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Original Article

Evaluation of Additive and Logistics Euroscore in Risk Assessment in Patients Who Have Coronary Artery Bypass Operation in Our Clinic

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Abstract

Aim: The aim of our study was to evaluate the additive and logistic EuroSCORE performance within different risk factors among years and determine the risk factors for the mortality in our clinic.

Materials and Methods: Additive and logistic EuroSCORE model was applied to 434 patients who underwent coronary bypass operations between May 2004 and December 2008 at the Cardiovascular Surgery Clinic Of Ondokuz Mayıs University Faculty of Medicine. Statistical analyses were made by Chi-square method.

Results: Additive EuroSCORE value of the 147 patients in low risk group was 0.82±0.81 and logistic EuroSCORE of the same group was % 1.15±0.31. In moderate risk group including 129 patients, additive and logistic EuroSCORE values 4.05±0.81 and % 3.16±1.01 respectively. Additive and logistic EuroSCORE values of 158 high risk patients were found to be 8.88±2.92 and % 16.36±15.45 respectively. Actualised mortality rates of these patients was %2 in low risk group, %9.3 in moderate risk group %26.6 in high risk group.

Conclusion: In the light of our results, we have found that additive EuroSCORE severely underestimates the actualized mortality rates but logistic EuroSCORE predicts mortality more precisely for our clinical results.

Keywords: EuroSCORE, assessment, mortality

CITATION

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INTRODUCTION

Importance of scoring systems in coronary surgery has gradually increased in recent years. They are used to obtain data on mortality, morbidity, intensive care time and cost before operation. Therefore, various scoring systems are developed. The study wherein EuroSCORE workgroup assessed 19030 patients has evaluated 49 risk factors affecting mortality and morbidity. Among these, 17 risk factors have been found to carry statistical meaning. Each one of these factors was assigned a coefficient for additive and logistic risk calculation (1,2). These risk factors include age, female gender, COPD, extracardiac arteriopathy, neurological dysfunction, serum creatinine level above 2.26 mg/dL, additive endocarditis, history of cardiac surgery, unstable angina pectoris, left ventricle disfunction (30% to 50% at moderate level, under 30% at high level), myocardia infarct in the last 90 days, pulmonary hypertension, emergency operation, operation other than coronary artery bypass, thoracic aorta surgery and VSD development after heart attack. As mentioned above, there are risk coefficients defined for each risk factor. The value derived by simple mathematical addition of these coefficients is the additive EuroSCORE value.

EuroSCORE workgroup has determined 13 factors affecting morbidity. These include inotropic support, general haemodynamic status necessitating IABP support, need for mechanical ventilation more than 24 hours, development of GIS complications, sepsis, pneumonia, mediastinitis, psychosis and meaningful confusion, intensive care stay more than 2 days, and developments resulting in move back to intensive care after release to service or in move to another hospital (1). According to EuroSCORE values the mortality rates are 0.8% for patients in

low risk group, 3% for patients in moderate risk group and 11.2% for patients in high risk group. The total mortality rate in general for all risk groups is determined at the level of 4.7%.

While application of logistic EuroSCORE calculation is particularly recommended for patients in high risk group, the more widely used scoring system today is additive EuroSCORE calculation due to difficulty of logistic calculations and lack of means to practically implement this method like in other scoring cases (3,4). The purpose of this study is to assess the performance of additive and logistic EuroSCORE methods in various risk groups changing across years, while also identifying the risk factors affecting mortality in our patients.

MATERIALS AND METHODS

Cases of 434 patients treated by coronary artery bypass operation under emergency and elective surgery conditions between May 2014 and December 2018 at the Coronary and Vascular Surgery Clinic of our Faculty were retrospectively reviewed. Additive and logistic EuroSCORE values of all patients were calculated using the EuroSCORE Matrix 1.0 Datamatrix Information Systems, Inc. Version 1.0, Build 5.0 software, based on Filemaker, sourced from the www.euroscore.org internet address.

The ethical approval of this study was taken from Samsun 19th May University in 2009.

Statistical Analysis

All values were expressed numerically, in kind of average standard deviation or percentile values. Factors affecting mortality were analysed by Chi-square method and "Student's T Test" in one way analysis. In addition, logistical regression analysis was performed for versatile analysis. The expected risk and realised risk levels under additive and logistic EuroSCORE scoring were compared against each other. Again, Chi-square test method used for this purpose. Again, expected risk and realised risk levels were compared for each risk factor. ROC graphs were calculated.

RESULTS

22 of the 434 patients were operated on with a working heart, while the rest were operated on under cardiopulmonary bypass. 40 patients were treated by single bypass, 110 patient were treated with double bypass, 167 patients were treated with triple bypass and 117 patients were treated with quadruple or more bypass. 55 patients received additional surgical procedures in addition to coronary artery bypass graft operation.

287 of the patients (66.1%) were male, while 147 (33.9%) were female. In the male patient group mortality rate was 11.5% with a total of 33 patients, while it was 16.3% in the female patient group with a total of 24 patients. No statistical meaning was identified in either patient group.

15 (8%) of the 180 operated patients of the age of 60 and under, 17 (12.7%) of the 133 operated patients between the ages of 60 and 70, and 25 (21.5%) of the 116 operated patients of the age of 70 and above were lost. No statistical meaning was identified between these groups ($p<0.0001$). According to one way analysis results, COPD, preoperative critical status, low injection fraction, pulmonary HT, MI in the last 90 days and operations additional to coronary artery bypass surgery were found to be statistically meaningful.

In assessment of multiple regression analysis risk factors including COPD, preoperative critical status, low injection fraction, pulmonary HT and operations additional to coronary artery bypass surgery were found to be statistically meaningful.

According to standard EuroSCORE the mortality rate expected in all groups was calculated as 4.71% ± 3.89%, while this value was calculated as 7.29% ± 11.61% according to logistic EuroSCORE.

Mortality rate in the low risk group is 2.0% with 3 cases, while it is at 9.3% with 12 cases in the moderate risk group and at 26.6% with 42 cases in the high risk group. In the low risk group the expected mortality rate was 0.82% ± 0.81% according to the additive risk model, and 1.15% ± 0.31% according to the logistic risk model. The mortality rate expected in the moderate risk group was 4.05% ± 0.81% according to the additive risk model, and 3.16% ± 1.01% according to the logistic risk model, while the mortality rate expected in the high risk group was 8.88%±2.92% according to the additive risk model, and 16.36%±15.45% according to the logistic risk model. According to these results statistical meaning was identified in and between these groups ($p=0.00$) (Table 1).

DISCUSSION

Many patients who were identified as inoperable and refused surgery in the past are today admitted for operation thanks to developments in the medical sciences and technology. Naturally, this results in higher rates of mortality, morbidity, intensive care time and hospital cost for high risk patients admitted to surgery in comparison to lower risk patients. This observation has led to development of risk scoring systems regarding mortality, morbidity, intensive care stay and cost calculations. To this extent a large number of risk classifications were developed (5,6).

In this study risk factors including age, COPD, pre-operation critical status, pulmonary HT, left ventricle dysfunction and operations additional to coronary artery bypass surgery were found to be statistically meaningful, while no meaningful result was identified for other risk factors. The lower rate of mortality we have seen in our patients with chronic renal failure which is defined at a higher level by the EuroSCORE workgroup is an indication that our protocol of three days of haemodialysis and intensive care haemodialysis as needed post operation implemented for this type of patient has been successful. In this study the mortality rate in the patient group treated with isolated coronary artery bypass surgery is 9.5%, while the mortality rate in the patient group treated with additional surgical procedures rises up to 38%. This indicates additional procedures cause a

Table 1. Patient numbers, risk factors and score percentages

Risk Factor	Patient Number (N)	Percentage (%)	EuroSCORE Percentage (%)	Number of patients lost (N)	P value
COPD	38	8.8	3.9	12	0.002
Extracardiac venous disease	36	8.3	11.3	5	0.525
Neurological dysfunction	5	1.2	1.4	1	0.507
High level of urea	25	5.8	1.8	4	0.421
Pre-operative critical status	45	10.4	4.1	20	<0.001
Angina pectoris	31	7.1	8	4	0.615
EF under 30%	70	16.1	5.8	17	0.004
EF 30-50%	93	21.4	25.6	21	0.003
MI in 90 days	114	26.3	9.7	25	0.002
Pulmonary Hypertension	63	14.5	2	22	<0.001
Emergency operation	30	6.9	4.9	5	0.357
Non-CABG operation	55	12.7	36.4	20	<0.001
Post MI VSD	3	0.7	0.2	1	0.345
Active endocarditis	-	-	1.1		
Thoracic aorta operation	-	-	2.4		

MI: Myocardia Infarct; CABG: Coronary artery bypass graft; VSD: Ventricular septal defect

meaningful increase in the mortality rate.

In assessment of realised mortality rates against the expected values according to additive and logistic EuroSCORE in all risk groups, we determined that additive EuroSCORE calculated the mortality rate under what is realised in our patient group, while logistic EuroSCORE provided results closer to reality. Comparison of mortality rates realised in risk groups against the mortality rates expected according to logistic EuroSCORE system show that values determined for high risk group are closer to reality, while expected mortality rate is lower than realised mortality rate in low and moderate risk groups. Sub-ROC area of logistic EuroSCORE was calculated as 79.1%. This shows that logistic EuroSCORE has good differentiation ability.

The study indicates female gender does not bring any meaningful difference regarding mortality, while mortality increases by a meaningful rate by age. Even though some studies have also indicated significant effect on mortality correlated to chronic renal failure, this effect was not observed in our patient group (7,8). In result of one way and versatile analyses on our patient group it is observed the most important risk factors affecting mortality include COPD, pre-operation critical status, left ventricle dysfunction, age, pulmonary HT and procedures additional to coronary artery bypass surgery.

