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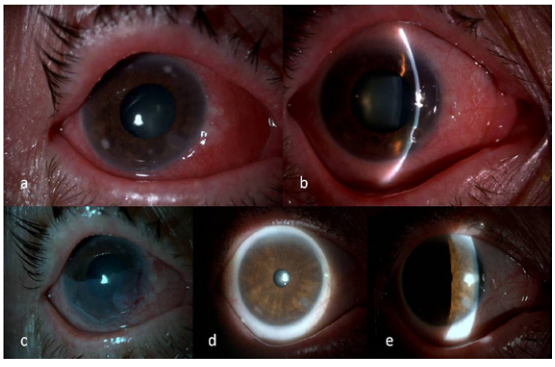

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Thiol disulfide homeostasis as oxidative stress marker in migraine patients

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ABSTRACT

Migraine is a very common disease. Annual prevalence of migraine in our country is reported as 16.4%. Oxidative stress is assumed to play a role in the pathophysiology of migraine. In many recent studies conducted on individuals with migraine, serum Oxidative Stress Index (OSI), Total Antioxidant Status (TAS), Total Oxidant Status (TOS) values were analyzed and it was indicated that the balance shifts towards oxidative direction. Thiol-disulfide homeostasis, which is an oxidative stress marker, was described in recent years and has been shown to have vital importance on cellular functions. In the light of this information, we aimed to examine the role of oxidative stress in pathogenesis of migraine disease with new biomarkers. The study was conducted on 36 cases of 24 patients (17 female, 7 male; mean age: 40.54±11.60) followed up with a migraine diagnosis and 12 people in the healthy control group with similar age and sex (10 female, 2 male; mean age: 38.17±10.80). Total thiol (μmol/L), native thiol (μmol/L) and disulfide level, disulfide/native thiol, disulfide/total thiol, native thiol/total thiol ratios were quantified in the patient and control groups. In the migraine group with aura, reduced ratio and thiol oxidation reduction ratio values were high and oxidized thiol ratio values were low (p = 0.010, 0.015, 0.048). This study focused on thiol-disulfide hemostasis, a new and reliable indicator in determining oxidative stress which is held responsible for the pathophysiology of migraine.

1. Introduction

Migraine is a very common disease characterized by moderate-severe throbbing headache attacks accompanied by nausea and/or vomiting, photophobia and phonophobia (Stewart et al., 1992; IHS, 2013). It is usually unilateral and its symptoms get worse with physical activity. One-year prevalence rate of migraine among adults in our country is reported as 16.4% (Ertas et al., 2012).

Oxidative stress is defined as the damage caused by reactive oxygen types (hydroxyl radical, superoxide radical and hydrogen peroxide) on organic molecules and cells (Blokhina et al., 2003; Valko et al., 2007). Oxidant–antioxidant balance disorders underlie several types of acute and chronic diseases of the central nervous system. It is believed that oxidative stress plays a role in the pathogenesis of migraine (Eren et al., 2015). In many recent studies conducted on individuals with migraine, serum Oxidative Stress Index (OSI), Total Antioxidant Status (TAS), Total Oxidant Status (TOS) values are analyzed and the results indicate that balance shifts towards oxidative direction (Alp et al., 2010; Oz et al., 2010; Yılmaz et al., 2011a; 2011b).

Thiols are a class of organic compounds known as mercaptans containing sulfhydryl (-SH) group, which has a critical role in preventing the development of any oxidative stress condition in cells (Tuncel et al., 2008). They eliminate reactive oxygen species (ROS) and other free radicals by enzymatic and non-enzymatic mechanisms and are an important component of the antioxidant cascade (Sen et al., 2000). When oxidative protein damage occurs, protein carbonyl levels increase, while protein thiol levels decrease (Caderas, 1989). It is important to measure total thiol levels in order to evaluate the excessive formation of free radicals (Hu, 1994).

Thiols cause formation of disulfide forms by oxidative reacting through oxidants. When oxidative stress increases, mixed disulfides are formed between thiols and protein thiol groups, however this formation is reversible. Dynamic thiol/disulfide homeostasis plays a role in cell signal mechanisms, transcription factors, enzymatic activation regulation, apoptosis and signal transmission, antioxidant protection and detoxification (Pasaoglu et al., 2004; Kayacan et al., 2018).

Thiol-disulfide homeostasis is identified as an oxidative stress marker in recent years and shown to have vital importance on cellular functions (Jones et al., 2009). Thiol is a term used for compounds containing sulfur, and the sulfur in its content is a very significant element for biological environments as it is also contained in amino acids, proteins and other biomolecules (Atmaca, 2004). According to a study conducted on healthy individuals, thiol protein groups constitute 52.9% of total antioxidant capacity in serum (Erel, 2004). Thiols, known as strong antioxidants, modulate glutathione-related antioxidant enzymes and remove free radicals from the environment (Atmaca, 2004; Eren et al., 2015). Studies report that dynamic thiol-disulfide homeostasis is associated with antioxidant protection, detoxification (Biswas et al., 2006), apoptosis (Circu et al., 2010), regulation of enzymatic activity and cellular signal mechanisms in the organism (Erel et al., 2014), as well as many diseases such as diabetes (Matteucci et al., 2010), chronic kidney disease, liver disorders (Rodrigues et al., 2012), cardiovascular diseases (Kundi et al., 2015) and stroke (Bektas et al., 2016).

In the light of this information, we aimed to investigate thiol disulfide hemostasis as a new marker for oxidative stress, which is assumed to be involved in the pathophysiology of migraine.

2. Materials and methods

Patient selection

The study was conducted on 36 cases of 24 patients (17 female, 7 male; mean age: 40.54±11.60) followed up with migraine diagnosis and 12 people in the healthy control group with similar age and sex (10 female, 2 male; mean age: 38.17±10.80). Patients with malignancy and systemic diseases, smokers, pregnant and lactating women, and patients who took any medication in the last 15 days were not included in the study.

Demographic characteristics of the patients were collected. Migraine patients were evaluated based on whether they had auras or not, whether they were in the ictal or interictal period, number of painful days per month, number of attacks per month and their life quality with EQ5D (with activity, self-care, ordinary, pain, anxiety, index and EQ5D VAS sub-groups).

Ethical committee approval of the study was obtained from Sakarya University Faculty of Medicine Ethical Committee. Informed consent was taken from the patients and control groups. All researchers hereby confirm the ethical standards of the Helsinki Declaration.

Blood samples

In pre-analytic period

In order to ensure that the samples in the tubes are in good contact with silica particles, the tubes were gently turned upside down 5-6 times and were never shaken.

Biochemical parameters

Blood serum analyses were performed by a fully automated Beckman Coulter AU 680 (serial no: 2016024580, Koutou-ku, Tokyo, Made in Japan) auto-analyzer. Rel Assay Diagnostics brand kit was used in the study. Samples were subjected to re-centrifuge (micro centrifuge) process as instructed in the kit insert. Total thiol (μmol/L) and native thiol (μmol/L) measurements in serums and the total measurements of thiols were recorded, and thiol/disulfide balance was determined.

Total thiol level (μmol/L) (TTL), native thiol level (μmol/L) (NTL) and disulfide level, disulfide/native thiol, disulfide/total thiol, native thiol/total thiol ratios were determined for the patient and the control groups. In this study, dynamic thiol-disulphide homeostasis in the serum samples was identified by an automated method recently developed by Erel et al. (2014). Total thiol (–SH+–S–S–) and native thiol (–SH) concentrations in the samples were measured by using Ellmann's and modified Ellmann's reagent. Native thiol content value was subtracted from the total thiol content value, and half of this difference gave the amount of dynamic disulphide bonds (–S–S). In addition, the (–S–S–) x 100 / (–SH), (–S–S–) x 100 / (–SH+–S–S–), and –SH x 100 / (–SH+–S–S–) ratios were calculated by using these parameters.

Analytical recovery

The percent recovery of the novel method was determined by adding 200 μM oxidized glutathione to the plasma samples. The mean percent recovery was 98–101%.

Linearity

The linearity of the native thiol measurement was the same as that of Ellman's reagent assay. Serial dilutions of the glutathione solution were prepared. The upper limit of

the linearity for the native thiol measurement was 4000 µM. Linearity of the total thiol measurement was also dependent on the amounts of $NaBH_4$ and formaldehyde concentrations. Serial dilutions of the oxidized glutathione solution were also prepared. The upper limit of the linearity for the disulphide measurement was 2000 µM. Dilution of plasma samples did not affect the novel assay.

Lower detection limit

The detection limit of the assay was determined by evaluating the zero calibrator 10 times. The detection limit, defined as the mean value of the zero calibrator + 3 standard deviations (SDs), was 2.8 µM (X).

Analytical sensitivity

As the slope of the calibration line, analytical sensitivity was found to be 7.9 × 10–4 Absorbance/Amount, [A × (µM)–1].

Interference

It was found that hemoglobin, EDTA, citrate and oxalate did not interfere with the assay, but bilirubin negatively interfered with the assay. Lipemic and uremic plasma samples did not interfere with the assay. Plasma and serum samples were used as samples.

Precision

To determine the precision of the novel assay, we assayed three levels of plasma pools. The plasma pool with high disulphide levels was obtained from the samples of patients with diabetes mellitus. The plasma pool with medium disulphide levels was obtained from the samples of healthy persons. The plasma pool with low disulphide levels was obtained from the samples of patients with urinary bladder cancer. Percent coefficient variation (%CV) was 4 ($\bar{X}$= 29.12 and σX=1.2) for high levels, 5 ($\bar{X}$= 16.03 and σX = 0.79) for medium levels and 13 ($\bar{X}$= 7.15 and σX = 0.98) for low levels.

Storage

Storage at 4°C for 1 day led to a 7% decrease in the native thiol amount and 170% increase in the disulphide amount (total thiol, native thiol and disulphide levels of fresh and stored plasma samples were 391 µmol/L, 357 µmol/L, 17 µmol/L and 391 µmol/L, 333 µmol/L, 29 µmol/L, respectively). Plasma native thiol, total thiol and disulphide concentrations were not affected by storage at –80°C for 3 months.

Statistical analysis

NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) was used for statistical analyses. Descriptive statistical methods (mean, standard deviation, median, frequency, and ratio) as well as Shapiro Wilks test and box plot graphs were used for the evaluation of the suitability of variables to normal distribution. Kruskal Wallis test was used for intergroup comparisons of parameters which do not indicate normal distribution, Dunn test was used for post-hoc evaluations, Mann Whitney U test was used for evaluations based on groups. Fisher's Exact test and Fisher-Freeman Halton test was used for comparison of qualitative data. Results were evaluated to be within a confidence range of 95% and a significance level of $p<0.05$.

3. Results

Demographic characteristics of cases are given in Table 1. Aura was observed in 50% (n=12) of migraine cases. With regards to the number of painful days per month, the ratio of cases with 1-5 days/month was 16.7% (n=4), 5-15 days/month was 54.2% (n=13), over 15 days/month was 29.2 % (n=7). There were 5 patients (20.8%) who had 1-3 attacks per month and 19 patients (79.2%) who had 3 or more attacks per month (Table 2).

Table 1. Evaluation of demographic characteristics by groups (Migraine (with/out aura) and Control).

