnemius muscle tissues of control and experimental groups

	G1-Control (n=8)			G2-Valproic Acid (n=8)			G3-Vitamin D (n=8)			p	Test Statistic*
VPA Calcitriol	**Median**	**Min.-Max.**	**Mean±SD**	**Median**	**Min.-Max.**	**Mean±SD**	**Median**	**Min.-Max.**	**Mean±SD**		
Congestion	0	0-1	0.13±0.4	3	1-3	2.5±0.8	1.5	0-2	1.38±0.7	**0.0001**	G1-G2 p=0.0001 G1-G3 p=0.003 G2-G3 p=0.013
Degeneration	0	0-0	0.0±0.0	2	2-3	2.38±0.5	0.5	0-1	0.5±0.5	**0.0001**	G1-G2 p=0.0001 G1-G3 p=0.025 G2-G3 p=0.001
Necrosis	0	0-0	0.0±0.0	2	1-3	2.0±0.8	0	0-1	0.38±0.5	**0.0001**	G1-G2 p=0.0001 G2-G3 p=0.002
Inflammation	0	0-0	0.0±0.0	2	1-2	1.88±0.4	0	0-1	0.38±0.5	**0.0001**	G1-G2 p=0.0001 G2-G3 p=0.001
Disorganization	0	0-0	0.0±0.0	2	1-3	2.0±0.5	1	0-2	0.88±0.6	**0.0001**	G1-G2 p=0.0001 G1-G3 p=0.003 G2-G3 p=0.004

*Mann Whitney U testi

Table 2. Statistical comparison of immunohistochemical data obtained from control and experimental gastrocnemius muscle tissues

	G1-Control (n=8)			G2-Valproic Acid (n=8)			G3-Vitamin D (n=8)			p	Test Statistic*
VPA Calcitriol	**Median**	**Min.-Max.**	**Mean±SD**	**Median**	**Min.-Max.**	**Mean±SD**	**Median**	**Min.-Max.**	**Mean±SD**		
Congestion	0	0-0	0.0±0.0	3	3-3	3.0±0.0	1	0-2	1.13±0.8	**0.0001**	G1-G2 p=0.0001 G1-G3 p=0.004 G2-G3 p=0.0001

*Mann Whitney U testi

DISCUSSION

This research provides essential findings supporting that Calcitriol positively affects muscle health. Vitamin D supplementation may be a supportive treatment option in myositis and other muscle damage conditions. The prevalence of vitamin D deficiency has increased, mainly due to low sunlight exposure, dietary habits, and lifestyle changes (7). Vitamin D supplementation may be an effective method to overcome this deficiency. Vitamin D deficiency has been associated with various health problems, including bone diseases, muscle weakness, immune system disorders, and cardiovascular diseases. Maintaining adequate vitamin D levels can help improve bone health and reduce cardiovascular risk factors. It also positively affects regulating the immune system and preventing inflammatory diseases (7, 8).

Several studies show that Calcitriol may be essential in reducing muscle damage and supporting muscle repair (14-16). The findings of our study suggest that calcitriol supplementation is beneficial in helping prevent the development of myositis in individuals with vitamin D deficiency. In our study investigating the reducing effect of calcitriol treatment on muscle damage in rats with valproic acid-induced myositis, we found that calcitriol treatment significantly reduced the histopathological degree of congestion, degeneration, necrosis, inflammation, and disorganization ($p<0.01$). These findings suggest that Calcitriol has a potential role in reducing muscle damage in rats with myositis. Calcitriol is involved in several biological processes necessary for muscle growth and repair. For example, Calcitriol promotes the proliferation and differentiation of muscle cells, supports muscle protein synthesis and recovery, and exerts anti-inflammatory and anti-apoptosis effects for muscle cells (19-21).

The findings of this study suggest that vitamin D deficiency may be a risk factor in the development of myositis (14-16). There is evidence that the risk of muscle damage may be higher in people with vitamin D deficiency. For example, one study found that people with vitamin D deficiency had a higher risk of muscle pain and weakness (22). Vitamin D supplementation and rats with myositis showed faster and more effective muscle recovery. Vitamin D contributes to the healing of muscle damage by promoting the rebuilding of muscle fibers and reducing inflammation. However, further research is needed on the effective dosage of vitamin D supplementation and duration of treatment (19-21).