We observed use of additive EuroSCORE model is not suitable for our patients due to the lower values it provides in comparison to realised mortality rates, while use logistic EuroSCORE provided values closer to reality in all groups, particularly in the high risk patient group.

Due to lack of mortality observation in patients treated with bypass surgery on working heart and the fact that such patients generally have serious left ventricle dysfunction , we believed left ventricle dysfunction can be excluded from assessment as a risk factor in calculation of EuroSCORE for patients treated with this type of surgery.

When mortality rates are assessed according to distal anastomosis figures, mortality rate shows a meaningful increase as the anastomosis figure rises, which leads us to believe the distal anastomosis number must definitely be included in the risk scoring system.

As to study constrictions; low number of patients and study being conducted at a sinle centre can be counted among these.

CONCLUSION

Patient populations differ in each country. Therefore scoring systems should be utilised for pre-operation assessment of patients considered for coronary artery bypass surgery in our country, but we should not be solely dependent on scoring systems.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: The ethical approval of this study was taken from Samsun 19th May University in 2009.

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Original Article

Effects of Different Oral Contraceptives On Ovarian Reserve, Histology, and Micrornas: An Experimental Study

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Abstract

Aim: The aim of the present study was to investigate the effects of different oral contraceptives containing androgenic and antiandrogenic progestins on ovarian follicle reserve, germinal epithelial fibrosis, and microRNA (miRNA) expressions in the ovary.

Materials and Methods: In this prospective study, 35 4-month-old adult female Wistar Albino rats weighing 190–220g and having a regular cycle were randomly divided into five groups during the estrus phase in a single-blind manner. Placebo tablets and oral contraceptives were delivered via gastric lavage for 3 months. Group 1 (control group) received placebo tablets, group 2 received ethinylestradiol (EE) 1.5mcg/day +drospirenone 150mcg/day (Yasmin®), group 3 received EE 1.5mcg/day +cyproterone acetate 100mcg/day (Diane 35®), group 4 received EE 1.5mcg/day +gestodene 3.75mcg/day (Ginera®), and group 5 received EE 1.5mcg/day + levonorgestrel 7.5mcg/day (Microgynon®). Bilateral oophorectomy was performed after 3months. The right ovary was used for the histological examination of the ovarian follicle pool (primordial, primary, secondary, tertiary follicle, fibrosis, corpus luteum [CL], and intra-CL angiogenesis) and surface epithelial change (germinal epithelial degeneration), and the left ovary was used to conduct genetic analysis of miRNAs (mir-21, mir-494, mir-191, and mir 145). Antimullerian hormone (AMH) was measured from intracardiac blood samples. For statistical analysis, the Kruskal–Wallis test was performed, followed by a pairwise comparison with the post-hoc Dunn's test, and p values of less than 0.05 were considered statistically significant.

Results: When compared with Group 1, no significant difference was observed in blood AMH levels in Group 2, but blood AMH levels were found to be significantly decreased in groups 3, 4, and 5. Light microscopy revealed that the number of primordial follicles was similar across the groups, while Group 4 had a significantly lower number of primary, secondary, and tertiary follicles than the control and other experimental groups. Fibrosis and germinal epithelial degeneration were significantly increased in all combined oral contraceptive (COC) groups compared to the control group. mir-21, mir-494, mir-191, and mir-145 expression levels were found to be significantly higher in all COC groups than in the control group.

Conclusion: Different progestin-containing COCs may affect ovarian reserve tests at different levels. Mir-21, mir-494, mir-191, and mir-145 are probably upregulated through the estrogen and progesterone receptor, due to the estrogen and progesterone containing oral contraceptives.

Keywords: Antimüllerian Hormone,Combined oral Contraceptive,Ovary Follicule Reserve,miRNA

CITATION

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INTRODUCTION

Combined oral contraceptives (COCs) have become one of the most common and frequently used birth control methods worldwide since their introduction to the market in 1960. The first COC contained higher estrogen and progestin concentrations than current COCs and caused insufferable side effects such as headache, nausea, weight gain, irregular bleedingand venous

thromboembolism episodes (1). While reducing the dose of the estrogen component ethinylestradiol (EE) in oral contraceptives and using new progestins with improved endocrine and metabolic properties have greatly reduced side effects such as androgenic effects and edema and COCs containing antiandrogenic progestins have been indicated for any hyperandrogenism associated with acne and hirsutism (2,3).

In addition to the frequent use of COCs worldwide, antral follicle count (AFC) and anti-Müllerian hormone (AMH) levels which are markers of ovarian reserve, are suppressed to varying degrees during COC use. Because of the suppression of the hypothalamohypophyseal axis, it will be difficult to distinguish "true" or "false" low ovarian reserve markers caused by COC use (4). However, it is unknown to what extent different progestin-containing COCs, which have different metabolic effects, suppress ovarian reserve tests.

The effect of COC use against ovarian cancer has also been proven, but the underlying mechanisms have not been clearly defined. According to the ovulation hypothesis, genetic damage to the ovarian epithelial cells may occur as a result of the degeneration and subsequent repair of the epithelium at each ovulation, leading to ovarian cancer (5–6).

Reproductive and hormonal factors such as COC use and pregnancy have been hypothesized to reduce the risk of ovarian cancer through the inhibition of ovulation. However, both of these factors confer much greater ovarian cancer protection than expected based on the number of ovulation cycles inhibited, suggesting that they may influence the risk of developing ovarian cancer via additional biological mechanisms (7).

Epigenetic editing refers to the inhibition of protein production to alter cellular functions without causing changes in the DNA sequence. In recent years, small non-coding microRNAs (miRNAs) have been shown to be important components of epigenetic regulators (8).

miRNAs are non-coding single-stranded RNAs that are approximately 22 nucleotides long. They can bind to the target messenger RNA (mRNA) and regulate its cleavage or translation (9).

miRNAs regulate various pathological and physiological processes, including pathogen infection, apoptosis, cell proliferation and cell differentiation. miRNAs control a variety of cellular processes in humans, including cyclical changes in the female reproductive system (10,11).

miRNA expression in the ovary depends on the stage of estrous cycle, cell type and cell function. miRNA is involved in primordial follicle formation, granulosa cell luteinization function and oocyte–cumulus cell interaction, corpus luteum (CL) development, maintenance, and regression, folliclar selection and atresia and. Understanding the expression patterns and functions of miRNA in the ovary will lead to the development of new therapeutics and potentially better contraceptives to improve ovarian dysfunction and infertility (12).

The aim of the present study was to investigate the ovarian reserve, surface epithelial changes, and miRNA levels in the ovarian tissue of rats that received androgenic and antiandrogenic progestin-containing COCs of different generations.

MATERIALS AND METHODS

Experimental Animals and Their Maintenance

The present experimental study was conducted in the laboratory of Fırat University Experimental Research Center. All procedures were carried out under the supervision of a veterinarian and with the approval of the Fırat University Ethics Committee (ethical approval reference number: 2013/1-15).

In total, 35 4-month-old adult female Wistar Albino rats weighing 190–220g and having a regular cycle were used in the present study. The rats were kept in at a constant temperature of 21 °C–23°C and fed with chow and water.

Experimental Procedure

In this prospective study, animals were divided into five groups randomly during the estrus phase in a single-blind manner.

Group 1 (G1) (n=7): The rats in the control group received placebo tablets.

Group 2 (G2) (n=7): EE 1.5mcg/day +drospirenone 150 mcg/day (Yasmin® Germany, Bayer Scherring Pharma) were administered via gastric lavage for 3 months.

Group 3 (G3) (n=7): EE 1.5mcg/day +cyproterone acetate 100mcg/day (Diane 35® Germany, Bayer Scherring Pharma) were administered via gastric lavage for 3 months.

Group 4 (G4) (n=7): EE 1.5mcg/day +gestodene 3.75mcg/day (Ginera tb® Germany, Bayer Scherring Pharma) were administered via gastric lavage for 3 months.

Group 5 (G5) (n=7): EE 1.5mcg/day +levonorgestrel 7.5mcg/day (Microgynon® Istanbul, Turkey Bayer Türk Kimya San. Ltd.) were administered via gastric lavage for 3 months.

After 3 months, oral feeding was discontinued 18 hours before the procedure, except water. To provide anesthesia, the rats were administered 400-mg/kg chloral hydrate intraperitoneally, and they were placed on the operating table in a supine position. A midline incision was used to cut open the abdomen, and bilateral oophorectomy was performed. The right ovary was fixed in 10% formaldehyde for histological examination, while the left ovary was stored at –80°C for RNA isolation. Intracardiac blood was taken from the rats under anesthesia for biochemical analysis, and serum AMH levels were measured.

Biochemical Analysis Methods

Intracardiac blood samples were drawn from the anesthetized rats using an injector and placed in glass tubes. These samples were centrifuged at 3,000 rpm for 10 minutes, and the sera were separated. The sera were drawn with a pasteur pipette and transferred into Eppendorf tubes before being stored in a deep freezer at −80°C for future analysis.

Serum samples were brought to room temperature and plasma AMH levels were analyzed in the Biochemistry Laboratory of Fırat University Faculty of Medicine using the rat Mullerian Inhibitory Substance/Antimullerian Hormone ELISA test kit (Eastbioharm Hangzhou Eastbiopharm co., ltd, Cat no: CK-E30083, China) in accordance with the kit procedure. The absorbances were measured spectrophotometrically at 450nm on the ELX800 ELISA reader. The BioTek ELX50 (BioTek Instruments, USA) automated plate washer was used for washing plates. The results were expressed in ng/mL. The measuring range was 0.1–40ng/mL with a sensitivity of 0.051ng/mL.

Tissue Preparation for Light Microscopic Examination

Ovarian tissues obtained from each group were fixed in 10% formaldehyde fixation solution for 24 hours and then washed under tap water. These tissues were then subjected to routine histological follow-up and embedded in paraffin blocks. The paraffin blocks were cut into 5–6-µm-thick sections. The sections were stained with Masson's trichrome stain. The slides were examined under a microscope, and the numbers of primordial, primary, secondary, and tertiary follicles and CL were determined and photographs were taken. In Masson's trichrome staining, fibrosis, germinal epithelial degeneration, and CL angiogenesis were scored using an ordinal scale ranging from 0 to +3. (none = 0, little =+1, moderate =+2, severe =+3).