		Groups		Test values
		Migraine (n=24)	**Control (n=12)**	**P**
Age (year)	Min-Max (Median) Mean±SD	19-68 (40) 40.54±11.60	20-51 (40) 38.17±10.80	Z:-0.185 [d] ***0.853***
Sex	**Female** **Male**	17 (70.8) 7 (29.2)	10 (83.3) 2 (16.7)	χ^2:0.667 [c] ***0.685***
Height (meter)	Min-Max (Median) Mean±SD	1.5-1.8 (1.65) 1.65±0.09	1.5-1.8 (1.63) 1.62±0.08	Z:-0.774 [d] ***0.439***
Weight (kg)	Min-Max (Median) Mean±SD	42-120 (74) 74.50±19.66	45-94 (61) 66.17±15.20	Z:-1.226 [d] ***0.220***
BMI (kg/m²)	Min-Max (Median) Mean±SD	18.6-42.9 (26.2) 27.22±6.60	20.3-33.5 (23.17) 24.87±4.36	Z:-0.889 [d] ***0.374***
	Normal **Overweight** **Obese**	10 (41.7) 8 (33.3) 6 (25.0)	9 (75.0) 1 (8.3) 2 (16.7)	
Education	**Primary School** **High School** **University**	10 (41.7) 8 (33.3) 6 (25.0)	4 (33.3) 1 (8.3) 7 (58.3)	χ^2:4.303 [b] ***0.113***
Exercise	**No** **Regular** **Irregular**	12 (50.0) 7 (29.2) 5 (20.8)	3 (25.0) 2 (16.7) 7 (58.3)	χ^2:4.664 [b] ***0.122***
Chronic Disease	**No** **Yes**	21 (87.5) 3 (12.5)	12 (100.0) 0 (0.0)	χ^2:1.636 [c] ***0.536***
Menstruation Age (n=26)	Min-Max (Median) Mean±SD	11-16 (13) 13.06±1.39	12-15 (12.5) 13.00±1.25	Z:-0.274 [d] ***0.784***
OCD (n=26)	**Yes** **No**	3 (18.8) 13 (81.3)	1 (10.0) 9 (90.0)	χ^2:0.362 [b] ***1.000***

[b] Fisher Freeman Halton Test [c] Fisher's Exact Test [d] Mann Whitney U Test
OCD: Oral Contraceptive Drug

Table 2. Clinical features of migraine patients.

Aura	**No**	12 (50.0)
	Yes	12 (50.0)
Frequency of aura (day per month)	**1-5**	4 (16.7)
	5-15	13 (54.2)
	≥15	7 (29.2)
Number of attacks (day per month)	**1-3**	5 (20.8)
	≥3	19 (79.2)

In the comparative evaluation of the control group, and the migraine groups with and without aura, no statistically significant difference was found based on the groups in EQ-5D scale "Activity", "Self-Care" and "Ordinary" sub-dimensions (p>0.05). A statistically significant difference was found in the "pain" sub-dimension (p=0.025; p<0.05). Incidence of pain was significantly higher in cases of migraine with and without aura, compared to cases of the control group (p=0.027; p=0.030; p<0.05). In "Anxiety/Depression" sub-dimension of EQ-5D scale, a statistically significant difference was found for the incidence of anxiety/depression (p=0.006; p<0.05). The rate of anxiety/depression incidence in migraine with aura group was significantly higher compared to the control group (p=0.004; p<0.01). A statistically significant difference was found between the EQ-5D index measurements (p=0.004; p<0.01). According to the paired comparison results conducted to determine the difference; EQ-5D index values of migraine groups with and without aura were found significantly lower compared to the cases of the control group (p=0.010; p=0.001; p<0.05) (Table 3).

A statistically significant difference was found between EQ-5D VAS measurements of cases based on groups (p=0.006; p<0.01). According to the paired comparison results conducted to determine the difference; EQ-5D VAS value of migraine group with aura was found significantly lower, compared to the cases of migraine group without aura and control group (p=0.019; p=0.005; p<0.05) (Fig.1).

In Table 4, TTL, NTL, Disulfide, Reduced ratio, oxidized thiol ratio and thiol oxidation reduction ratio values are shown in accordance with the groups.

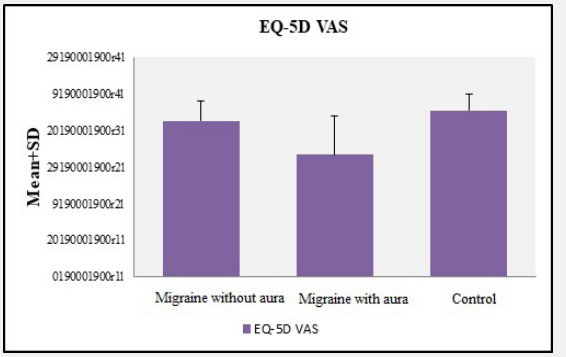

Fig. 1. Distribution of EQ-5D VAS measurements by groups (Migraine with aura, Migraine without aura and Control).

A statistically significant difference was found between the Reduced Ratio measurements of the cases based on groups (p=0.027; p<0.05). Reduced Ratio values of cases in the migraine group with aura were statistically higher than cases in the migraine group without aura (p=0.010; p<0.05). A statistically significant difference was found between Oxidized Thiol Ratio measurements of the cases based on groups (p=0.036; p<0.05). Oxidized Thiol Ratio values of the cases in the migraine group with aura were statistically lower than the cases in the migraine group without aura (p=0.015; p<0.05) (Fig. 2). A statistically significant difference was found between Thiol Oxidation Reduction Ratio measurements of the cases based on the groups (p=0.048; p<0.05). Thiol Oxidation Reduction Ratio values of the cases in the migraine group with aura were statistically higher than the cases in the migraine group without aura (p=0.021; p<0.05) (Fig. 3).

Table 3. Evaluation of EQ-5D scale according to groups (Migraine with aura, Migraine without aura and Control).

EQ-5D		Groups			Test Value	Test Value	Test Value	Test Value
		Without aura[1]	With aura[2]	Control[3]	*p*	p^{1-2}	p^{1-3}	p^{2-3}
Mobility	**No problem in walking**	10 (83.3)	10 (83.3)	12 (100.0)	χ^2:2.292	χ^2:0.000	χ^2:2.182	χ^2:2.182
	Some problem in walking	2 (16.7)	2 (16.7)	0 (0.0)	[b]0.517	[c]1.000	[c]0.478	[c]0.478
Sef care	**No problem**	11 (91.7)	12 (100.0)	12 (100.0)	χ^2:1.874	χ^2:1,043	χ^2:1.043	-
	Some problem	1 (8.3)	0 (0.0)	0 (0.0)	[b]1.000	[c]1.000	[c]1.000	-
Usual activities	**No problem**	12 (100.0)	11 (91.7)	12 (100.0)	χ^2:1.874	χ^2:1.043	-	χ^2:1.043
	Unable	0 (0.0)	1 (8.3)	0 (0.0)	[b]1.000	[c]1.000	-	c1.000
Pain	**No**	5 (41.7)	5 (41.7)	11 (91.7)	χ^2:9.777	χ^2:1.074	χ^2:6.750	χ^2:6.521
	Moderate	7 (58.3)	6 (50.0)	1 (8.3)	[b]0.025*	[b]1.000	[c]0.027*	[b]0.030*
	Extreme	0 (0.0)	1 (8.3)	0 (0.0)				
Anxiety/ Depression	**No**	6 (50.0)	3 (25.0)	11 (91.7)	χ^2:12.169	χ^2:2.683	χ^2:5.042	χ^2:10.531
	Moderate	6 (50.0)	7 (58.3)	1 (8.3)	[b]0.006**	[b]0.240	[c]0.069	[b]0.004**
	Extreme	0 (0.0)	2 (16.7)	0 (0.0)				
EQ-5D index	**Min-Max (Median)**	0.59-1 (0.66)	0.18-1 (0.66)	0.66-1 (1)	χ^2:11.190	Z:-1.089	Z:-2.573	Z:-3.208
	Mean±SD	0.79±0.19	0.65±0.27	0.97±0.10	[a]0.004**	[d]0.276	[d]0.010*	[d]0.001**
EQ-5D VAS (Health state)	**Min-Max (Median)**	60-100 (85)	30-100 (65)	70-100 (90)	χ^2:10.402	Z:-2.353	Z:-1.493	Z:-2.823
	Mean±SD	85.00±10.87	66.67±21.03	90.83±9.00	[a]0.006**	[d]0.019*	[d]0.135	[d]0.005**

[a]Kruskal Wallis Test [b]Fisher Freeman Halton Test [c]Fisher's Exact Test [d]Mann Whitney U Test *p<0.05 **p<0.01

Table 4. Evaluation of thiol variables according to groups (Migraine with aura, Migraine without aura and Control).

			Groups			Test Value	Test Value	Test Value	Test Value
			Without aura[1] (n=12)	With aura[2] (n=12)	Control[3] (n=12)	*p*	p^{1-2}	p^{1-3}	p^{2-3}
Thiol Values	TTL	Min-Max (Median) Mean±SD	1107-1671 (1335) 1372.67±193.86	938-1644 (1383) 1353.08±174.31	1133-1608 (1393) 1412.67±124.91	χ^2:0.582 [a]0.748	Z:-0.144 [d]0.885	Z:-0.665 [d]0.506	Z:-0.635 [d]0.525
	NTL	Min-Max (Median) Mean±SD	470-633 (516.5) 536.17±63.56	376-601 (512) 499.33±70.31	439-685 (528) 540.5±69.51	χ2:1.613 [a]0.446	Z:-0.983 [d]0.326	Z:-0.144 [d]0.885	Z:-1.185 [d]0.236
	Disulfide	Min-Max (Median) Mean±SD	318.5-522 (41.25) 416.83±64.87	281-521.5 (438.75) 421.18±68.2	347-487.5 (440) 435.5±35.76	χ^2:0.785 [a]0.675	Z:-0.433 [d]0.665	Z:-0.954 [d]0.340	Z:-0.289 [d]0.773
	Reduced Ratio	Min-Max (Median) Mean±SD	37.19-42.46 (39.56) 39.S44±1.79	34.5-41.6 (37.15) 37.62±1.83	34.5-44.08 (38,18) 38.2±2.36	χ^2:7,238 [a]0.027*	Z:-2,570 d0.010*	Z:-1,905 [d]0.057	Z:-0,693 [d]0.488
	Oxidized Thiol Ratio	Min-Max (Median) Mean±SD	28.77-31.41 (30.22) 30.3±0.89	29.96-32.75 (31.37) 31.2±0.79	27.96-32.75 (30.91) 30.9±1.18	χ^2:6.650 [a]0.036*	Z:-2.425 [d]0.015*	Z:-1.905 [d]0.057	Z:-0.577 [d]0.564
	Thiol Oxidation Reduction Ratio	Min-Max (Median) Mean±SD	105.33-147.57 (129.22) 128.16±12.19	105.33-133.81 (117.59) 118.75±6.93	105.33-157.65 (123.53) 124.02±12.97	χ^2:5.384 [a]0.048*	Z:-2.309 [d]0.021*	Z:-1.270 [d]0.204	Z:-1.011 [d]0.312

[a]Kruskal Wallis Test [d]Mann Whitney U Test *p<0.05 TTL: Total Thiol Level NTL: Native Thiol Level

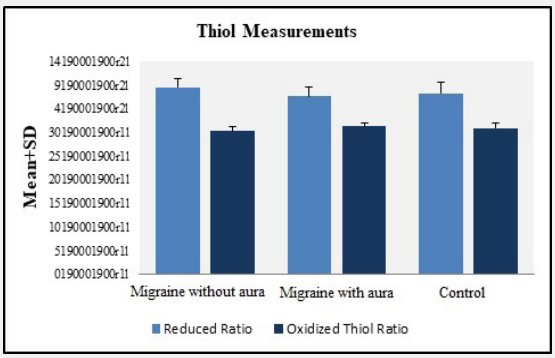

Fig. 2. Distribution of reduced ratio and oxidized thiol ratio measurements according to groups (Migraine with aura, Migraine without aura and Control).