Hurme T et al. analyzed the healing of gastrocnemius muscle injury in rats ultrastructurally and immunohistochemically (23). In the histopathological examination of the skeletal muscle sections of our study, we observed disorganization, degeneration, inflammatory cell infiltration, vascular congestion, and intense edema in the structure of muscle fibers in the gastrocnemius muscle in the group in which myositis was formed. In the group in which myositis was induced and Calcitriol was administered, we found a significant decrease in degeneration, inflammatory cell infiltration, and vascular congestion in the muscle tissue in histopathological sections. In the statistical comparison of the groups, $p<0.01$ was found statistically between myositis+ control and myositis groups.

Apoptosis is a genetically controlled form of cell death that occurs in many biological processes. Skeletal muscle cells are fully differentiated and multinucleated. Apoptosis has been described in developing myoblasts and, more recently, in mature myotubes. Mammalian neonatal muscle cells and myoblasts preferentially induce apoptosis in response to noxious stimuli (24). In our study, calcitriol treatment decreased muscle apoptosis in rats with myositis ($p<0.01$).

There are various studies on skeletal muscle in the literature. Bilgiç et al. investigated the protective effect of Montelukast against acute ischemia-reperfusion injury in the skeletal muscle of rats. In the histopathological examination of ischemic muscles, edema, polymorph infiltration, and erythrocyte extravasation levels were statistically significantly higher in the control group than in the Montelukast group. They observed that edema, polymorphonuclear infiltration, and erythrocyte extravasation levels decreased significantly in the treatment group compared to the control group (25). It has also been shown that the conductivity of the nerves in the muscles decreased after ischemia-reperfusion injury, but this conductivity was preserved in the crocin groups (26). Skeletal muscle is the most abundant tissue in the human body. Its main feature is its capacity to regenerate after injury through inflammatory response, regardless of the cause of injury (27).

No nutritional supplements or minerals are effective in treating valproic acid-associated myopathy. However, some studies have shown that creatinine, beta-hydroxybutyrate (BHB), and Coenzyme Q10 (CoQ10) may help relieve the symptoms of this type of myopathy (28-30). Creatinine is an amino acid found in muscles that helps with energy production. In a study of mice with valproic acid-associated myopathy, creatinine supplementation reduced muscle weakness and fatigue (28). BHB is a ketone

body produced in the liver. It aids energy production and may help reduce muscle damage. In a study of mice with valproic acid-associated myopathy, BHB supplementation increased muscle strength and endurance (29). CoQ10 is a coenzyme that plays an essential role in cell energy production. In a study conducted in mice with valproic acid-associated myopathy, CoQ10 supplementation was shown to reduce muscle damage (30). These studies demonstrate the potential benefits of supplemental nutrient or mineral supplements in treating valproic acid-associated myopathy. However, more research is needed to demonstrate the efficacy of these supplements in humans.

This study has several limitations. First, our study had a small sample size. Studies with a larger sample size would help us more accurately assess the effects of calcitriol treatment on myositis. Second, our study was of short duration. Longer-term studies will help us assess the long-term effects of calcitriol treatment on myositis. Third, our study was conducted in a non-human model. More research is needed to assess the effects of calcitriol treatment on myositis in humans.

The findings of this study suggest that calcitriol treatment has a potential role in reducing muscle damage in rats with myositis. Future research in this area will help us better understand the effects of calcitriol treatment on myositis. This research may include evaluating whether calcitriol treatment can help prevent the development of myositis and how it could be applied in humans.

CONCLUSION

This study in myositis-induced rats demonstrates the positive effects of Calcitriol against muscle damage. Vitamin D supplementation may be a potential strategy to support muscle health and accelerate the healing process of muscle damage. However, more clinical studies are needed to assess its effectiveness in humans. Such studies could determine vitamin D's appropriateness in treating muscle damage and provide a valuable treatment option in clinical practice.

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Ethical approval: This study was approved by the Local Animal Experiments Ethics Committee (Protocol No: 725/2023).

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