Quantitative RT-PCR Method (qRT-PCR)

In the study, the qRT-PCR method was used to detect differences in the expression levels of the following miRNAS: mmu-miR-21 (Assay ID 002493, Applied Biosystems, USA), mmu-miR-191 (Assay ID 002576, Applied Biosystems, USA), rno-miR-494 (Assay ID 462468, Applied Biosystems, USA), and rno-miR-145 (Assay ID 463225, Applied Biosystems, USA). First, the PureLink™ RNA Mini Kit (Catalog No: 12183018A, Invitrogen, USA) was used for the isolation of total RNA from rat ovarian tissue samples stored at −80°C. RNA isolation was performed as per the protocol recommended by the manufacturer. The RNA concentrations were determined using the Qubit® 2.0 Fluorometer (Invitrogen, Australia). RNA samples from each group were collected in their own pools, containing equal levels of total RNA. For complementary DNAs (cDNAs), 10µL of pooled RNA samples from each group were used. cDNA synthesis was performed using the High-Capacity cDNA Reverse Transcription Kit (Applied Biosystems, USA) as per the manufacturer's instructions. The obtained cDNA samples were stored at −20°C. The resulting cDNAs were amplified via qRT-PCR in the presence of sequence-specific primers. When examining miRNA expression levels in rat ovarian tissue samples, 4.5S rRNA (Assay ID 001716, Applied Biosystems, USA) was used as the reference gene. qRT-PCR analysis was performed in triplicate on 96-well plates with a total volume of 10µL. This analysis was performed using TaqMan® Gene Expression Master Mix (Assay ID 4369016, Applied Biosystems, USA) in the Applied Biosystems 7500 Real-Time PCR system as per the manufacturer's instructions. At the end of the analyses, the $2^{-\Delta\Delta CT}$ method was used to calculate the differences in miRNA expression.

Statistical analysis

Statistical analysis of the data was performed using the SPSS 21.0 program. The numerical data were expressed as median (min-max). The Mann-Whitney U test was used to compare two groups. In the comparison of more than two non-parametric groups that did not conform to the normal distribution, the Kruskal–Wallis test was used, followed by a pairwise comparison with the post-hoc Dunn's test. A p value of less than 0.05 was considered statistically significant.

RESULTS

Serum AMH Levels

At the end of the experiment, there was no significant difference between G1 and G2 in terms of AMH levels in blood samples obtained from the rats. However, G3, G4, and G5 had significantly lower AMH levels than G1 (Table 1).

Light Microscopy Findings

Light microscopic examination of Masson's trichrome-stained samples revealed a normal appearance of ovarian tissues in G1 (Figure 1). When compared to G1, fibrosis (red star) and germinal epithelial degeneration (red double arrow) were significantly increased in G2, G3, G4, and G5 ($p<0.05$). In addition, ovarian reserve was determined by counting the numbers of primordial (black arrow), primary, secondary, and tertiary follicles in the ovarian tissues of all groups. When the number of follicles were counted to estimate ovarian reserve, a significant decrease was observed in the number of primary, secondary, and tertiary follicles in G4 when compared with G1 ($p<0.05$). Histological findings of all groups are summarized in Table 1.

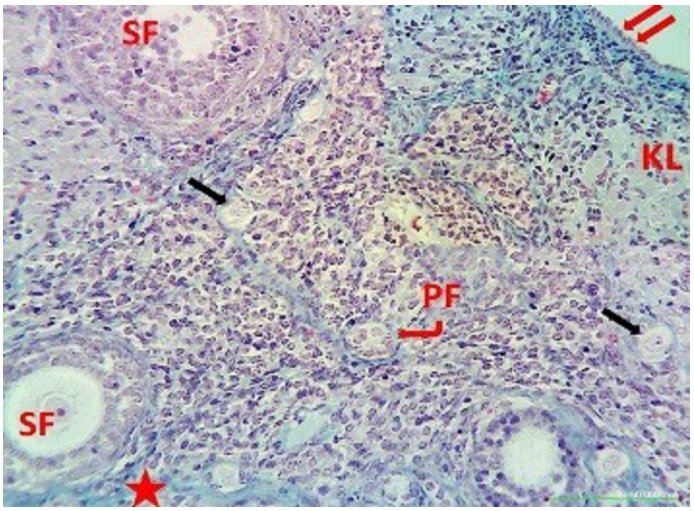

Figure 1. Growing follicles and epithelial findings in light microscopic examination in the control group (G1). Scale bar: 50 µm. Germinal epithelium (red double arrow), fibrosis (star), primordial follicle (black arrow), primary follicle, corpus luteum, and secondary follicle

Table 1. Comparison of the number of ovarian follicles (primordial, primary, secondary, tertiary) and ovarian fibrosis, germinal epithelial degeneration, and intracorporeal angiogenesis results between groups

	G1	G2	G3	G4	G5	P*
AMH	3.83(3.2-4.6)[a]	3.84(2.8-5.5)[a]	3.04(2.4-4)[b]	3.01(2.4-3.6)[b]	2.97(2.3-3.6)[b]	0.42
Primordial	19.8(17-23)[a]	20(18-23)[a]	18(15-21)[a]	18(17-20)[a]	17(14-20)[a]	0.161
Primary	14(13-15)[a]	13(11-15)[a]	12.7(12-14) [a]	6(5-7)[b]	13(12-14)[a]	<0.001
Secondary	10(9-11)[b]	15(13-17)[a]	10.1(8-12)[b]	8(7-9)[c]	11(10-12)[b]	0.001
Tertiary	4(3-5)[a]	3(2-4)[a]	3(2-4)[a]	1(0-2)[b]	4(3-5)[a]	<0.001
Fibrosis	0[b]	0.5(0-1)[a]	0.5(0-1)[a]	1(0.5-1.5)[a]	1.4(0.5-2)[a]	<0.001
Degeneration of Germinal Epithelium	0[c]	1.4(0.5-2)[b]	2.3(1-5)[b]	1.4(0.5-2)[b]	3(2-4)[a]	0.078
CL angiogenesis	1[a]	0.5(0.5-1)[a]	0.5(0-1)[a]	0.5(0-1)[a]	0.5(0-1)[a]	0.042

AMH: Antimullerian hormone CL: Corpus luteum * Kruskal–Wallis test. a,b,c: According to the post-hoc Dunn's test, the same letters indicate statistical insignificance

miRNA Findings

The t-test revealed that mir-21, mir-494, mir-191, and mir-145 expressions in the ovarian tissue were found to be significantly increased in G2, G3, G4, and G5 compared to those in G1. The miRNA findings of all groups are presented in Table 2.

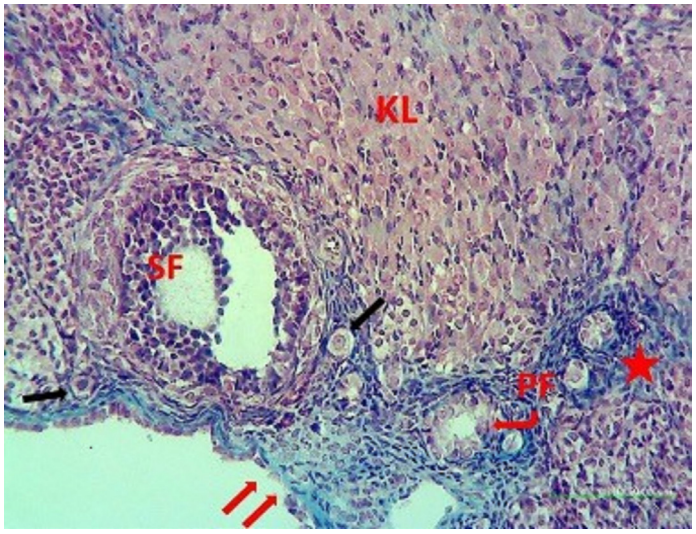

Figure 2. In the ethinylestradiol+ drospirenone group (G2), epithelial degeneration (red double arrow) and growing follicles. Scale bar: 50 µm. Fibrosis (star), primordial follicle (black arrow), primary follicle, corpus luteum, and secondary follicle

Table 2. Fold increase in miRNA expression of all groups

	Control	Ginera	Yasmin	Microgynon	Diane35	p
mir 21	1	18584	2878	448	6931	<0.001
mir 145	1	86	20	6	33	<0.001
mir 191	1	92	3	5	16	<0.001
mir 494	1	116	2	2	49	<0.001

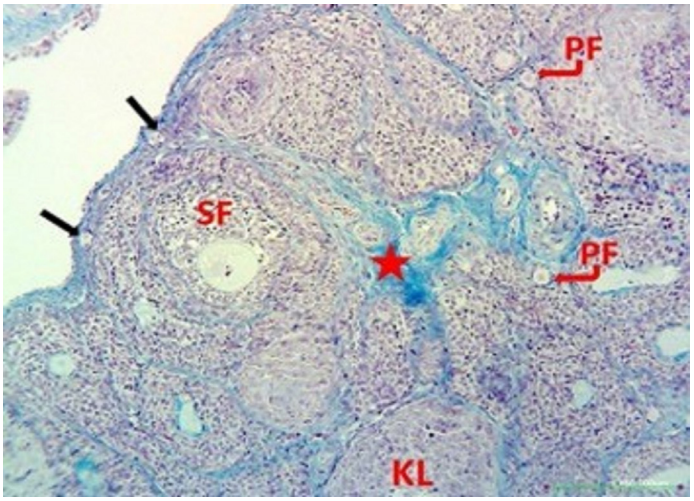

Figure 3. Growing follicles and fibrosis (star) are observed in the ethinylestradiol + cyproterone acetate group (G3). Scale bar: 50 µm. Primordial follicle (black arrow), primary follicle, corpus luteum, and secondary follicle