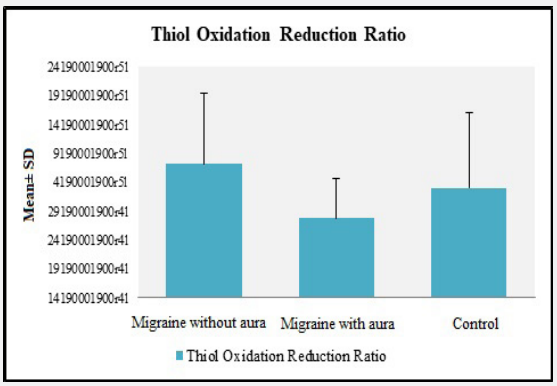

Fig. 3. Distribution of thiol oxidation reduction ratio measurements according to groups (Migraine with aura, Migraine without aura and Control).

Based on ictal or interictal period of the migraine patients and when compared with the control group, no statistically significant difference was found between TTL, NTL, disulfide, reduced ratio, oxidized thiol ratio and thiol oxidation reduction ratio values (p>0.05) (Table 5).

Table 5. Evaluation of melatonin and thiol variables by groups (Interictal, Ictal and Control).

			Groups			Test value
			Interictal (n=18)	Ictal (n=6)	Control (n=12)	p
Thiol Values	TTL	Min-Max (Median) Mean±SD	938-1671 (1382) 1344.22±175.7	1224-1671 (1391.5) 1418.83±200.02	1133-1608 (1393) 1412.67±124.91	χ^2:1.060 [a]0.589
	NTL	Min-Max (Median) Mean±SD	376-631 (512) 511.44±55.97	376-633 (545.5) 536.67±100.83	439-685 (528) 540.5±69.51	χ^2:1.460 [a]0.482
	Disulfide	Min-Max (Median) Mean±SD	281-521.5 (433) 416.39±62.23	318.5-522 (432.25) 426.87±79.05	347-487.5 (440) 435.5±35.76	χ^2:0.853 [a]0.653
	Reduced Ratio	Min-Max (Median) Mean±SD	34.5-42.46 (37.62) 38.19±1.88	37.15-42.46 (39.29) 39.55±2.19	34.5-44.08 (38,18) 38.2±2.36	χ^2:2.329 [a]0.312
	Oxidized Thiol Ratio	Min-Max (Median) Mean±SD	28.77-32.75 (31.19) 30.9±0.94	28.77-31.24 (30.47) 30.28±0.87	27.96-32.75 (30.91) 30.9±1.18	χ^2:2.678 [a]0.262
	Thiol Oxidation Reduction Ratio	Min-Max (Median) Mean±SD	105.33-147.57 (120.61) 123.87±9.95	105.33-147.57 (120.16) 122.22±14.12	105.33-157.65 (123.53) 124.02±12.97	χ^2:0.317 [a]0.853

[a]Kruskal Wallis Test

4. Discussion

It is believed that migraine pathophysiology is related to primary neuronal mechanisms. Under the light of the data presented in recent years, it is suggested that migraine is a neurovascular disease caused by cortically spreading depression, neurogenic inflammation and vasodilatation (Boran et al., 2013; Noseda et al., 2013). Additionally, oxidant-antioxidant balance disorders and resulting oxidative stress is believed to play a role in pathogenesis in migraine as well as many central nervous system diseases (such as epilepsy, stroke, neurodegenerative diseases) (Bockwski et al., 2008; Gruber et al., 2010; Tetik et al., 2010; Méndez-Armenta et al., 2014; Oz et al., 2014; Sharma et al., 2014; Kurt et al., 2017).

In a study, TOS levels of individuals with migraine with aura were found to be higher, while their TAS levels were found to be lower; this data suggested that oxidative/antioxidative balance of individuals with migraine shifted to oxidative direction (Alp et al., 2010). It was suggested that oxidative stress in migraine is related to increased nitric oxide levels (Bockwski et al., 2008). Nitric oxide (NO) causes trigeminovascular activation that plays a role in cerebral vasodilatation at the onset of migraine attacks (Lance, 1993). It is assumed that delayed inflammatory response at durometer, inducible nitric oxide synthase (iNOS) expression, and increase of proinflammatory cytokines such as IL-1 and IL-6 have a role in the pathophysiological mechanism of this activation (Reuter et al., 2001). In a recent study, it was reported that the plasma asymmetric dimethylarginine (ADMA) and NO levels were higher in individuals with migraine compared to healthy groups (Uzar et al., 2011). In the study by Yılmaz et al. (2007), malonaldehyde (MDA), nitrate and nitrite levels among oxidative stress indicators were studied in the thrombocytes of 22 migraine patients without aura and 14 migraine patients with aura during their attack periods, and compared to 36 healthy control cases. The findings illustrated that MDA, nitrate and nitrite levels were higher in migraine patients during the attack periods, compared to the healthy control cases, while there was no difference outside the attack period (Yılmaz et al., 2007).

Tuncel et al. (2018) found that plasma MDA levels and similar superoxide dismutase (SOD) and catalase (CAT) activities were higher in migraine patients compared to the control group. In the study conducted by Erol et al. (2010), SOD, CAT, glutathione peroxidase (GSH-Px) activities known as antioxidants were measured in erythrocytes of children with migraine outside the attack periods. Compared with healthy control cases, SOD activity was found to be similar, while CAT and GSH-Px activities were lower. As the common result of all these studies, it can be suggested that there is a decrease in the activity of antioxidant mechanisms, a shift in the balance towards oxidative direction and development of an oxidative stress environment in individuals with migraine.

In our study, serum disulphide levels were found to be lower in migraine patients compared to the control group (Migraine without aura: 416.83±64.87; Migraine with aura: 421.18±68.2; Control: 435.5±35.76). This situation can be explained by the insufficient number of cases, as well as the studies conducted on antioxidant efficacy of exercise in the literature. While 75% of the patients exercised in our control group, the rate was 50% in the migraine group (Kayacan et al., 2019).

In a study that analyzed the oxidative/antioxidative balance in migraine patients, it was shown that the total thiol levels were low in migraine patients without aura and there was a negative correlation between thiol levels and duration of headache (Alp et al., 2010). In their study conducted on migraine patients, Eren et al. (2015) found that serum TTL in individuals with migraine were lower than those of the healthy control group, whereas TAS, TOS and OSI levels were similar. In the same study, thiol levels were found to be similar between the patients with migraine with and without aura (Eren et al., 2015). In a study conducted on 63 migraine patients, higher TTL and NTL were obtained in comparison to the healthy control group; and as thiols affect the physiological conditions of the organism and they are dynamic molecules in this case, it was concluded that these findings supported the idea that they act like pro-oxidant molecules (Gumusyayla et al., 2016). In our study, reduced ratio and thiol oxidation reduction ratio values were found to be higher and oxidized thiol ratio value was found to be lower in the migraine group with aura (p=0.010, 0.015, 0.048). With these values, we can come to a conclusion in favor of increase in TOS especially in the migraine group with aura, which supports the role of oxidation in pathophysiology of migraine.

This study focused on thiol-disulfide hemostasis, a new and reliable indicator in determining oxidative stress which is held responsible for the pathophysiology of migraine. The reduced ratio, oxidized thiol ratio and thiol oxidation reduction ratio values gave statistically significant results in favor of oxidation, especially in the migraine group with aura, and shed light on the literature. Further studies to be conducted with a larger number of patients will support the presence of oxidative stress in development of migraine.

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Can we use waist circumference in the first trimester to screen for gestational diabetes?

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ABSTRACT

Maternal obesity is known to be associated with a higher risk of gestational diabetes mellitus and ad-verse perinatal outcomes. The aim of this study was to investigate whether waist circumference meas-urement is an alternative screening test for gestational diabetes. This is a prospective cohort study at a single clinic at Ondokuz Mayıs University Hospital in Samsun, Turkey, between January 2011 and September 2012. All subjects with a singleton pregnancy were eligible for the study at 11–14 weeks' gestation. After statistical evaluation of the data we have found out that wider waist circumference measurements in the first trimester leads to an impaired 50 g oral glucose tolerance test in the second trimester. In the end waist circumference measurement is a cheap screening tool to foresee a high-risk population under threat of gestational diabetes.

1. Introduction

Maternal obesity is associated with more undesirable perinatal outcomes (Solomon et al., 1997). It is highly likely to cause gestational diabetes mellitus (Ehrenberg et al., 2004; Surkan et al., 2004). Pregnancy diabetes (GDM) occurs first during pregnancy and returns to normal after birth. In pregnancy diabetes, glucose tolerance and carbohydrate intolerance cannot be altered (Wong et al., 2001). The incidence of gestational diabetes is 2 to 9 percent in all pregnancies and is associated with many complications (Hoffman et al., 1998). The babies of mothers with gestational diabetes face certain health risks. These are bad mind performance, the possibility of developing obesity afterwards, and impaired glucose tolerance (Petitt et al., 1985; Silverman et al., 1995).

GDM creates more risk factors and possibilities for pregnancy. It is associated with many unwanted complications related to pregnancy. It is known to be associated with diabetes. These complications are vasculopathy, polyhydramnios, intrauterine growth

retardation and macro-somia. Other complications are pre-eclampsia, urinary and genital tract infections, polyhydram-nios and sudden intra-uterine death (Ng et al., 1990; Wong et al., 2001). The main purpose of screening tests, early diagnosis and blood tests in GDM is to prevent its harmful effects as soon as possible like macrosomy, all other concerned complications. Therefore, it is important to predict deficiencies such as impaired fasting glucose and impaired glucose tolerance in order to prohibit these probable complications during pregnancy (Pridjian et al., 2010). It is important to identify a simple screening test that can be performed in the first trimester and seek patients at risk for developing GDM. The aim of our study was to search for an alternating and basic way to detect GDM.

2. Material and methods

Pregnant women with singleton pregnancies participating antenatal clinic who were not known to be diabetic were included in this present study. We completed a prospective cohort study on 148 patients at a single clinic at Ondokuz Mayıs University Hospital in Samsun, Turkey, between January 2011 and September 2012. Total 148 pregnant women of 11±14 weeks of gestation were including to the present study. Patients with type 1 or type 2 diabetes or other disorders known to affect glucose metabolism prior to pregnancy, women with a positive history of alcohol or drug abuse during their current pregnancy, women older than 40 years of age, and women with a previous history of GDM were excluded. Patients with type 1 or type 2 diabetes prior to pregnancy, those alcohol users in their current pregnancy, women with a history of drug addiction, women more than 40 years old, and women previously known to have a history of diabetes were excluded from this study. All participants signed the informed consent form. The Hospital Ethics Committee approved this study according to the Helsinki Declaration. Waist circumference measurement was performed 11–14 with respect to the standard procedures of the Airlie conference. The measurement was made at the mid-distance between the iliac crest and the final rib edge after a normal expiration while standing.

Biochemical analysis

Participants were asked to fasting for 12 hours during the first three months of pregnancy (11-14 weeks of gestation). Pregnancy's haven't breakfast for this test. they did not eat the previous evening. Blood samples were taken from the antecubital vein the next day after fasting for one night at 08:00–09:00 hours. Plasma was separated immediately by centrifugation (2,000 rpm, 20 min, 4°C). Following centrifugation, plasma glucose concentrations were evaluated by the glucose oxidase method (YSI 2300-STAT; Yellow Springs Instrument, Yellow Springs, OH) immediately after blood was drawn. Plasma total triglyceride amounts using enzymatic hydrolysis, on a Multiparity Analyzer CX7 (Beckman Instruments, Fullerton, USA). Then glucose tolerance tests were scheduled. Blood glucose levels were also screened at 0 and 60 minutes after a 12-hour fasting. 50 g oral glucose tolerance test performed at 24–28 weeks of gestation as designated by the American Diabetes Association in 2016.