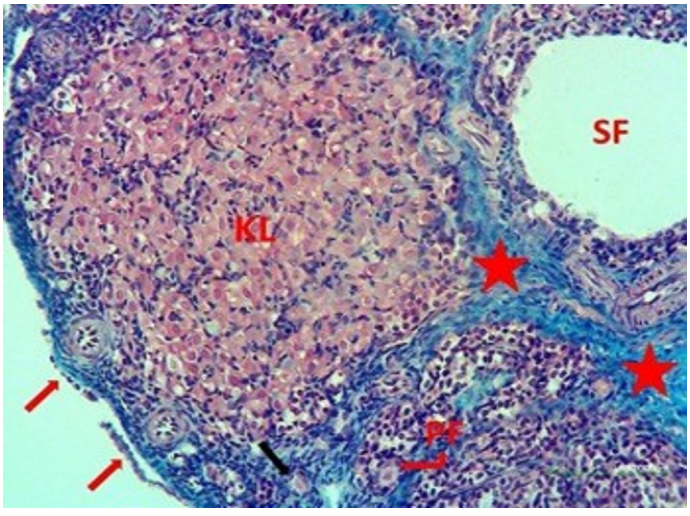

Figure 4. In the group that received ethinylestradiol + gestodene (G4), separation of germinal epithelium (red double arrow) and increased fibrosis (star) were observed. Scale bar: 50 µm. Corpus luteum and secondary follicle

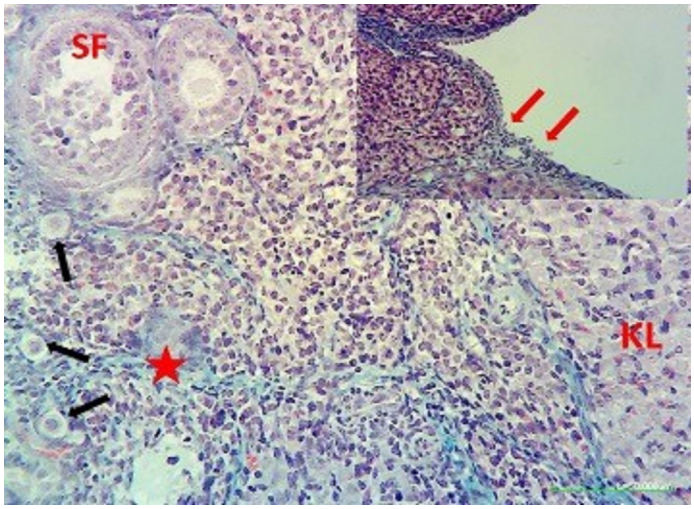

Figure 5. Germinal epithelial degeneration (red double arrow), fibrosis (star), and ovarian follicles in the ethinylestradiol + levonorgestrel group (G5). Scale bar: 50µm. Primordial follicle (black arrow), corpus luteum, and secondary follicle

DISCUSSION

When compared to G1, no significant difference was observed in blood AMH levels in G2, while blood AMH levels were found to be significantly lower in G3, G4, and G5. Light microscopic examination revealed that the number of primordial follicles was similar across the groups, while the number of primary, secondary, and tertiary follicles was found to be significantly decreased in G4 compared to that in G1 and other experimental groups. Fibrosis and germinal epithelial degeneration were significantly increased in all COC groups compared to G1. Compared to G1, all COC groups exhibited significantly increased mir-21, mir-494, mir-191, and mir-145 expressions.

Estimation of ovarian reserve complicates the interpretation of ovarian reserve markers during COC use (13).

Ovarian reserve is evaluated using two main markers that indirectly indicate the true primordial follicle pool: serum AMH level and AFS (14).

A large-scale, cross-sectional study by Bentzen et al, involving 228 COC users and 504 non-users showed that AMH and AFC values were 30% lower in COC users than in non-COC users (15).

Similarly, a cross-sectional cohort study conducted with 27,125 participants showed that compared to non-users, AMH levels were lower not only in participants using oral contraceptives but also in those using vaginal rings, hormonal intrauterine devices, implants, and progestin-only contraceptive pills at variable percentages (16).

In our study, the AMH level of G2 was found to be similar to that of G1, while it was found to be lower in the other COC groups. Preantral and antral follicles were found to be lower in G4 than in the control and other COC groups.

Progesterone and synthetic progestins in hormonal contraceptives interact not only with the progesterone receptor but also with other steroid receptors. Some progestins also bind to androgen receptors and induce androgenic or antiandrogenic effects (17).

If androgen induces the ligand-activated androgen receptor, FSH activity in developing granulosa cells may be modulated. Therefore, they contribute as important modulators of follicle maturation and granulosa cell differentiation, especially in the FSH-dependent early antral stages (18).

In other words, androgens work synergistically with FSH during the early follicular phase. Therefore, using an androgenic progestin to benefit from a COC will prevent the gonadotropin effect necessary for follicle development while also exposing it to the androgenic effect. These two effects negatively affect follicle development. Initially, androgens promote follicle growth, but the absence of FSH causes the growing follicle to undergo atresia. In this context, Barad et al. (19) discovered a significant decrease ovarian reserve test parameters and in the number of oocytes collected after ovarian stimulation in high androgenic COC users, including young patients. Gestodene is a third-generation synthetic progestin with androgenic properties. In our study, the androgenic effect was found to be responsible for a significant decrease in the number of primary, secondary, and tertiary follicles in G1. Similar suppression was not observed in the other group that received COC containing levonorgestrel, another androgenic progesterone.

It is necessary to characterize the androgenic profiles of different progestins to gain insight into their pharmaceutical potential. The androgenicity of synthetic progestins has been analyzed in animal experiments, such as those conducted on ventral prostate, seminal vesicles, ,and levator ani muscles of rats (20).

Gestodene has approximately two times higher androgen-receptor affinity than levonorgestrel, a progestin known to be androgenic (21). The absence of similar findings in the group containing two androgenic progestins may be because of these effects.

Progestins are classified into four successive generations, with the fourth generation designed to have a greater affinity for the P4 receptor (PR) and exert biological effects more similar to P4 than progestins from previous generations (22).

A new generation progestin, drospirenone, has antiandrogenic properties. Combinations of drospirenone and EE alone suppress ovulation but do not completely suppress follicle development (23)

In a study by Barad et al. (19), no difference was found between the number of oocytes obtained between the patients using COCs containing drospirenone and cyproterone acetate and the control group, while a significant decrease was observed in the group that received androgenic COCs. In our study, no difference was observed in both AMH levels and follicle pools between G2 and G1.

In a previous study, changes in ovarian morphology were studied in 32 sterilization patients who received COCs for 1–8 months. Histological examination of the ovaries revealed flattening of the epithelial wall; increased fibrosis of atretic follicles; dispersion of granulosa cells, luteinization of the follicular cyst; vacuoles in luteinized cells; hypercellularity of its cortex, fibrosis of the cortex; increased vascularity; hyaline material inside mature, degenerating follicles; increased edema; and atretic follicles at various stages of degeneration (24). Similarly, the present study found increased fibrosis and germinal epithelial degeneration in all COC groups compared to G1.

In a randomized study by Rodriguez et al. (25) conducted on female monkeys for 3 years investigating the protective effects against ovarian cancer and involving the control, estrogen-only, and estrogen +progestin (levonorgestrel) groups, a single line was observed on the basal layer of the ovarian surface epithelium in the control and estrogen groups, and apoptotic cells were scarcely observed. In addition, typical morphological findings were reported in the estrogen + progestin group; the tendency to detach from the ovarian surface in the form of patches has been reported as the separation of cells with sparse cytoplasm from the ovarian surface. Immunohistochemical examination revealed a dramatic increase in apoptotic cells. This finding suggests that the progestational agent increased the rate of apoptosis. Similar to that study, germinal epithelial degeneration was found to be significantly increased in all COC groups when compared with that in G1 in the present study. Morphologically, similar separations were observed in the epithelium.

In our study, mir-21, mir-494, mir-191, and mir-145 expressions were found to be significantly increased in all COC groups compared to those in G1.

miR-21 was one of the first miRNAs discovered in mammals. miR-21 is a regulator of cell apoptosis and follicular development. It is found in higher concentrations in CL collected on day 10 of the estrous cycle than on day 4. This suggests that it is also involved in the luteinization process (26). Simultaneously, inhibition of miR-21 reduces the ovulation rate by inducing apoptosis in both mouse granulosa cells and ovaries and (27). mir-21 is an androgen-regulated miRNA. It has been shown that the binding of androgen to the AR element of the miR-21 promoter leads to an increase in miR-21 expression by the anabolic–androgenic steroid R1881 in LNCaP and LAPC-4 cells (28). Considering the antiandrogenic effects of oral contraceptives, a decreased mir-21 expression is expected. The increased mir-21 levels in our study can be explained in several ways. Firstly, higher levels of miR-21 were found in ER+ and PR+ breast cancers compared with ER- and PR-negative receptor status (29). Considering that all of the COCs used in the present study are estrogen/progesterone-containing COCs, it is easier to understand why mir-21 expression increases significantly as a result of COC treatment. The upregulation of mir-21 expression by COCs by ER and PR receptors seems to be the most likely underlying mechanism.

miR-191 is an estrogen-inducible onco-miR that promotes several malignancy properties in breast cancer, including enhanced cell migration , proliferation, , chemotherapy resistance, and survival in the tumor microenvironment. mir-191 has an ER-receptor binding site in the promoter region (30,31).

The increased mir-191 levels in our study can be attributed to the binding of estrogen in COC preparations to the mir191 promoter via ER receptors and the resulting upregulation of gene expression.

miR-494 can treat as a tumor suppressor or an oncogenic miRNA in various tumor types. miR-494 is underexpressed in ovarian malignancy(32,33).

E2 has been shown to induce miR-494 expression via ER alpha in female mouse cardiomyocytes and myocardium (34). Although it is unknown whether a similar mechanism exists in ovarian tissue, the increase in mir-494 in the present study can be explained by the upregulation of mi-494 by the estrogen contained in the oral contraceptives. Further research into this mechanism is needed.

miR-145 supports proliferation, differentiation, and steroidogenesis of granulosa cells and plays an important role in ovarian physiology and pathology. It is involved in the formation of the primordial follicle pool in fetal and neonatal mouse ovarian tissues (35,36).

In a recent study, it was shown that progesterone inhibits the proliferation of endometrial epithelial cells by inducing miR-145/miR-143 expression. Although it is not known whether there is a similar mechanism in the ovarian tissue, the inhibition of primordial follicle development by oral contraceptives via increased mir-145 expression appears to be a likely mechanism (37).

In summary, the main mechanism underlying the increase in the four miRNAs analyzed in our study, in which the mirRNAs we analyzed were generally upregulated in different cells and tissues by estrogen or progesterone due to the use of oral contraceptives, is the most likely mechanism through estrogen/ER and progesterone/PR. is seen as. Although the evidence suggests that these mechanisms are likely, there is a need for studies analyzing these mechanisms in a cell-specific way in ovarian tissue. This may provide insight into the epigenetic regulation of the relationship between COC use and anticancer effects. However, the function of miRNA may be time-, tissue-, and species-specific.

Furthermore, most of our knowledge of miRNA activity is based animal models. Although animal models are extremely effective in understanding the function of miRNA in ovarian follicular development, species-specific differences in miRNA expression and function may reveal a difficulty to the use of miRNA detection in human applications. Studies with human ovary and specific cell cultures are promising in terms of understanding the relationship between COCs and miRNA.

CONCLUSION

In conclusion, this study showed that COCs containing drospirenone did not affect AMH levels or follicle counts, while COCs containing gestodene suppressed both AMH levels and follicle counts compared to other COCs. Preparations containing drospirenone can be preferred, especially in ovulation induction protocols. It should be noted that both AMH levels and AFC can be severely suppressed in women who take gestodene-containing COCs.

Competing interests: The authors declare that they have no competing interest.

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Ethical approval: All procedures were carried out under the supervision of a veterinarian and with the approval of the Fırat University Ethics Committee (ethical approval reference number: 2013/1-15).

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Original Article

Comparison of Meperidine and Tenoxicam For Pain Management in Trauma Patients

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Abstract

Aim: The aim of this study was to compare the effectiveness and side effects of meperidine and tenoxicam, either alone or in combination for the pain management of trauma patients.

Materials and Methods: This was a prospective, single-center, single-dose, randomized, double-blind study in trauma patients (age≥16) with Glasgow coma scale (GCS) 15, stable hemodynamics and initial visuel analog scale (VAS) score of 50 mm or higher. Sixty patients were randomized to one of the three treatment groups. All patients vital signs, VAS scores and adverse events were recorded before the drug administrations and at 15, 30, 60 minutes of applications.

Results: The mean initial VAS for meperidin, tenoxicam and meperidin + tenoxicam groups were 83±13, 82±15 and 76±15, respectively. The mean final VAS for these gruops were 5.0±1.8, 4.9±2.2 and 4.3±2.3, respectively. The decreases of VAS for all groups and time periods were statistically significant and there were not any significant difference between the groups. Furthermore, no serious adverse events were observed.

Conclusion: In conclusion, in addition to it's advantages like rendering possible intravenous administration and not having direct effects on vital functions, tenoxicam is as effective as meperidine for acute severe pain.

Keywords: Trauma, pain management, tenoxicam, meperidine

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INTRODUCTION

Trauma is usually associated with moderate to severe degree of pain (1). Recently, several studies were performed to reduce the mortality and the morbidity in this patient group, and pain management studies in trauma patients constitute an important aspect of this area.

Posttraumatic pain may help the diagnosis, provide immobilization and prevent additional injuries and pain leads elevation of the heart rate and the blood pressure by inducing catecholamine release, and thus, facilitating blood flow to vital organs especially during hypovolemia. On the other hand, it is known that inadequate pain management, increases stress response to trauma which includes cytokine and acute phase reactants release, causes impaired coagulability, altered immune response and potentiates the adverse effects on normal physiological functions such as ventilation, and gastrointestinal system and renal functions, resulting in higher morbidity and mortality. Furthermore, inadequately treated acute pain can lead to the development of chronic, neuropathic pain (2,3). However, sufficient early analgesia leads to a much better therapeutic outcome and decreases the hospitalization time (4).

Opioids are the drugs of choice for severe and moderate pain management. But most physicians hesitate to use opioids at emergency department (ED) with the fear of deterioration at respiration or hypotension at potentially critical patients like trauma. Thus, a safety and effective pain management strategy has to be defined for these patients.

As it is true for all a nonsteroidal antiinflammatory drugs (NSAID), tenoxicam may have adverse effects on the renal functions and platelet functions, and has the risk of gastrointestinal system irritation or bleeding. These effects, however, generally occur during long-term use.

The visual analog scale (VAS) is a pain rating scale based on patients' self-reported measures recorded with a single handwritten mark placed at one point along the length of a 100 mm line. The scale represents a continuum between the two ends—"no pain" on the left end (0 mm) of the scale and the "worst pain" on the right end of the scale (100 mm).(5)

This study was designed to compare the effectiveness and side effects of meperidine and tenoxicam, either alone or in combination in the emergency department patients with trauma.

MATERIALS AND METHODS

Trauma patients with > 16 years of age, Glasgow Coma Scale (GCS) of 15, stable hemodynamics and whom reporting an initial visual analog scale (VAS) score of 50 mm or higher were included in this prospective, randomized, double-blind study. Patients with an initial systolic blood pressure below 90 mmHg, GCS < 15, patients who received analgesics before admission and had probability for major surgery were excluded. Besides patients with displaced fractures and dislocations were excluded from the study although they had analgesic requirement because of the need for emergency reduction which could effect VAS during the procedure. The patients were randomized to one of these study groups;

Group 1 received Meperidine 1 mg / kg iv + 3 cc saline iv

Group 2 received Tenoxicam 20 mg iv + 3 cc saline iv

Group 3 received Meperidine 0.5 mg /kg iv + Tenoxicam 20 mg iv.

All patients received analgesics at the first half hour of their arrival to the ED after a closed envelope with the name of the drug was randomly drawn and then prepared and applied by a nurse. As two drugs were administered together in Group 3, 3 cc saline solution was co-administered with the drugs in the 1st and 2nd groups. Following the administration of the drug, the patients were assessed for vital functions, adverse events and pain relief by the emergency physician working at the ED whom did not know the contents of the injection until the end of the study period.

Statistical analysis

Statistical analysis of the data was performed using SPSS for Windows Ver. 10.0 Statistics software. Wilcoxon test was used. 15., 30., 45. and 60. minute VAS values were compared with the baseline VAS value, within each group. Kruskal-Wallis test was used to compare three drug groups. Mann-Whitney's U-test was performed for comparing two groups after the Kruskal Wallis test, in case of finding significances. For the analysis of the variables (age, ISS) Kruskal Wallis test was used. The results were presented as mean ± standard deviation (SD). Statistical significance was set to $p < 0.05$.

This study received institutional review board of Uludag University Medical Faculty. Ethical approval was obtained from Ethics Committee Uludag University Faculty of Medicine. (reference no.2004-10/5).

RESULTS

A total of 132 trauma patients were evaluated while the study period. Seventy two patients were excluded from the study for various reasons (Figure1).

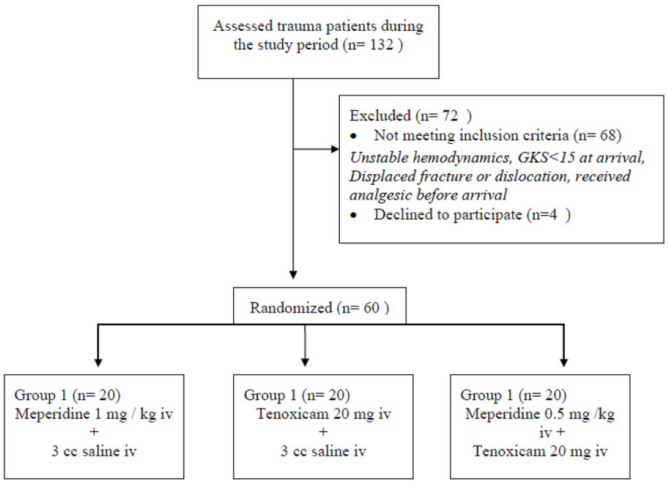

Figure 1. Flow diagram

Sixty patients were included in the study and twenty patients were randomized to each group. The mean age was 37.9 (17-83) years and the majority (%75) of the patients was male. The mean injury severity score (ISS) of the patients was 10.1±7.5. There was no significant difference between the drug groups, in terms of age distribution and ISS scores. The general characteristics of the drug groups are shown in Table 1. Most common indications for analgesia were extremity fractures, back-pain, rib fracture and soft tissue injuries (Table 2).

Table 1. Distribution of the groups in terms of age, gender, and ISS*

		Group 1	Group 2	Group 3	Total
Mean age		37.9	37.7	37.8	37.8
Gender	Male	15	16	14	45
	Female	5	4	6	15
ISS		11.5±9.7	11.4±6.5	7.35±4.7	10.1±7.5
Number of patients		20	20	20	60

*ISS= Injury Severity Score

Table 2. Indications for analgesics administration

Extremity fracture	**37**	**61.7**
Soft tissue injury	9	15
Back pain	12	20
Rib fracture	9	15
Others	4	6.7

*Some of the patient had more than one indication for analgesia

The mean initial VAS value was 80±10.4 for all patiens. This value was 83±13 for meperidine, 82±15 for tenoxicam and 76±15 for meperidin + tenoxicam group and there was no significant difference between the initial VAS scores of the groups (p=0.9). The reduction in the VAS levels at all time periods (15, 30, 45, and 60 minutes) were also statistically significant for all groups, but without a significant difference between the groups (p<0.001). The changes in the VAS levels for all drug groups were shown in Table 3.