Statistical analysis

Statistical analyses were conducted using SPSS for Windows, version 21.0 (Chicago, IL). Data are expressed as mean ± standard deviation and median. Correlations between variables were analyzed by Spearman correlation. To verify the model's statistical significance, analysis of variance, F test, was performed and the model was considered to be statistically significant with a p value of $p<0.05$, variables added to the model were also found to be statistically significant ($p<0.05$, t test). Model is found to be 54% explanatory. Waist girth and triglyceride concentrations of the participants were measured. The waist girth cut point of 85 cm was chosen based on the definition of the hyper triglyceridemic waist. Triglyceride concentrations cut point of was 200 mg/dl.

3. Results

The mean age, waist circumference and body mass index of the patients were 28.4, 87.7, and 24.9, respectively. The characteristics of the 148 participants included in the study are shown in Table 1. After statistical evaluation of the data, we have found out that there is positive correlation between glucose and triglycerides (R:0.567; $p<0.05$) and positive correlation between glucose and waist circumference (R:0.465; $p<0.05$) which shows us that wider waist circumference measurements in the first trimester leads to an impaired 50 g oral glucose tolerance test in the second trimester. The difference between each 2 variables was significant. We also found correlation between triglyceride and waist circumference. Likewise, increased triglycerides also impair glucose tolerance and as an added note. We have also observed a positive correlation between increased waist circumference and BMI (R:0.411; $p< 0.05$). Table 2 shows the correlations between these variables.

Table 1. Characteristics of patients (n:148).

	Mean (SD)	Median (range)
Age, (years)	28.4 (3.8)	28.1 (20–37)
Waist circumference, (cm)	87.7 (13.6)	86.3 (69–152)
Body mass index, (kg/m2)	24.9 (4.8)	23.9 (16.7–42.2)
Total triglycerides, (mg/dl)	102.6 (46.9)	97.3 (35.3-265.4)
***Glucose (mg/dl)**	127 (50.89)	126 (70-182)

* Plasma glucose concentrations were also measured at 60 minutes after a 12-hour fasting 50-g oral glucose tolerance test.

Table 2. Correlations.

	Waist circumference (cm) *r P value	Glucose (mg/dl)	Total triglycerides (mg/dl)
Age (years)	r:0.396 p:0.700	r:-0.018 p:0.839	r:0.465 p:0.765
Total triglycerides (mg/dl)	r:0.417 p:0.000	r:0.567 p:0.000	
Glucose (mg/dl)	r:0.465 p:0.000		
BMI (kg/m²)	r:0.411 p:0000		

*r: Correlation coefficient

4. Discussion

GDM is one of the most important health problems. Pregnancy diabetes (GDM) represents a growing and urgent public health problem. It is the most common pregnancy complication affecting 7-17% of pregnancies worldwide. It may cause unwanted results in terms of mother and baby. These results can be seen in short or long term.

In addition, GDM is conventionally screened and diagnosed at the beginning of the third trimester. This situation increases the need for early detection of high-risk women for GDM (Guariguata et al., 2014; Zhu et al., 2016). Impaired glucose tolerance and fasting glucose can be classified as a metabolic disorder that exists between glucose tolerance and diabetes. Together, both are considered risk factors for the development of cardiovascular disease and diabetes. This risk factor, as written in the literature, can cause diabetes in life. The patient may have to live with diabetes (Giugliano et al., 2016).

Several attempts have been made to find an early screening test to facilitate the diagnosis of gestational diabetes and to make an early diagnosis. However, it has not yet identified a practical method for performing an easily accessible screening for the diagnosis of gestational diabetes in a very short time. Current studies show that positive and negative predictive values for first trimester fasting glucose and insulin have been determined for the detection of diabetes in the next pregnancy. Studies have been continuing on this subject (Riskin et al., 2009; Hao et al., 2017).

Most of these studies have been performed among women at risk for pregnancy diabetes. However, these screening tests and studies should be performed in women population with different risk factors for gestational diabetes and repeated. Aside from pregnancy, a person with normal fasting glucose should be informed about glucose intolerance or diabetes criteria during an oral glucose tolerance test. Moreover, there is no specificity of the instruments used to measure adipose tissue. There are several differences between the studies performed about this subject (Gur et al., 2014; Shinar et al., 2019).

A present study in the literature showed that abdominal visceral adiposity, especially in pregnant women, is associated with the risk of developing gestational diabetes in early pregnancy (De Souza et al., 2014). In addition to ultrasonography, there are various tools for measuring adipose tissue. Ever Since 1990, Nowadays, computed tomography is accepted as one of the gold standard methods used to measure the thickness of adipose tissue. Riberio et al. evaluated computed tomography as a better option to measure adipose tissue rather than ultrasonography (Ribero, 2003). Then, both ultrasound and computed tomography compared to assess visceral obesity in a non-pregnant population to predict cardiovascular risk ingratiation's associated with abdominal obesity. Martin et al. reported that ultrasonographic measurement of abdominal adipose tissue thickness in 64 pregnant women in the first trimester was associated with obesity in early pregnancy and impaired glucose tolerance in subsequent pregnancies (Martin, 2009). Unlike our study, Soo Lim et al. utilized computerized tomography (CT) to compare insulin sensitivity in women with past GDM history and measure visceral adipose tissue (Lim et al., 2007). In our work group, we preferred a different approach rather than these two methods. We utilized Airlie conference standardized procedures to evaluate the waist circumference, using an extremely basic and inexpensive measure method. Similar to our results, in their study , Lemieux et al. stated that the waist circumference is a simple feasible screening method to foresee high-risk population under atherogenic risk factors such as smoking, hypertension, hypercholesterolemia, diabetes mellitus, hyperlipidemia, hyperinsulinemia and previously coronary heart disease (Lemieux et al., 2000). Contrary to our study, in predicting GDM, Pontual et al. did not find waist circumference better than pre-pregnancy BMI measurement (Pontual et al., 2016).

In our study, we have found out that there is positive correlation between glucose andtriglycerides and positive correlation between glucose and waist circumference. We have also observed that increased waist circumference and triglyceride measurements in the first trimester increases 50 g glucose intolerance in later pregnancy. Our findings were in similar range with (Martin et al., 2009; Brisson et al., 2010; Lemieux et al., 2010).

In present study, we observed that the presence of raised waist circumference and hyper-triglyceridemia in the first trimester was associated with a significantly increased risk for subsequent glucose intolerance of the pregnant woman. In addition to, the raised waist circumference also positively correlates with BMI and age.

As a result, we found that first trimester waist circumference measurement is a method that can be applied without the need for expert staff. It is also

inexpensive, easy, effortless, non-invasive, functional method to evaluate impaired glucose tolerance. We are aware of some limitations of our study. The present study reported herein should be considered in the light of some limitations. Small sample sizes and the heterogeneity of the studies are the main limitations. The results of this study were limited by its comparatively small sample size. The lack of previous research studies on the subject is another limitation.

Therefore, comprehensive, prospective and large-scale randomized controlled studies are needed to accept waist circumference measurement as a screening method in GDM.

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The satisfaction level in cases with gynecologic cancer

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ABSTRACT

The aim of this study was to determine the level of satisfaction in gynecological cancer patients and to increase the awareness of the disease in the community. This descriptive study was carried out on 280 patients treated at our Gynecological Oncology Center between May 2018 and January 2019. As a data collection tool, descriptive information and satisfaction questionnaire were prepared by the researchers based on the literature and the demographic parameters of the patients were asked. In the analysis of the data: descriptive statistics, t test, Mann Whitney U Test and Spearman correlation coefficient were used in SPSS 25.0 statistical program. It was understood that 51.4% of the participants did not hear this type of cancer before being diagnosed. It was learned that 61.4% of the participants did not have any routine screening program against cervical and/or breast cancer. 42.1% of the participants did not know the tests and 39.3% of them did not know that they did not have access. 85.7% of the cancer patients who participated in the study received the disease-related diagnosis from the gynecologist. 33.4% of the patients stated that it took a long time to diagnose. 46.4% of the patients stated that they had not been informed by the doctor about their illness and options. In addition, 49.3% of the patients were not satisfied with the approach taken in this information and 50.7% wanted to obtain more effective and comprehensive information. Patients' expectations from the doctors are more understanding, better communication with the patient, receiving emotional support, and decision-making about the disease and treatment is also the time for the doctor to support the patient, to respect him, to spend more time. The patients think that the health personnel have difficulty in giving information about the treatment process and its side effects, the likelihood of recurrence of the disease, the effects of the disease on the psychological state, prognosis, how long the treatment will take and what the disease is and why. For this reason, patients feel themselves lacking. It is important for health personnel to inform the patient, to listen to the patient and to support them in all stages of the disease and treatment, and to support the survival of this chronic disease.

1. Introduction

Nowadays cancers are the most common diseases. It is very important not only because it causes a decrease or a loss in the reproductive ability of the woman, but also because it affects many functions of the woman as a whole (Saevarsdottir et al., 2010). Therefore, health

practitioners serving gynecological oncology patients have many responsibilities. Gynecologic oncology patients are now oncology patients after uneventful postoperative period. After that, a quality care service should be provided to the oncology patients.

Gynecology oncology doctors apply the best protocols by performing the operations required by their disciplines in the best way. However, it should be kept in mind that they are family physicians who make the first diagnosis of the woman, who will best understand the woman. Besides, medical oncology doctors who follow the treatment processes and the palliative care team are parts of required elements. All of this team, need to determine its approach by wholly examining the gynecological cancer diagnosed women, taking into account the sensitivity of the disease and the patient (Catt et al., 2005). If we examine the studies that contribute to studies in gynecologic oncology; it appears that the studies are mostly about discharged times, cost effectiveness studies and work towards solving psychosocial problems. However, studies that include evaluations in terms of patient satisfactions are rare. Changes in mood changes in women in the gynecological cancer treatment process can be seen depending on many factors. Factors such as uncertainty about the treatment process, the risk of spreading to other organs and fears of death, female identity, changes in body image and sexuality, and difficulty in activities of daily living can cause anxiety (Sang et al., 2007). In addition to mood changes that may occur due to lack of emotional support, radical hysterectomy may also present as symptoms of genitourinary atrophic disorders and psychiatric symptoms due to the loss of estrogen and ovarian menopause. Women may experience intense sadness especially after hysterectomy because of their belief in the effect they have on the woman's identity and the meaning they attach to the uterus. For many women in traditionally dependent societies, the uterus is still a symbol of womanhood, sexuality, fertility and motherhood. When the ovaries are removed, the woman fears that her sexual desire and will decrease and that she will get older (Steele and Fitch, 2008).

It is known that cancer patients need information, during the diagnosis, treatment and follow-up period, is widespread. Patients have suspicions about future conditions, diseases, examinations and treatment. How healthcare professionals define the limit, type and path of information to be given to patients, is an important issue (Catt et al., 2005; Saevarsdottir et al., 2010). Defining communication and information needs of patients will be guiding in practice. The timely treatment and prevention of side effects in cancer treatment will improve the quality of patient care, if the patient's supportive care needs are met. The mood disorders and sexual dysfunctions associated with the cancer treatment process are important problems that should be considered in terms of affecting the quality of life, physical, social and emotional health. The majority of women in the post-treatment period with gynecological cancer, stated psychosocial and sexual problems as primary necessities. The importance of employment for people with cancer appears to go beyond meeting the financial requirements and makes women feel good in every sense.

Identification and management of unmet supportive care needs of patients is the main component of health care. Cancer causes different effects on all levels of life of both the patient and the family (Evans et al., 2006). Effective, high-quality cancer care cannot be limited to the implementation or treatment of surgical treatment alone. Care refers to a more holistic approach, individualized care and closeness to oncology patients and their families. It is seen that the material and emotional needs of cancer patients during the diagnosis period are not investigated adequately, in the diagnosis, treatment and post-treatment period. There are still difficulties in the diagnosis of patients' needs, standardization of measurements and determination of unmet supportive care needs and levels (Bekar et al., 2013). Lack of studies on this subject has also been identified in gynecologic oncology patients. In our study, we investigated gynecologic oncologic cancer patients who had undergone surgical operation and are still under treatment, their sources of information, their information needs, their expectations from the health personnel and the effect of cancer on these parameters.