Hypotension (<90 mmmHg) was observed at one patient in meperidine group and nausea was observed at 3 patients in meperidine group and 2 patients in meperidin + tenoxicam group.

Table 3. Values of VAS and p over time in drug groups

Groups	VAS1 0.min	VAS2 15.min	VAS3 30.min	VAS4 45.min	VAS5 60.min	p value*
1. group (n = 20)	83±13	70±14	62±15	62±15	50±18	a_p=0.001 b_p=0.001 c_p=0.001 d_p=0.001
2. group (n = 20)	82±15	72±17	65±18	57±16	49±22	a_p=0.001 b_p=0.001 c_p=0.001 d_p=0.001
3. group (n = 20)	76±15	66±17	54±19	49±20	43±23	a_p=0.001 b_p=0.001 c_p=0.001 d_p=0.001

*a_p=VAS2 - VAS1, b_p=VAS3 -VAS1, c_p=VAS4 - VAS1, d_p=VAS5 - VAS1

DISCUSSION

Pain management, especially in trauma patients, is one of the most important issues in the emergency patient care all over the world. A fast, reliable, and effective analgesia is a prerequisite for a good patient care and patient satisfaction. Various studies, however, report that trauma patients receive insufficient and inappropriate analgesic treatment (6,7,9-11).

Opioids are still the first-line drug for the treatment of severe acute pain, including the trauma patients (1-8). However, due to their major adverse effects, there are several studies investigating alternative drug choices or the use of combinations of opioids with other drugs, also known as "multimodal analgesia"(12-16). Wheeler reported that with the administration of multiple drugs, a better patient comfort is achieved, and fewer side effects are observed (13). Javery et al. reported that for postoperative pain management, sufficient analgesia could be achieved with less amount of morphine if combined with ketamine, and that side effects are occur much less frequently (14). In this study, in addition to meperidine and tenoxicam groups, we also formed a third group where meperidine dosage was reduced and combined with tenoxicam. We found no significant difference between the groups in terms of sufficient pain control, as well as side effects.

There are few studies in the literature comparing opioids with NSAIDs for the pain management of trauma patients in the ED. Rainer et al. compared intravenous ketorolac with intravenous morphine in patients admitted to the ED due to extremity injuries and found that the analgesic effect of ketorolac was at least as potent as morphine, and reported less frequent and less severe side effects with this drug (15). Cordell et al. determined that intravenous ketorolac alone or in combination with meperidine is more effective than intravenous meperidine alone in the treatment of renal colic pain (16). Holdgate, in his meta-analysis of 20 studies comparing the effectiveness of NSAIDs and opioids on patients receiving analgesia for renal colic, reported that NSAIDs provide a more effective analgesia, less additional analgesia is required in the early stage in the NSAID group and side effects such as nausea and vomiting occur more frequently with opioids (17). Tenoxicam was chosen in this present study as it is shown before as a safe and effective drug in preoperative and postoperative analgesia. In our study tenoxicam was as effective as meperidine for pain control in trauma patients,

as significant decreases of VAS was observed for both drug groups. On the other hand, Stahmer reported the decrease of VAS should be at least 13 -15 mm to detect clinically significant pain relief (18). This degree of decrease was possible at fifteenth minute of injection at tenoxicam –meperidine combination group and it was possible at 30 minutes of injection at tenoxicam and meperidine alone group in our study.

LIMITATIONS

Our study was a single-center low-population study, conducted in a tertiary care hospital. Therefore, reproducing it on larger sample sizes will improve its generalizability. Another limitation is that adverse effects in this study were only examined up to 60 min after the administration of tenoxicam. Some of the well-known adverse effects of tenoxicam include renal injury and gastrointestinal bleedings, which were not evaluated in this study.

CONCLUSION

Traumatic injuries vary in severity from minimal soft tissue injuries to life-threatening multiple fractures. Adequate analgesia is an important component of trauma management. Patient-specific pain management considering age, chronic illnesses, appropriate pain evaluation, cognizance of adverse effects medications and major surgery requirement is essential. Tenoxicam was as effective as meperidine in pain management of trauma patients if used alone, or in combination with the half-dosage of meperidine in our study. Therefore tenoxicam may be a good drug of choice for proper trauma patients in the emergency department for pain management.

Author Contributions: F.O. and M.B. researched literature and conceived the study. F.O. , S.A.A and O.K. collected and anaylsed the data. F.O. and M.B. wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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Original Article

Foreign Bodies Found in Various Locations and the Treatment Methods Used

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Abstract

Aim: The aim of the study was to present the treatment of foreign bodies found in various locations in our patients.

Materials and Methods: The files of 11 patients who presented to the Kafkas University Departments of General Surgery and Orthopedics and Traumatology between November 2015 and July 2022 were reviewed retrospectively. Demographic characteristics, etiological factors, endoscopic evaluation, radiological imaging results, surgical treatment and results, and postoperative complications were recorded.

Results: There were 5 female (45.45%) and 6 male (54.55%) patients found to have a foreign body. The distribution was a swallowed battery in 1, a swallowed needle in 4, a metal piece in the hand and wrist in 2, a metal needle in the foot in 2, a piece of wood in the hand in 1, a glass piece in the elbow area in 1, and a sewing needle in the foot in 2 patients. Radiological imaging methods and endoscopic procedures were used in all of our patients to determine the location of the foreign body. Patients found to have a needle in the intestinal region by abdominal X-ray examination were hospitalized and followed up for at least five days. No foreign body was detected in the ambulant direct abdominal radiography during the follow-up of our patients who had swallowed needles, and no surgical intervention was planned for these patients. All foreign bodies detected in the upper and lower extremities were removed with surgical intervention. No complications developed in any of our patients.

Conclusion: Foreign bodies detected in various parts of the body should be located by endoscopic or imaging methods and appropriate treatment should be provided before any complications develop.

Keywords: Foreign body, endoscopy, plain radiography

CITATION

Allahverdi TD, Allahverdi E. Foreign Bodies Found in Various Locations and the Treatment Methods Used. Int Target Med J. 2022;1(3):67-9.

INTRODUCTION

The presence of foreign bodies within the body as a result of swallowing or various accidents at work or home is a common clinical problem. The complications that may occur in patients who have swallowed a foreign body include gastrointestinal bleeding, intestinal perforation, and intestinal obstruction. Patients with a swallowed foreign body close to the surface may present to the hospital with a feeling of difficulty swallowing or painful swallowing, while those with a foreign body in various parts of the body may present pain, limitation of movement, and symptoms consistent with an abscess (1). Foreign body injuries with objects such as glass and metal may occur in the extremities. Whether surgical intervention is required can be decided on by endoscopy and radiological imaging methods (1,2). We aimed to retrospectively review the file records of patients who had swallowed foreign bodies or were found to have foreign bodies in various parts of the body, and present our experience and results.

MATERIALS AND METHODS

The files of 11 patients who had presented to the Kafkas University Departments of General Surgery and Orthopedics and Traumatology's emergency and outpatient units between November 2015 and July 2022 were retrospectively reviewed. Demographic characteristics, etiological factors, endoscopic examination and radiological imaging results, surgical treatment and results, and postoperative complications were recorded. Permission to conduct the study was obtained from the Kafkas University Faculty of Medicine Ethics Committee (decision no. 80576354-050-99/178 dated 26-06-2019).

RESULTS

There were 5 female (45.45%) and 6 male (54.55%) patients found to have a foreign body. The mean age was 53.4 for the female patients and 43.4 for the males. The symptoms and complications varied according to the location of the foreign

body. Symptoms such as dysphagia, difficulty swallowing, nausea, and abdominal pain were observed in patients with a swallowed foreign body while pain, limitation of movement, and symptoms related to an abscess were reported in patients with foreign bodies in the upper or lower extremities. The distribution was a swallowed battery in 1, a swallowed needle in 4, a metal piece in the hand and wrist in 2, a metal needle in the foot in 2, a piece of wood in the hand in 1, a glass piece in the elbow area in 1, and a sewing needle in the foot in 2 patients (Figure1, 2, 3, 4) .

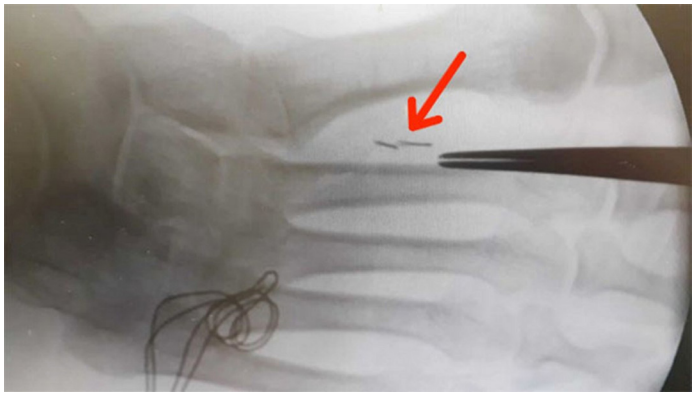

Figure 1. a metal needle in the hand

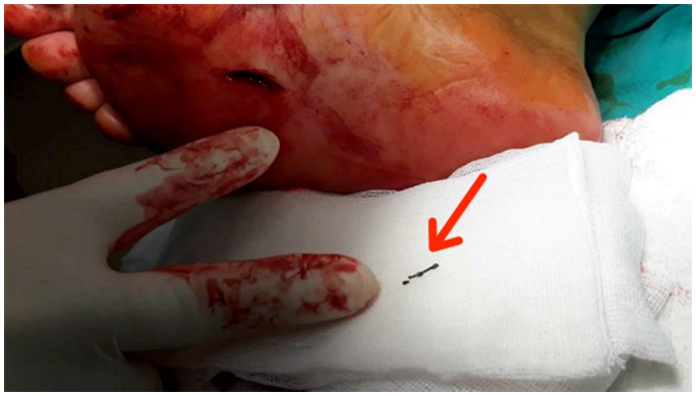

Figure 2. a metal needle in the foot

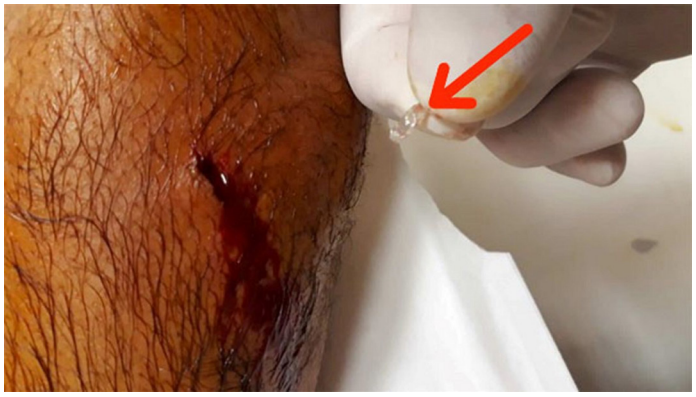

Figure 3. a glass piece in the elbow area

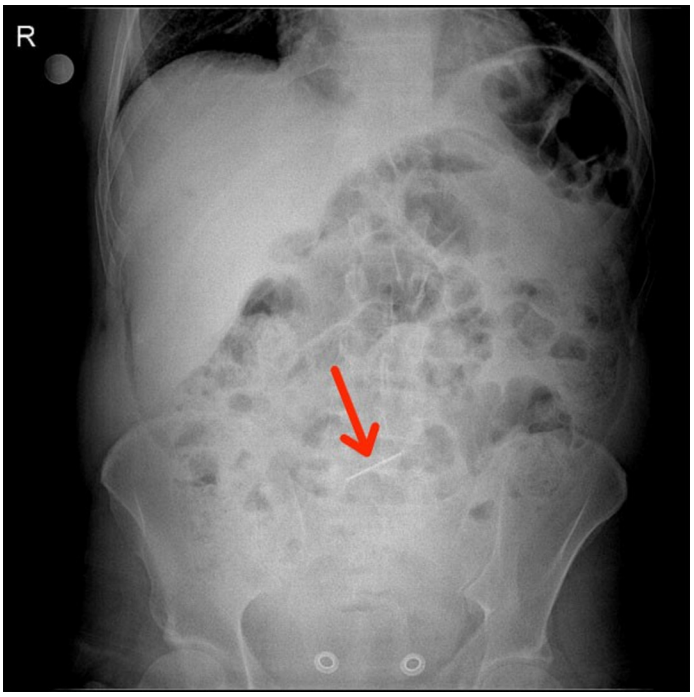

Figure 4. a metal needle in the abdomen

Radiological imaging methods and endoscopic procedures were performed in all patients to detect the location of the foreign body. The patients who underwent endoscopy had an uncertain fasting period as they had been urgently referred from an external center. We did not detect any foreign body in the endoscopic examinations we performed. The abdominal X-ray examination revealed a battery in the stomach region in one patient and a needle in the intestinal region in another patient. The patient with a battery in the stomach location was taken to surgery; the battery was removed and the stomach repaired with a primary suture. The patients with a needle in the intestinal region on direct abdominal X-ray examination were hospitalized and followed-up for at least five days. No foreign body was detected in abdominal X-ray examination during the follow-up of the patients who had swallowed needles and no surgical intervention was necessary. All foreign bodies detected in the upper and lower extremities were removed by surgical intervention and the mean follow-up duration in these patients was three days. The abscesses that had developed in our patients with a foreign body detected in the extremities underwent debridement and evacuation during the surgical intervention. No complication developed in any of our patients who had undergone surgery.

DISCUSSION

Adult patients who present to emergency departments with a swallowed foreign body are mostly in prison or have a dental prosthesis. While those in prison mostly swallow foreign bodies voluntarily, those with a dental prosthesis present with food getting stuck in the pharynx.It should not be forgotten that other problems such as mediastinitis, fistula development, perforation,

and abscess might occur if the foreign body remains in the esophagus and stomach for a long time. Therefore, the foreign body should be detected by radiological imaging and endoscopic methods and then removed as soon as possible. As long as foreign bodies remain in the stomach and esophagus, swallowing difficulties and ulcerations in the esophagus and stomach may occur (3,4). Foreign bodies in the small intestine and stomach are usually removed by the body itself. However, emergency surgical intervention should be performed in patients who develop acute abdomen symptoms following complications such as perforation (5). Laparotomy should be performed in cases where peritoneal irritation findings are detected and the foreign body has remained in the same place for 48 to 72 hours (6). The transit duration of foreign bodies from the digestive tract has been reported to be 3.6 to 5.1 days (5).

Extremity foreign body injuries may occur due to materials such as glass, wood, and metal (7-10). The foreign bodies appear radiopaque on plain radiographs, and it is possible to detect glass fragments larger than 2 mm in 99% of the investigations (8). Ultrasonography should be the first choice in case of radiolucent bodies such as wood and plastic (2). If the piece of wood is fragmented, it may not be seen during ultrasonographic imaging due to the edema and abscess that develops in the soft tissue. If the foreign body is not detected with plain radiographs or endoscopic procedures, it can be located by using Computed Tomography or Magnetic Resonance (1,2). If the foreign body is not removed, complications such as pain, cellulitis, infection, and delayed healing may occur. However, it may also be possible to leave foreign bodies in their current location when they have been present for a long time and do not cause any obvious dysfunction (2).

We did not detect any foreign body in the endoscopic examinations, the patient who was found to have a foreign body on abdominal X-ray examination that could not be detected on endoscopy due to a full stomach was taken to surgery and two batteries were removed from the stomach. No surgery was necessary in the other patients. No surgical intervention was necessary in the patients with a history of swallowing needles since the needle was not seen in the abdominal X-ray examination and no acute abdomen signs developed during follow-up.Our patients were followed-up for at least 6 days and then discharged. Plain radiographs were taken in all of our patients with a history of a foreign body in the extremities in order to determine the location of the foreign body. Surgery was performed in patients found to have a foreign body in an extremity on plain radiographies. Plain radiographs did not reveal a foreign body in the patient who was found to have a piece of wood in an extremity. However, the piece of wood was removed by surgical intervention as an abscess had developed.

CONCLUSION

In conclusion; foreign bodies in various parts of the body should not be considered simple injuries. Appropriate imaging methods should be used to determine the patients who need to be monitored or require surgery. Surgery should be performed when necessary according to the location of the foreign body. For foreign bodies detected in the gastrointestinal tract, surgery should be performed if complications such as obstruction and perforation develop, while patients without any complication should be monitored.

Competing Interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

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Case Report

Rapid Depreciation of Cryptocurrencies and Suicide: A Case Report

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Abstract

The relationship between economic crises and suicide has been analyzed in the medical literature. Cryptocurrency, which has recently occurred with the increasing technological advances, attracts people's attention and can be noticed as an investment tool. However, rapid rises and declines can be seen in cryptocurrencies such as Bitcoin. Financial losses can negatively influence people's mental health and induce suicide. In this case report, after the rapid devaluation of Bitcoin in the first two weeks of June/2022, a case that committed suicide by jumping from a height and applied to the emergency room (ER) by ambulance was presented and discussed.

Keywords: Blockchain, suicide, emergency room, mental health

CITATION

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INTRODUCTION

With the increasing technological development, various economic instruments have emerged. Bitcoin is one of the most popular instruments in the world, also called virtual money or cryptocurrency in terms of market size. Bitcoin is the first new currency to acquire popularity a few years after its launch, the largest cryptocurrency on the market, and its pricing also seem unpredictable (1).

There are publications that show a link between bankruptcy and suicide (2). Judi et al. also reported a significant association between patients who presented to the emergency room (ER) with a suicide attempt and experienced financial bankruptcy within two years prior to admission and within two years after admission (3).

This essay discusses a case with Bitcoin investments who was admitted to the ER because he committed suicide by jumping from a height after the large drop in the value of Bitcoin in June 2022.

CASE REPORT

A 32-year-old male patient is married with two children and works as a civil servant in a public institution. According to his family, he uses his financial savings by investing in the cryptocurrency Bitcoin. He has no known chronic illness and no history of psychological treatment. After Bitcoin reached a value of $31,148 on 06/06/2022, it quickly lost value and fell to $22,120 on 06/14/2022. He fell into depression and jumped to the fifth floor of a building on 06/14/2022, committing suicide by throwing himself down and was seriously injured by hitting the concrete floor. The patient was intubated and taken by ambulance to Sakarya Training and Research Hospital (SEAH). His general condition was poor, he was unconscious, his Glasgow Coma Score was three, his pupils were dilated and midline, no light reflex, blood pressure was 78/47 mmHg, heart rate was 130/min, and SpO2 was 81-88. The patient's physical examination and imaging results revealed diffuse cerebral edema, traumatic subarachnoid hemorrhage, burst fracture of the L3 vertebra, displaced rib fracture of the sixth and seventh ribs on the right side, pneumothorax measuring three cm at the widest part of the right hemithorax, and emphysema in the subcutaneous tissue of the right hemithorax. Abdominal examination and imaging were unremarkable, and comminuted fractures of the right pelvic bone, right acetabulum, and pubic bone were noted, along with a severe hematoma in the adjacent muscle tissue. On the extremities, displaced shaft fractures of the right and left humerus and an open shaft fracture of the distal left tibia were noted. After bladder catheterization, the patient was found to have hematuria. The patient's laboratory results presented hemoglobin 11.1 g/dL, WBC 24 K/uL, PLT 339 K/uL, neutrophils 19.8 K/

uL, lymphocytes 3.9 K/uL, glucose 286 mg/dL, ALT 181 U/L, AST 192 U/L , CK-MB 363 U/L, hsTn I 109.3 ng/L, INR 1.74, lactate 7.9 mmol/L. Radiologically, no extravasation was noted in the pelvic region. Control hemoglobin was measured one hour later at 6.5 g/dL. The patient, whose red blood cell suspension transfusion was initiated, was admitted to the intensive care unit in the second hour after admission to the ER. One hour later, the patient, who suffered cardiac arrest in the ICU, died.