2. Material and methods

The European Society of Gynaecological Oncology (ESGO) is the leading European organisation with more than 2.500 professionals involved in prevention, treatment, care and research of gynaecological cancers. Our study group consisted of patients diagnosed with gynecologic cancer in 5-year period and admitted to gynecologic oncology outpatient clinic between May 2018 and January 2019 at Tepecik Education and Research Hospital, which is accredited by ESGO (n=280). The patients over 18 years of age and could be communicated easily, were included in the study. The Local Ethics Committee approved the study. The universal principles of the Helsinki Declaration were implemented. The patients were first told to study and to collect data, all patients were given a sociodemographic information form and satisfaction questionnaire including age, educational status, marital status, duration of disease, diagnosis of cancer. While responding to the questions, patients were asked to respond in a closed room, in order to prevent them from being directed. After the data were collected, the data were recorded by a different person without patient names. After the questions containing the

demographic data, the main survey questions were passed. The questions in the awareness and prevention subgroup indicated whether they had information about gynecologic cancers and whether they had any tests on these cancers. The subgroup form of the patients' expectations from the health personnel was prepared by the researchers based on the literature. The questionnaire included 8 questions about the sociodemographic characteristics of the patients (age, gender, BMI, number of pregnancies, educational status, economic status, working status, marital status). 9 questions about the characteristics of the disease (diagnosis, stage, when diagnosis was made, current health status, how to obtain information about the disease, the type of cancer, the methods of screening for cancer, whether or not the screening, the causes of the disease, how and by whom the diagnosis was made), 2 questions about whether the health institution sends educational articles, 2 questions about whether the treatment is late, 7 questions about how the medical personnel evaluate the communication, 2 questions about the complementary help during diagnosis, 1 question about the impression of the healthcare team in the patient, 1 question to determine the information requirements, 25 questions about the expectations of the patients from the health care personnel, 1 question about whether they are aware of the scientific studies, and a total of 58 questions. Three experts received their opinions for the questionnaire. Five cancer patients were pre-applied to the questionnaires. There are five options in the form of I strongly disagree, disagree, neither agree nor disagree, agree, absolutely agree. The corresponding scores are 1, 2, 3, 4,5 respectively. The total score is calculated by summing the points given for each item. The total score is between 14 and 35, and the scores from each of the subscales range from 1 to 5. When the total score is calculated, the high scores indicate that the satisfaction level is high. The respondent is asked to mark a single score for each item.

Evaluation of data

Statistical analysis of the data obtained in our study was performed with SPSS (Version 25.0, SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed as mean ± standard deviation or median (min-max) for continuous variables according to data distribution, number and percentage for categorical data. Normality distribution was evaluated by Shapiro-Wilk and Kolmogorov-Smirnov tests. Student t test was used for comparison of two independent variables when Gaussian distribution was proved, and nonparametric Mann-Whitney U test was used for comparison of independent variables these parameters could not be met. This study is limited to adult patients in the various cancer diagnostic groups and who give consent to participate in the trial. In the study, the relationship between satisfaction questionnaire score and age, educational status, social support status, duration of disease and clinical features were evaluated by Spearman correlation coefficient and test.

3. Results

As shown in Table 1, 9.6% of the participants were between the ages of 30-39 and 23.5% were over 60 years of age. The mean age of the participants was 52.32 ± 9.69 (min: 30- max: 73). 80.7% of those examined were married; 62.1% were graduated from primary school, 19.3% were university graduates. 58.9% of the participants were retired and 13.6% were employed. 33.2% of the respondents had a household income of $ 500-1000 and participants with a household income of more than 1500 dollars were 19.3%. It was found that 89.3% of the participants were multiparous. According to the BMI of the participants, 52.5% were overweight and 3.2% were obese. Table 2 presents the distribution of the characteristics of the participants. Of the participants, 12.1% were diagnosed with cervical cancer, 20.7% with ovarian cancer, 3.6% with vulva cancer, 0.7% with vagina cancer, 60% with endometrial cancer, 2.9% with tubal cancer. 56.1% of the cancer was found in the second stage. 20.4% of the participants received diagnoses and treatment one year ago, 26.7% of them 1 year-3 years ago, 52.9 of them received 3 years-5 years ago. It was learned that 93.6% of the patients continued their treatments.

In Table 3, the distribution of the disease levels, information levels and diagnostic characteristics of the participants were presented. It was determined that 51.4% of the participants did not hear this type of cancer before the diagnosis and that from the cancer prevention tests they were aware of mostly Pap smear test which is a cervical cancer screening test with rate of 27.9% and ovarian cancer markers with 56.4%. It was learned that 61.4% of the participants did not undertake any routine screening program against both cervix and breast cancer. It was determined that 42.1% of the participants didn't do it because they didn't know about the tests and 39.3% of them didn't do it because they didn't have access. It was understood that 39.3% of the cancer diagnosis of the participants was recognized because of their continuous health problems. A large proportion (85.7%) was diagnosed by a gynecologist. Table 4 presents the distribution of the expectations of the participants from the doctors and nurses in the diagnosis and treatment of their diseases.

The majority of the participants (36.4%) stated that the first speech after the diagnosis was good but was in a great shock to evaluate the information given; 92.1% stated that no written document was sent after speech and 83.6% stated that it would be beneficial to send the

written document. There was no statistically significant relationship between the expectation and duration of disease in patients (p> 0.05). 44.3% of the participants stated that the family physician could not diagnose the disease and 34.3% stated that it took a long time to diagnose. 52.1% of the participants stated that they had to wait 1-2 months for diagnosis. 20% of the participants disagreed with the section 'I was very informed about the disease and options by my doctor/nurse at the hospital', 20% of the participants did not agree with the section 'My doctor explained all possible side effects of the treatment and / or all possible effects', 18.6% did not agree with the section 'my doctor / team told us about the possible recurrences and symptoms of the disease', 17.2% did not agree with teh section 'I am satisfied with the communication with my doctor', 15.7% did not agree with 'I think that I have answered all my questions and concerns', 35% were undecided to 'I'm sure of my doctor choice'. 16.5% did not agree with the section 'my doctor was understanding to me and the difficulties I had experienced'. 46.4% of the participants stated that they were offered many treatment options, 60% said that they were offered psychological support, 57.9% said that the team made them feel safe, 45.7% said that psychological support was incomplete and diagnosis and treatment helped them feel better, 9.3% stated that their needs were not met. All of the patients stated that they did not know if there was any ongoing clinical study in the duration of the illness and did not receive a clinical study proposal, and would like to participate if there was any such study. 35% of the participants stated that the oncologist should have had spent more time explaining the side effects of the treatment, and 44.3% stated that they had no desire or regret, they were satisfied with the team's choices. 39.3% of the participants stated that they wanted the nurses to spend more time for each patient, that it was not their options, but that the lack of time negatively affected. Patients would like to receive information primarily about the side effects of treatment (35%), the likelihood of recurrence (6.4%), regular follow-up (2.9%), duration of treatment (6.4%). In our study, it was determined that the

Table 1. The distribution of some descriptive and demographic characteristics of the participants.

	Number (n=280)	(%)*
Age Groups		
30-39	27	9.6
40-49	94	33.5
50-59	93	33.2
60 years and older	66	23.5
Marital status		
Married	226	80.7
Single	16	5.7
Divorced	38	13.6
Education status		
Primary school graduate	174	62.1
Middle school high school graduate	52	18.6
Graduate from a university	54	19.3
Operating status		
Full time work	38	13.6
Working part-time	32	11.4
Does not work due to health condition	45	16.1
Retired	165	58.9
Monthly total household income		
Up to $ 500	49	17.5
$ 500- $ 1000	93	33.2
$ 1000- $ 1500	84	30
More than $ 1500	54	19.3
Pregnancy		
Multiparous	250	89.3
Primipar	30	10.7
Body mass index (BMI kg/m^2)		
Normal (BMI 18-24 kg/m^2)	124	44.2
Overweight (BMI 25-29 kg/m^2)	147	52.5
Obese (BMI 30-34 kg/m^2)	9	3.2

Table 2. The distribution of the characteristics of the participants related to their diseases is presented.

	Number (n=280)	(%)*
Type of cancer		
Cervical cancer	34	12.1
Ovarian cencer	58	20.7
Vulvar cancer	10	3.6
Vagina cancer	2	0.7
Edometrial cancer	168	60.0
Tuba cancer	8	2.9
Cancer stage		
Stage 1	100	35.7
Stage 2	157	56.1
Stage 3	23	8.2
How many years ago have you been diagnosed?		
Less than 1 year	57	20.4
1-3 years	75	26.7
3-5 years	148	52.9
What is your current health condition?		
I'm under treatment	262	93.6
My treatment is complete	2	0.7
My disease has relapsed	16	5.7

Table 3. The distribution of knowledge and diagnostic characteristics of the participants of the study.

	Number (n=280)	(%)*
Have you heard of this cancer before the diagnosis?		
Yes	136	48.6
No	144	51.4
Have you heard of any of the following screening or methods to help prevent the type of cancer you are caught?		
Cervical cancer HPV test	2	0.7
Cervical cancer HPV vaccine	4	1.4
Cervical cancer HPV DNA test	4	1.4
Pap smear test for cervical cancer	78	27.9
Weight control for endometrial cancer	22	7.9
Ultrasonography control for endometrial cancer	12	4.3
Tumor markers for ovarian cancer	158	56.4
BRCA test for ovarian cancer	0	0
Have you done any routine screening programs for cervical or breast cancer?		
I had cervical and breast cancer tests.	24	8.6
I only had breast cancer	12	4.3
I had both cervical and breast cancer tests	72	25.7
I didn't have a cervical or breast cancer routine scan.	172	61.4
If you never had any of the routine screening programs for cervical or breast cancer, what is the main reason?		
I didn't know them	118	42.1
I knew it, but I didn't have access	110	39.3
I knew them, but I'm not good enough	10	3.6
I knew these things, but I didn't see myself worthy.	42	15.0
How were you diagnosed with cancer?		
Self-examination and suspicion	94	33.6
Due to persistent health problems	110	39.3
Through regular inspection / scanning	76	27.1
Who puts the diagnosis?		
Family doctor	38	13.6
Gynecologist	240	85.7
Surgeon	0	0
Radiologist	2	0.7

Table 4. The distribution of the expectations of doctors and nurses in the diagnosis and treatment process related to the diseases of the participants.