DISCUSSION

Garry Smith points out that the link between gambling and bankruptcy, addiction, and suicide is not considered a major problem in Canada (4). Although there are significant differences between online betting and day trading and cryptocurrency investing, there are also studies on strategies to protect and prevent harm to inexperienced investors (5). Vicente Rodríguez et al. find that financial fraud has a negative impact on people's mental health during the economic crisis (6). Bankruptcy and unemployment during the Asian economic crisis have been reported to have a negative impact on mental health and may lead to an increase in suicide rates (7). Our amateur crypto investor, who works as an official in support of the publications listed here, committed suicide by jumping from a height in the face of a Bitcoin loss of approximately 50% within a week and died, although he was taken to the ER.

CONCLUSION

New economic instruments can attract people for investment purposes. Investment instruments such as cryptocurrency, which can experience rapid price increases and losses, can cause people to commit suicide because of financial losses. It is believed that developing strategies to protect the mental health of investors will become increasingly important.

Limitation

The limited information about how much money this case lost is a limiting factor.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Informed Consent: Written consent was obtained from the his parents.

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Review Article

Gastroesophageal Reflux Disease During Pregnancy

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Abstract
Gastroesophageal reflux is the most common gastrointestinal symptom in pregnancy. Although it is normal for pregnant women to have it during pregnancy, there is treatment and it can be prevented. Reflux that reaches a maximum of 60 minutes during the day is called physiological reflux, which is defined. Its frequency is up to 80% in some studies during pregnancy. Reflux symptoms include epigastric burning sensation, bitter water in the throat, and nausea are available. Endoscopy is generally needed in the diagnosis of reflux symptoms during pregnancy, which does not happen. In the treatment, lifestyle changes are used in the majority of patients, and it works. Elevating the head of the bed, avoiding acidic spicy foods stopping, frequent and less food consumption are recommended. In cases where lifestyle changes do not work, medical agents are used. Our aim in this review is to examine gastroesophageal reflux disease in pregnancy.

Keywords: Pregnancy, gastroesophageal reflux, heartburn

CITATION
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INTRODUCTION

The regurgitation of the gastric content, mainly consists of acid, to the esophagus, is defined as Gastroesophageal reflux (GER) (1). Physiological reflux is short-term reflux, which can reach a maximum of 60 minutes during the day. Reflux esophagitis occurs if physiological reflux is accompanied by histological differences. This is a rare condition. Pregnancy reflux is described as reflux that arises for the first time during pregnancy (2). When the literature data was examined, it was found that GER was present in 30% to 50% of all pregnancies presenting with epigastric burning3,4. However, in a 2003 report published by Richter and colleagues, the prevalence of GER was shown to be 80% throughout pregnancy (5). The unavailability of a standard diagnostic criteria accepted worldwide is to blame for the discrepancy between the studies (6).

The clinical manifestation of GER typically begins in the first trimester and continues until the third trimester. The majority of them are not seen following the postpartum period (7).

Symptoms

There is no difference in GER symptoms between pregnant and non-pregnant women. The disease involves symptoms such as epigastric burning sensation, bitter or sour liquid in the throat, nausea, vomiting, nutritional disorders, and periodontal diseases. In certain pregnant women, these may even be mistaken with symptoms of laryngitis or asthma. Some pregnant women may have sleep issues as a result of burning sensations (8). Among all these symptoms, the most common symptom is the epigastric burning sensation.

Etiopathogenesis

It has been suggested that more than one factor may have a role in the development of GER during pregnancy. Some studies attribute the reason to a decrease in lower esophageal pressure (LES), while others attribute it to insufficient lower esophageal sphincter pressure against increasing intra-abdominal pressure (9,10). Furthermore, although the specific reason is unclear, it is suspected that GER arises as a result of elevated gastrin during pregnancy (11).

Hormonal changes during pregnancy have been blamed for low LES pressure in pregnant women. Estrogen and progesterone are considered to be particularly responsible for increasing serum concentration (12).

Risk Factors

GER disease risk factors

Consuming foods high in unsaturated fatty acids, as well as acidic and spicy foods (13-15)

Short period of time between meals and bedtime.

Increased waist circumference

Advanced gestational week (16)

Multiparity

Body mass index before pregnancy

Weight gained during pregnancy

Race

Adolescent pregnancy (17)

Diagnosis

Anamnesis is usually sufficient to diagnose GER. Due to the risk of radiation exposure, barium X-ray examinations are not recommended for diagnosing GER during pregnancy. Although it is mentioned that it is not essential, esophageal manometry and pH measurements are proven to be safe during pregnancy. Endoscopy and biopsy are, nevertheless, recommended in cases wherein complications are suspected (18). Mahadevan has demonstrated that endoscopy is safe to utilize during pregnancy (19). If an endoscopy is required during pregnancy, it should be avoided as much as possible during the first trimester. Pregnancy category C drugs such as meperidine and fentanyl can be used for sedation during endoscopy. It has been reported that midazolam and diazepam, both are group D medications, can be used during pregnancy. If conscious sedation is insufficient, propofol, a group B medication, can be used to induce profound sedation (20).

Therapy

The aim of GER therapy is to alleviate symptoms and avoid consequences. The pregnant woman's lifestyle changes becomes important in primary care therapy. Raising the head of the bed, avoiding foods like chocolate, spices, and acids in meal choices, eating less frequently, limiting the quantity of meal if possible, selecting for steeper pillows while lying down, and quitting smoking should be among these (21,22). Acupuncture and placebo comparisons have also revealed that there are no negative effects of using acupuncture and that it improves the patient's GER symptoms (23,24).

The utilization of pharmacological agents is increased in second-line therapy. The usage of antiacid or alginic acid should be prioritized. It is suggested that pregnant women use these medications only when symptoms arise, rather than on a regular basis (25,26). Furthermore, no fetal abnormalities induced by the use of these medications has been identified in the research available in the literature (27,28).

In 2003, a European council stated that calcium-based antiacids had a lower risk of hypertension and preeclampsia (29). Furthermore, no maternal or neonatal negative effects were seen in the short term (30). However, milk alkali syndrome has been related to the consumption of more than 1.4 grams of calcium when using calcium-containing products. It is also stated that the usage of bicarbonate-containing products may result in fetal or maternal metabolic acidosis (16,31,32). When using magnesium-containing goods, fetal hypotonisite, kidney stones, respiratory depression, and cardiovascular issues may develop (29,33). In light of all of this data, it is stated that it is safe to use calcium and magnesium-containing antiacids during pregnancy, that it is necessary to avoid long-term high dose use of magnesium-containing products, and that the use of sodium bicarbonate-containing antiacids is not safe during pregnancy (34).

Metoclopramide reduces GER by enhancing gastric discharge and improving acid clearance in the esophagus. Its usage during pregnancy is intended to alleviate nausea and vomiting by inhibiting the medullar chemoreceptor region. Furthermore, when the literature is examined, there are no neonatal complications associated with metoclopramide (35,36).

Cisapride, which is known for its resemblance with metoclopramide, functions by enhancing acetylcholine release. Until 2000, it was used to prevent GER during pregnancy. However, it is no longer administered since it induces cardiac arrhythmia.

Although FDA permission for usage in pregnancy is still in place, Domperidon, which functions via peripheral antidopaminergic blockage before the blood-brain barrier, is known to produce significant cardiac adverse effects (37,38).

In cases where antiacid medication fails, the use of H-2 receptor blockers is recommended. Several research on the use of H-2 receptor blockers during pregnancy found no increase in fetal anomalies. However, some studies have found that using simetidine raises the risk of embryonic heart abnormalities marginally (39-41). The majority of physicians who are concerned about the use of H-2 blockers consider that simetidine may be administered safely during pregnancy. Other H-2 blockers, such as nizatidine, famoditin, and ranitidine, can also be used safely during pregnancy (42).

It has been reported that medications that function by suppressing gastric acid secretion, such as omeprazole, lansoprazole, pantherorazole, and rhabeprazole, can be administered safely in pregnant women in cases when H-2 blocker treatment is not beneficial. Proton pump inhibitors(PPI) are medications that lower acidity in the stomach by blocking the enzyme H,K-ATP. The studies found no increase in the risk of fetal anomaly (43). It has been found that their use during pregnancy does not raise the risk of fetal abnormalities and these medications are among the safest and most effective medications (44). No side effects are expected during their use. Furthermore, no increase in the likelihood of adverse effects or abnormalities is anticipated with long-term treatment (42). However, it has been observed that

PPI administration during pregnancy may increase the risk of allergies and asthma in children. The cause for this issue is that the fetus becomes more sensitive to allergens with the passage of maternal immunoglobulin E through the placenta and develops a phenotype that is more prone to allergies owing to the mother's cytokines (39).

Complications

There are normally no complications associated with GER during pregnancy, however esophagitis or stricture may occur on rare occasions (42).

A research of 405,586 pregnant women published in Korea in 2021 demonstrated that the presence of GER increased the risk of preterm delivery (43). Another study, conducted in Vietnam and published in 2021, reported that sleeplessness was more likely among GER illness patients who had a short time to go to bed after eating (44).

CONCLUSION

GER is very common during pregnancy. However, for the vast majority of patients, a lifestyle adjustment prior to pharmacological treatment prevents the symptoms.

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