	Number (n=280)	(%)*
How would you describe your first conversation with your doctor / nurse / health care team?		
They told me everything about my good and very clear disease and treatment.	94	33.6
Good but not clear - information was not clear	76	27.1
It's not very clear and clear.	8	2.9
Good, but I'm too shocked to evaluate the information.	102	36.4
Did your health care provider send a written instructor document after your first conversation?		
Yes	22	7.9
No	258	92.1
Do you think these tutorials would be useful if they were sent?		
Yes	234	83.6
No	46	16.4
Have you experienced any of the following problems?		
Diagnosis took a long time	96	34.3
Family physician couldn't diagnose my disease	124	44.3
I'm not satisfied with my doctor, I changed my doctor	16	5.7
I had to wait for the tests	42	15.0
I was not satisfied with the health institution and I had to change	2	0.7
How long did you have to wait for your treatment?		
Less than a week	6	2.1
1-2 weeks	16	5.7
Up to 1 month	50	17.9
1-2 months	146	52.1
More than 2 months	62	22.1
I was well informed about my illness and options by my doctor at the hospital		
I strongly disagree	0	0
I do not agree	12	4.3
Neither agree nor disagree	44	15.7
I agree	130	46.4
Absolutely I agree	94	33.6
My doctor explained all possible side effects and / or delayed effects of treatment		
I strongly disagree	0	0
I do not agree	10	3.6
Neither agree nor disagree	46	16.4
I agree	134	47.9
Absolutely I agree	90	32.1
My doctor / team explained the possible recurrence and symptoms of the disease		
I strongly disagree	0	0
I do not agree	14	5.0
Neither agree nor disagree	38	13.6
I agree	134	47.9
Absolutely I agree	94	33.6
I am satisfied with the communication with my doctor		
I strongly disagree	0	0
I do not agree	10	3.6
Neither agree nor disagree	38	13.6
I agree	138	49.3
Absolutely I agree	94	33.6
I think you answered all my questions and concerns		
I strongly disagree	0	0
I do not agree	10	3.6
Neither agree nor disagree	34	12.1
I agree	142	50.7
Absolutely I agree	94	33.6

I'm sure about my choice of doctor.		
I strongly disagree	0	0
I do not agree	14	5
Neither agree nor disagree	84	30
I agree	152	54.2
Absolutely I agree	30	10.7
My doctor was sympathetic to me and the difficulties I had.		
I strongly disagree	0	0
I do not agree	8	2.9
Neither agree nor disagree	38	13.6
I agree	134	47.9
Absolutely I agree	100	35.7
Which of the following options is suitable for your diagnosis and treatment?		
Many treatment options were offered to me	130	46.4
I was offered to see another specialist doctor against my illness	44	15.7
The following procedures were described after my treatment	106	37.9
Have you been offered any complementary help?		
Psychological support	168	60.0
Social support	72	25.7
Nutritionist assistance	24	8.6
Sexual counseling	2	0.7
Rehabilitation program	0	0
Palliative care of existing patient organizations or support programs	0	0
Patient organizations	14	5.0
How did your doctor and doctor's team make you feel?		
Safe	162	57.9
Guilty	30	10.7
Frightened	26	9.3
Uncertain	20	7.1
Confused	42	15.0
Responsible / accountable	0	0
Not alone	0	0
Do you think any of the options below are missing and will help you better diagnose and treat?		
Suggestions about sexuality	40	14.3
Social support suggestions	56	20.0
Dietary recommendations	16	5.7
Psychological support	128	45.7
Information on treatment options and steps	40	14.3
Which of the following options is suitable for your treatment? My doctors: my medical team:		
She talked to me about my emotional tide.	68	24.3
He offered to help me during my treatment	40	14.3
He offered to help me after my treatment	40	14.3
He offered to help me improve my life	10	3.6
He offered me and / or my wife psychological help and counseling	15	5.4
She offered to help me cope with the personal side effects of my illness / delayed side effects	30	10.8
He talked to me about possible sexual dysfunction following treatment of my illness	19	6.8
He offered regular follow-up after my treatment was completed	32	11.4
Followed my needs	26	9.3
Do you know if there is any ongoing clinical study during your illness?		
Yes	0	0
No	100	100
Have you been offered to participate in a clinical trial?		
Yes	0	0
No	280	100
If yes, how would you describe the information you received about it?		
I received very detailed information and I think I decided based on information.		
I got some information, but I still have a lot of questions in my mind and I don't think I've decided based on knowledge.		
I didn't get a lot of information, but I did a lot of research and I trust my decision.		
I didn't get much information, but it doesn't matter. I was ready to participate in any clinical study.		
Would you agree if a clinical trial was offered?		
Yes	280	100
No		
What would you like your doctor to do differently?		
I would like my family physician to listen to me more carefully when I first consult with him about the problem.	12	4.3
I'd like him to spend more time telling the side effects of my oncologist.	98	35.0
My oncologist. I'd like him to tell me how long my treatment is going to take.	18	6.4
After my treatment was complete, I felt lonely. I'd like to give me regular follow-up.	8	2.9
I would like more support for delayed side effects.	2	0.7
I'd like to know about the possibility of disease recurrence.	18	6.4
I am not satisfied with the choice of the team that provided me the treatment.	124	44.3
What would you like the nurses to do differently?		
I would like the nurses to be more careful when giving my medication with more focus on what I am treated for.	2	0.7
I would like nurses to spend more time for each patient. I realized this was not in their possession, but the lack of time affected me negatively.	110	39.3
I would like the nurses to talk more clearly to me about all the effects of my illness, such as psychological and even death / life expectancy.	30	10.7
I didn't want them doing anything different. The nurses have always been attentive to my needs and I am very satisfied with the nursing team that provides me treatment.	138	49.3

satisfaction scores of the patients were above the middle level. As seen in Table 5, there is a statistically significant ($p < 0.05$) relationship between the satisfaction survey questions of cancer patients and the income status, on the other hand there was no significant relationship between the general satisfaction score and age, marital status, cancer stage, level of education, work status, sick leave, and disease duration variables ($p > 0.05$).

4. Discussion

Gynecological cancers are one of the most important causes of mortality and morbidity in women after breast cancer. Although the incidence of gynecologic cancers increases all over the world, the most important reason for the decrease in the mortality rate in recent years is the development of early diagnosis and treatment methods (Steele and Fitch, 2008). One of the most important problems caused by the diagnosis and treatment methods applied during the treatment of gynecologic cancers is the problems that can occur after the surgery and these problems can negatively affect the quality of life of women both during the treatment phase and when they start their daily lives (Wenzel et al., 2003). The perception of gynecological cancers as a chronic disease causes lifestyle changes in women. These changes in women's lifestyle can lead to psychological difficulties and problems that may cause emotional, mental, and behavioral reactions. Generally, uncertainties of cancer may cause confusion, panic and fear in patients. The requirements of the patients from all health teams are multidimensional and determining these requirements will reduce the patient's stress, poor quality of life, and dissatisfaction with care; prevent the use of health services and increase the cost (Evans et al., 2006; Steele and Fitch, 2008). While supportive care is used to describe care given to those with conventional disease in oncology, the applicability to the gynecological cancer patients who are increased in numbers in recent years, in every stage of the disease, should be considered in recent years.

Surgical interventions such as radical hysterectomy, vulvectomy, total pelvic exenteration in gynecologic cancer; treatments such as radiotherapy and chemotherapy lead to significant health problems that adversely affect a woman's life. Parker et al. (2003) reported that women diagnosed with gynecological cancer had lower well-being than other cancer diagnoses (Parker et al., 2003). In a study of gynecological cancer patients whose primary treatment was completed and at least one year after diagnosis, unmet requirement rate was found to be 55.6% (Urbaniec et al., 2011). In our study, the unfulfilled expectation rate was 9.3%. The reason for this low rate may be due to computerization of follow-ups and reduction of delays and disruptions during follow-up. In addition, thanks to the careful work of the archivist and oncology nurse of our gynecology oncology clinic, regular follow-up of the follow-up process is ensured. Similar to our study, Vellone et al. (2019) found no significant relationship between the expectation level and duration of disease in patients (Vellone et al., 2019). Another study suggests that oncologists patients should be sensitive to what the patients want to hear during the treatment of cancer and help patients to define their expectations and they discuss an approach to this issue (Evans et al., 2006). In our study, no relationship was found between the patients' operation durations and expectations. The fact that there was no statistically significant relationship between the expectation and duration of the disease in the patients suggests that the positive or negative effects obtained during the treatment period of the disease may not have been clearly perceived by the patients. This finding may be interpreted as the fact that cancer patients are always open to encouraging hope and can be referred to this issue.

In another study conducted in gynecological cancer patients, general well-being and quality of life of the women were examined and it was observed that the most adverse effects were in emotional and social terms in functional situations (Anderson and Lutgendorf, 1997). In our study, it was reported that most of the patients' needs, especially psychosocial needs, were not handled by the treatment team in gynecologic cancer patients and the necessity to address them in the early period was revealed. In our study, psychological and emotional need ratio was 45.7%. In studies of women with ovarian cancer who received cancer treatment, psychological and emotional needs were reported in 57-63% of patients. The need to talk to someone about irritability, sadness, fear and feelings is expressed in order (Fitch et al., 1999). Psychosocial care and more information are among the most frequently reported requirements. Care that helps the patient and his family cope in the course of diagnosis, during treatment, in follow-up or in advanced stage, palliation during terminal period, is supportive care (Ekman et al., 2004). This care includes activities and health services that help the patient to maximize the benefits of treatment and to live as high as possible with the effects of the disease.

In our study, it was determined that the satisfaction scores of the patients were above the middle level. It was also found that patients had higher satisfaction scores as their income levels increased. This suggests that the level of income and the ability to reach the doctor may also affect the patients' coping behaviors and hence the level of hope. Felder et al. (2004) found that patients' levels of hope were high in studies in which they investigated the level of hope in cancer patients (Felder, 2004). Jo et al. (2004) found that patients with cancer maintained their hopes in the disease process (Jo and Son, 2004). The results of these studies are consistent with the results of our study. Cancer patients do not have low level of hope. In our study the rate of meeting of patients' expectations with follow-ups was high.

Another important issue; the patients stated that the lack of communication and information as their unmet needs and their dissatisfactions. Sutherland et al. (2009) found in their study that the unmet supportive care needs of patients diagnosed with various cancers are related mostly to the lack of information about testing, treatment and side effects (Sutherland et al., 2009). Information has functions of gaining control, reducing anxiety, improving cohesion, determining realistic expectations, participating

in self-care and raising morale, feeling safe. In many studies related to the subject, it has been shown that the patient's biggest complaint is the need for information about disease, prognosis and treatment (Sanson-Fisher et al., 2000; Hodgkinson et al., 2007). Supportive active participation in the decision rather than the submissive attitude, unlike the beliefs that the decision should be made by the physician as in the previous years and considering the treatment as a partnership between the patient and the professional worker, increase patients' need of information. At this stage, health professionals need to feel responsible for diagnosing patients' information needs and meeting their individual knowledge needs, as well as other needs of patients. It is understood that patients need information in every period and this is not frequently met (Sanson-Fisher et al,. 2000). Harrison et al. (2009) reported in their rewiev, information (11-97%), psychosocial (21-89%), daily living activities (4-89%), supportive care (13-86%), psychological (18-85%).) physical (21-70%), sexuality (49-63%), communication (2-57%) and economic (13- 54%) requirements of cancer patients were not met during the treatment period (Harrison et al., 2009). These results indicate that the needs of cancer patients are multidimensional and variable. These unmet needs should be identified and approached by a team work in order to optimize the care that will be offered to these patients. In this context, other health professionals (psychologists, physiotherapists, nutritionists and dieticians, etc.) should take part in this process as well as their main duties in the diagnosis and treatment processes of physicians.

In our study, the general well-being and quality of life of the women were examined and it was seen that there were mostly emotional and social negative effects in functional situations. In the study conducted by Harrison et al. (2011) it is indicated that unmet needs and rates of the patients were activities of daily living (41-47%), communication (30%); economic (5-13%), information (6-83%), physical (26-52%), psychosocial (8-17%), supportive care (38-53%) and sexuality (33-34%) (Harrison et al., 2011). In our study, 57.9% of the patients who had gynecologic oncology surgery stated that they were safe and 64.9% of them stated that they were satisfied with the choice of doctor. In their study conducted with 199 patients who had surgery 1-8 years before and survived in order to assess long-term psychosocial outcomes and supportive care needs two-thirds (68%) reported a positive quality of life and relationship adjustment. However, approximately one third (29%) of them reported symptoms of anxiety at the clinical level, and about 90% reported a 4-fold increase in their unmet needs in such a diagnosis. In the study that Beesley et al. (2013) evaluated the women with ovarian cancer from 6 months to 2 years after the diagnosis it is reported that system / information, patient care and sexuality requirement scores decreased by 2 years, psychological and physical requirements continued (Beesley et al., 2013). Browall et al. (2004) reported that patients with ovarian cancer had little change in information requirements at the time of diagnosis, after completion of therapy, and 6 months after completion of therapy and found that they need information about the most likely improvement in all measurements, stage and spread of the disease, different treatment options (Browall et al., 2004).

Although the initial stage of the disease is important in adherence to the whole process, the supportive care needs and meeting status of newly diagnosed cancer patients in this period have not been adequately investigated in terms of treatment and post-treatment period. When we look at the studies in the literature, it is seen that physical, psychosocial and information requirements are common. It is seen that most cancer patients have physical supportive care needs related to the symptoms during the diagnosis period. The patient who had to wait more than 2 months for the initiation of treatment was 22.1% and the rate of participants who expressed their discomfort regarding the diagnosis of the patients was long was 33.4% in our study. This can be attributed to the inconvenience of organizations and the inadequacy of oncology hospitals in the diagnosis and treatment phase. In another study conducted by Billet and Crossing (2003), the problems related to the organization of treatment in the opinions of the women who are receiving breast cancer treatment were the delay of the treatment process, meeting with different doctors at each control, long waiting time in the clinic, inadequate coordination of treatment (Billett and Crossing, 2003).

Among all the needs of women with gynecological cancer, it is seen that the needs of the sexual field are mentioned at the forefront. It is reported that cancer treatments affect sexuality but both patients are uncomfortable in expressing this need and health professionals do not ask questions about their sexual needs. In our study, the need for sexuality was 14.3%. Crothers et al. (2005) investigated the relationship between social support and hope in cancer patients, and found that patients' satisfaction with their support was statistically significantly associated with their hope (Crothers et al., 2005). Consistent with these findings, Dansuk et al. (2002) found that hopelessness and loneliness level increased as family and social support decreased in patients with cancer (Dansuk et al., 2002). In our study, the need for social support was 20% and no effect of the need for social support on satisfaction scores was found statistically.

In a study conducted by Steele and Fitch (2008) with gynecological cancer women; 69% of women fear that the cancer will recur, 66% fear that the cancer will spread, 54% fear of the uncertainty about the future

(Steele and Fitch, 2008). Concerns about uncertainty about the future due to the fear of recurrence and spread of cancer in gynecologic cancer patients cause anxiety and sadness. In our study, 7.1% of the patients stated that their status was uncertain and 9.3% stated that they were scared. There is a positive correlation between income level and expectations of patients. It was emphasized that people with low incomes have many obstacles for screening programs, not only screening programs are sufficient and timely monitoring is very important when abnormal test results are obtained (Bierman et al., 2012). For the above reasons, health research and cancer screening programs should be systematically disseminated to the whole society. In our study, it was observed that satisfaction ratio increased as income level increased.

It was found that patients who quit their jobs needed more psychological support. In the study conducted by McCorkle et al. (2006) it is found that 21% of women diagnosed with cervical cancer suffered from depression and women who experienced changes in the terms of spouses, work and finance tend to be more prone to depression (McCorkle et al., 2006). One month after the start of treatment, patients usually expressed profession loss as job loss, loss of connection with employer, loss of work purpose or permanent loss of ability to work. While the cancer does not allow the individuals to earn money, the need for resources increases due to the cost of treatment and can cause cancer patients and their families to experience financial crisis (Amir et al., 2007). Apperently, studies about cancer and financial requirements are not enough in numbers. After the diagnosis and treatment of cancer, which has significant effects on the financial situation, the experience of change in work life (reducing working hours, interruption of work, change of workplace, etc.) or stopping the work was determined as 70% (Spelten et al., 2002). The need for financial resources increases for unemployed and / or patients who are inadequate to meet their daily lives. Patients with low socio-economic status find it more difficult to meet financial needs (Amir et al., 2007). Although the cost of cancer treatment imposes a large financial burden on the state economy, only a small part of this burden is imposed on patients.

The rate of patients seeking information about side effects and protection against side effects was 20%. Among the biological problems that cause anxiety and anxiety in women during the gynecological cancer process are abnormal metabolic processes that may develop due to the side effects of their treatment. In the process of coping with cancer; women should be informed about the characteristics of the cancer such as stage, diagnosis time, location, symptoms, treatment methods and their ability to combat should be supported (Steele and Fitch, 2008). In our study, 0.7% of the patients discontinued follow-up from their own treatment center and 5.7% of the patients changed their first doctor. Unsatisfactory requirements arise when there is a mismatch between perceived needs of cancer patients and the appropriateness of the service provided. The level of meeting the health care needs is directly related to the low level of patient satisfaction and quality of life. The level of meeting the health care needs is directly related to the low level of patient satisfaction and low quality of life. Studies on supportive care needs of cancer patients have shown that unmet needs are high (Harrison et al., 2009; Polikandrioti and Ntokou, 2011). In addition, patients' perceptions about unmet needs can vary throughout the cancer process, at all stages of cancer, and according to different types of cancer, stages, and age of the individual. We could not find any relationship between age, different types of cancer, duration, stages and satisfaction score.

Our positive contributions with this cross-sectional descriptive study; diagnosing unmet needs can provide impetus for improving resources for patients with cancer in improving resources and rescheduling services. Considering the lack of gynecological oncology centers and the patient statements indicating that they are in search of a more reliable health institution and the institutions where these services are provided well, there are still deficiencies at the point of meeting the abovementioned needs of this institution shows that it is important to investigate this issue. The sharing of information to be obtained through such studies with oncology centers and the more active sharing of non-governmental organizations on cancer in this subject will lead to possible impaired self-esteem in gynecological cancer patients and the presence of healthy body perception. These results suggest that it is important to maintain the expectation level that supports positive prognosis in cancer patients and to plan appropriate approaches of health care professionals during the diagnosis, treatment and follow-up of gynecological cancer patients.

In our study, firstly, although we have a retrospective design, we compare a homogeneous situation. We have limited the duration of cancer to 5 years in order to prevent the patients from remembering the events that occurred many years ago and also to avoid biased and incorrect information. Patients whose history and obstetric and gynecological history were not reassuring, especially those, whose file and information were inconsistent, were excluded. There are several other values in the context of the possible outcome of the present study. All subjects were analyzed by the same doctor throughout the study period and for the entire study group. These factors are less likely to affect the outcome of the study, as the above exclusion criteria are applied perfectly and exclusion of such cases. There were some limitations in our study, which were conducted in a single institution. The performance of multicentre studies on this subject will strengthen our results.

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Case Report

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Anaphylaxis developing with sugammadeks in pediatric case

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ABSTRACT

Bronchospasm developed in a 21-month-old that underwent bronchoscopy due to foreign body aspiration immediately after sugammadex which was applied for short-term decurarization. We thought this was due to anaphylaxis. Peripheral oxygen saturation and pulse decreased, breathing pattern disturbed, and a rash appeared on upper part of the body and the face in the patient. Deep sedation was achieved and the patient was treated with methylprednisolone, pheniramine, theophylline, and inhaler bronchodilator application.

1. Introduction

Sugammadex is a selective agent which reverses the effects of aminosteroid group of muscle relaxants like rocuronium and vecuronium by encapsulation method (Schaller et al., 2013). It acts at a rate of under two minutes. Renal clearance and dosage are independent of age and fat distribution but dependent on bodyweight and deepness of neuromuscular block (Sanfilippo et al., 2013). Although it is used in many countries, the evidence for the safety of the drug, the risks it poses and the hypersensitivity reactions are not enough.

Despite a large number of cases showing that sugammadex has the capacity to induce allergic reactions, it is not yet clear whether it is more allergenic

than the commonly used anesthetic agents (Baldo et al., 2014). We present a 21-month-old case that developed anaphylaxis after recurarization with sugammadex sugammadex which was performed after bronchoscopy due to foreign body aspiration.

2. Case

Emergency bronchoscopy was performed to a 21-month-old and 11 kg child with no previous history of a chronic disease with an indication of foreign body aspiration due to the information that he might have aspirated a peanut. There was a congenital lesion on the forehead, starting from between the eyebrows and extending through the frontal region to the scalp (Fig. 1). For anesthesia induction IV midazolam 0.1 mg/kg, fentanyl 1μg/kg, propofol 2.5 mg/kg, rocuronium 0.6 mg/kg and prednisolone 2 mg/kg were used. After the operation which lasted approximately 10 minutes, 2 mg/kg sugammadex was administered. His spontaneous respiration returned, and s/he was extubated. At this time, diffuse redness and a rash in the form of blistering occurred at his/her neck, bilateral supraclavicular regions and on the face (Fig. 1). Simultaneously, peripheral oxygen saturation and pulse rate decreased and breathing pattern deteriorated. Inability to hear the respiratory sounds suggested that angioedema might have developed. This condition was interpreted as a bronchospasm which developed due to anaphylaxis after sugammadex. Sedation was deepened with 15 mg propofol and assisted mask ventilation was performed. Additional prednisolone of 10 mg was given. After IV 10 mg pheniramine and salbutamol inhaler was administered, 5 mg/kg aminophylline infusion was initiated. Thus, ventilation of the patient who has difficulty in ventilation was achieved. After a period of assisted-mask ventilation spontaneous respiration was returned without a need for reintubation. He was followed in the recovery room about 90 minutes and sent awake to the ward. After the controls in a pediatricsclinic, he was discharged on the first postoperative day.

Fig. 1. Congenital skin lesion. Skin findings in the face and neck region.

3. Discussion

Early recognition of anaphylaxis signs and symptoms is important for prognosis. Monitoring of the patients during anesthesia application and presence of a patent IV line provides advantages to anesthesiologists to deal with such reactions. Although there are direct monitors patient's face, neck, and upper extremities are followed indirectly for heat, pulse, rash and color changes. Despite all the advanced monitorization methods indirect follow upis indispensable for anesthesiologists during follow up and crisis management.

It is generally advised to administer adrenaline first to the patient in an emergency situation such as anaphylaxis (Harper et al., 2009). But the initial dose and the methodology to be applied is controversial. Because the treatment should be shaped according to the anatomy of the patient, the clinical features and the response received in the emergency intervention (Mertes et al., 2011). We didn't approach aggressively due to the advantage of monitoring the patient. Because respiratory sounds were lost and pulmonary ventilation decreased during intervention with medications we thought a bronchospasm due to histamine discharge and achieved respiratory control by deepening sedation. Vital signs rapidly improved because hypoxia was prevented at an early period. Because the patient was being closely followed and gave a response to early intervention adrenalin was not given after the response. Priorities in the treatment should be stopping the possible cause, informing the surgeon, calling for help, maintaining the airway and continuing oxygen treatment. Although corticosteroids and antihistamines are used for continuation of treatment there is not sufficient and strong evidence (Choo et al., 2010). Inhaled β2 adrenergic receptor agonists or nebulized adrenaline should be administered in cases of bronchospasm without arterial hypotension (Dewachter et al., 2009). There are controversial issues about treatments that can be used and we used corticosteroid, antihistaminic and inhaler agent.

In the prospectus of the drug including sugammadexas an active agent (Bridion®, Merck Sharp Dohme Corporation, Istanbul), use in children below 2 years of age is not recommended; however, our patient was nearly 2 years old. Because of the severe damage to the lungs due to foreign body aspiration and surgical manipulation recovery was expected to be delayed. In addition, the decision to use sugammadex was made because neuromuscular antagonism with anticholinesterase and anticholinergic combination could cause fluctuations in hemodynamic values of the patient. The operation finished in a short time. However, we thought that anaphylaxis in this patient developed due to sugammadex because we didn't use any medications before or simultaneously with sugammadex during the extubation phase.

The most effective way to deal with anaphylaxis which is commonly seen in both children and adults is to follow them closely even if they are monitored and to make quick decisions. We are of the opinion that it is necessary to be alert and prepared for anaphylaxis with use of sugammadex in children.

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Case Report

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An atypical presentation of Streptococcus pyogenes keratitis

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ABSTRACT

The purpose of this report is to present a case of multiple peripheral keratitis associated with chronic dacryocystitis and to discuss its management. A 58-year-old woman with redness, pain, and decrease of vision in her right eye that remained refractory to medical therapy with antibiotics and cycloplegics was referred to our clinic. The patient had history of chronic dacryocystitis for two years. Ocular examination revealed conjunctival injection, diffuse corneal edema and multiple peripheral corneal infiltrates two of which were associated with corneal thinning. Streptococcus pyogenes was isolated from the corneal and conjunctival cultures. Since there was no any clinical improvement and corneal thinning continued despite medical treatment, external dacryocystorhinostomy (DCR) and amniotic membrane transplantation (AMT) were performed at the same session. After surgery, the patient responded well to medical treatment, symptoms relieved and corneal findings improved. Streptococcus pyogenes can cause multiple peripheral keratitis with corneal thinning in the patient with chronic dacryocystitis. The surgical treatment for dacryocystitis may be necessary for management of the keratitis.

1. Introduction

Streptococcus pyogenes is a gram-positive group-A streptococcus within the group of β-hemolytic streptococci. It induces the disease by three mechanisms: Suppuration, as in pharyngitis; toxin elaboration, as in streptococcal toxic shock syndrome; or immune-mediated inflammation, as in acute rheumatic fever or post-streptococcal uveitis (Nizet and Arnold, 2008). It also can cause marginal keratitis with direct infection (Kim and Ostler, 1977) or hypersensitivity reaction (Cohn et al., 1979). We present a case with multiple peripheral keratitis associated with chronic dacryocystitis that was culture positive for Streptococcus pyogenes and its surgical management.

2. Case

A 58-year-old woman with redness, pain, and decrease of vision in her right eye was examined in Ondokuz Mayis University ophthalmology department. She had admitted to another hospital with same symptoms 15 days before. Topical moxifloxacin and syclopentolate were initiated at that time. Because the patient's signs and symptoms worsened despite this treatment the ophthalmologist referred her to a tertiary clinic. The

patient had past ocular history of chronic dacryocystitis in her right eye for 2 years.

On presentation, the visual acuity was 4/10 Snellen lines in her right eye and 10/10 in her left eye. Slit lamp examination was significant for conjunctival injection, diffuse corneal edema, and multiple peripheral circumferential corneal infiltrates on the right. There was a clear corneal zone between the infiltrates and the limbus. Two of these infiltrates were associated with corneal thinning (Fig. 1a, 1b). Purulent material came out through the punctum by digital pressure over the lacrimal sac.

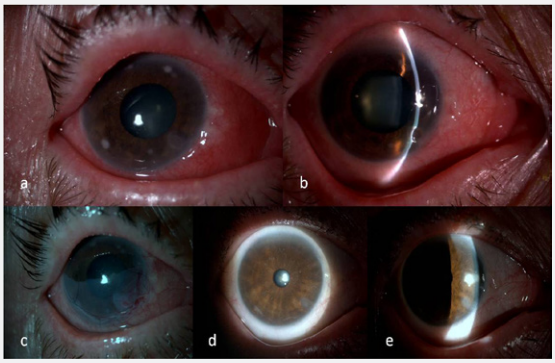

Fig. 1. Streptococcal marginal keratitis. a, Conjunctival injection, mild corneal edema and multiple peripheral corneal infiltrates separated from the limbus by a clear corneal rim. b, Corneal thinning at the corneal periphery. c, Appearance on postoperative day 1. Amniotic membrane on the inferior cornea. d, e, Appearance on postoperative 1st month. The cornea healed with residual leucoma.

Corneal scrapings and conjunctival swabs were collected for the cultures. Nasolacrimal irrigation confirmed the diagnosis of chronic dacryocystitis. Vancomycin (50 mg/mL) and ceftazidime eye drops (50 mg/mL) were initiated topically every hour and cyclopentolate hydrochloride three times a day. Nasolacrimal irrigation with sefazoline was performed twice a day. The following day fluorometholone 0.1% eye drops was added to her therapy with the thought that the keratitis could be caused by bacterial exotoxins. Streptococcus pyogenes was isolated from both the corneal and conjunctival cultures. It was susceptible to vancomycin according to the antibiogram. Despite this suitable therapy, there was no improvement at slit lamp examination on day 5. Corneal thinning also progressed. Fluorometholone was discontinued and topical cyclosporine was initiated as an anti-inflammatory agent. Chronic dacryocystitis may have prevented the healing process so external dacryocystorhinostomy (DCR) was performed. Because the corneal thinning at 5 o'clock and 8 o'clock positions was still present, amniotic membrane was sutured on inferior hemi field of cornea in the same session with DCR (Fig. 1c).

The same topical treatment and nasolacrimal irrigation with antibiotics were continued after surgery. Because her symptoms improved the patient was discharged on postoperative day 3 and called for follow-up. The next visit was on postoperative day 10. The amniotic membrane was still on its place. Nasolacrimal passage was patent. The patient did not have any complaints. Antibiotic therapy was continued for two more weeks. Corneal thinning healed with a residual leucoma at the periphery and patient's vision increased to 10/10 on postoperative first month (Fig. 1d, 1e).

3. Discussion

Streptococcus pyogenes can cause ophthalmic pathologies such as dacryocystitis (Chaudhary et al., 2010), post-streptococcal uveitis (Leiba et al., 1998) or corneal ulcers (Millender et al., 2012). There are two reports in the literature mentioned about streptococcal marginal ulcers. Both of them were associated with chronic dacryocystitis and conjunctivitis caused by Streptococcus pyogenes in a similar way with our case (Kim and Ostler, 1977, Cohn et al., 1979). Kim and Ostler (1997), suggested that the keratitis was because of direct infection with bacteria but, Cohn et al., (1979) thought that a hypersensitivity or toxic response to streptococcal superantigens may have been the major cause of these marginal problems such in staphylococcal marginal keratitis. The mechanism underlying the development of staphylococcal marginal keratitis is thought as a result of a reaction against staphilococcal superantigens. The lesions are sterile and steroid responsive (Kanski, 2007). Besides Staphylococcus aureus, Streptococcus pyogenes can produce superantigens. So, it is possible that streptococcus pyogenes can be the cause of these lesions like in staphylococcal marginal keratitis.

Since this case presented to us like a staphylococcal marginal keratitis, we started the treatment with antibiotic and steroid. After a few days, culture results revealed Streptococcus pyogenes in both corneal and conjunctival samples. Streptococcus pyogenes is not a common cause of chronic dacryocystitis. It was accounting for 3.77% of culture positive chronic dacryocystitis according to another study (Chaudary et al., 2010). The chronic dacryocystitis may induce abnormal bacterial colonization in the eye. Despite the suitable antibiotics according to the antibiogram and steroid were used, this abnormal bacterial colonization may have prevented the healing of the corneal ulcers. The corneal healing after surgical treatment corroborated this assertion. In addition, AMT surgery may have helped the process by preventing the contact between cornea and bacterial exotoxins and by facilitating the wound healing.

Streptococcus pyogenes is not a common cause of either chronic dacryocystitis or marginal keratitis. The abnormal bacterial colonization may trigger keratitis by causing direct infection or toxic reaction. In case of medication resistant peripheral keratitis, surgical treatment may be necessary for treatment of both keratitis and chronic dacryocystitis.

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Case Report

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Massive carbuncle in a patient with diabetes mellitus

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ABSTRACT

Carbuncle is a skin infection with deep subcutaneous tissue involvement and can lead to sepsis and death if not properly treated. Wound care, control of co-morbid diseases that affecting the immunity are as effective as antibiotic treatment in the treatment of the carbuncle. Here, a case of carbuncle of the gluteal area is reported in a 75-year-old woman with concomitant diabetes and chronic renal failure.

1. Introduction

A carbuncle is the collection of furuncles that affects deeper subcutaneous tissue with purulent drainage from multiple follicules (Sommer et al., 2018; Stevens et al., 2014). It manifests as painful, tender, fluctuant, erythematous nodules surrounded by a rim of erythematous swelling. A carbuncle may result with bacteremia that can cause life threatening infections like endocarditis and osteomyelitis. Diabetes Mellitus (DM), immunologic abnormalities, trauma and intravenous drug use are important risk factors but it can also develop in healthy individuals (Gira et al., 2004; Kars et al., 2005). Most commonly involved areas are nape of neck, face, axillae and buttocks. Although s. aureus alone comprises up to 75% of the cases, multiple organisms can be isolated in perioral and anogenital infections (Summanen et al., 1995). Diagnosis is based primarily on clinical appearance, bacterial cultures and gram stains of the lesion. Although simple furuncles may heal only with warm compresses, a carbuncle often requires systemic antibiotic therapy, incision and drainage.

2. Case

A 75-year-old female was admitted with the complaint of red, tender mass with fluid leakage on her left perianal gluteal region accompanied by fever. Dermatological examination showed approximately 15cmx15cm sized

tender, fluctuating mass with multiple suppurating papules on erythematous base almost completely covering the left gluteal area (Fig. 1). She has DM and chronic renal insufficiency. Her initial laboratory tests revealed values of creatinine: 2.64 mg/dL, WBC:11900/uL, ESR:67 mm/hr, CRP:0.97 mg/dl, glucose 244 mg/dl. Three punch biopsies were taken from the lesion for bacterial culture, gram stain and histopathological examination. Empirical ampicillin-sulbactam was started 1 gr three times daily. Incision and drainage were also performed. A magistral drug containing acetate aluminum, lanoline anhydrite, distilled water and petrolatum jelly was applied for daily dressing of exposed wound surface. Polymorphonuclear leukocyte rich mixed type necrotizing inflammation starting from surface and extending into deeper subcutaneous tissue with fistula formation were seen in histopathological examination. Since the bacterial culture revealed S. aureus proliferation susceptibility to oxacillin, we gave ampicillin sulbactam therapy for three weeks as the lesion regressed (Fig. 2). One month later, patient had no complaints and dermatological examination was unremarkable with approximately 4x2 cm sized scar tissue (Fig. 3).

Fig. 1. Approximately 15cmx15cm sized tender, fluctuating mass with multiple suppurating papules on erythematous base almost completely covering the left gluteal area.

Fig. 2. The lesion after ampicillin sulbactam therapy for three weeks.

Fig. 3. One month later, dermatological examination was unremarkable with approximately 4x2 cm sized scar tissue.

3. Discussion

In this case report, a gluteal carbuncle case is presented in a patient with both chronic renal failure and uncontrolled diabetes. One of the three punch biopsies taken was gram-stained for rapid diagnosis, followed by antibiotherapy; tissue culture was performed with the second one, and antibiotherapy was planned according to the (culture) result. Antibiotic treatment continued because of the oxacillin sensitive S. aureus growth. The third tissue was sent to pathology, and the tissue was examined for diseases found in the differential diagnosis, such as pyoderma gangrenosum, which could be escaped the attention. During this treatment, the patient received IV fluids for chronic renal failure and his blood glucose levels were tightly controlled. Although incision and drainage have been suggested in some publications in the presence of immunosuppression, the presence of comorbidities and rapid progression of cellulite, in this case, we did not prefer these and have observed that drainage has been performed with the help of dressing to the lesions (Chou et al., 2015). With the control of comorbid diseases, effective wound care, and systemic antibiotic treatment, the patient's lesion was regressed and an obvious improvement in her general condition was observed.

In conclusion, a carbuncle is a significant skin infection that can reach massive size in diabetic and immune compromised patients. When followed incautiously it may cause sepsis or even death. Appropriate therapy, alertness about sepsis and management of accompanying disease are important in the management of these patients.

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