How is the effect of planned training given to women with preeclamptic pregnancy on oxidative stress and anxiety levels?: non-randomised controlled-study

ABSTRACT

Purpose: This study aimed to studying the effects of planned training given to women with preeclamptic pregnancy on stress-anxiety and oxidative stress levels.

Materials and methods: A non-randomised controlled-study study, carried out in Gynecology and Obstetrics Clinics of Research and Application Hospital of one university. In the study, 28 preeclamptic patients matching the sampling criteria were taken as the experimental group and 22 other preeclamptic patients who also match the sampling criteria constituted the control group. Questionnaire, scale application and laboratory evaluation for the control group were performed only once.

Results: In the experimental group, there is a statistically significant difference between the TAS (mmol trolox equ./L) ($t = -9.71$ $P = 0.00$) and the TOS (lmol H_2O_2 equ./L) ($t = 6.56$ $P = 0.00$) measurements before and after the training and there is a statistically significant difference between the State-Trait Anxiety Inventory ($t = 3.64$ $P = 0.00$) before and after the training.

Conclusion: It has been determined in the study that the planned training given to the pregnant women who received a diagnosis of preeclampsia has decreased their oxidative stress levels and state anxiety levels.

Highlights

- In the experimental group, has decreased the TOS levels of the pregnant women in the experimental group significantly and increased the TAS levels significantly as against the control group.
- A significant decrease has been determined in the pre and post-training state anxiety

levels of the women.

- This positive effect towards this important and dangerous disorder in pregnancy is important in terms of preventing complications.
- It is important that this study is the first in literature evaluating oxidative stress markers after training.

Key Words: Anxiety,Oxidative stress, Pre-eclampsia, Pregnancy.

What's already known about this topic?

Oxidative stress increases in preeclampsia patients. This has been proven in many studies. Various medical treatment methods are available for preeclampsia patients.
Our research is offers a different perspective to patients by researching with planned training.

What does this article add?

This study aimed to studying the effects of planned training given to women with preeclamptic pregnancy on stress-anxiety and oxidative stress levels. It has been determined in the study that the planned training given to the pregnant women who received a diagnosis of preeclampsia has decreased their oxidative stress levels and state anxiety levels.
When evaluated from this point of view, the importance of planned education has been proven in our research. It is important that this study is the first in literature evaluating oxidative stress markers after training. We think that researching the literature will contribute significantly.

Introduction

Preeclampsia serious pregnancy-specific disorder accounts for a major part of perinatal and maternal morbidity worldwide and affects up to 5-7% of all pregnancies in developed countries and many more in developing countries, leading to as many as 8,370,000 cases worldwide per year [1-3].

Pregnancy is related with significant chronic stress. In particular, risky pregnancies such as preeclampsia are associated with stress [4,5]. It was hypothesize that mental distress conditions during pregnancy can induce preeclampsia by increasing cortisol levels and reducing lym phocyte sensitivity to glucocorticoids. High cortisol levels could also induce hypertension and endothelial dysfunction, features observed in preeclampsia [6]. Such psychosocial stress may evoke neuroendocrine responses favouring an increase in arterial pressure. Psychological events such as high stress levels, anxiety or depression may directly or indirectly affect pregnancy and may thus lead to preeclampsia [7]. It was indicated in studies, that perceived stress during pregnancy was associated with increased rates of preeclampsia [7-12].

Psychological stress and lack of social support together with the adverse effect of high risk medical status as a preeclampsia [5]. Another factor that causes preeclampsia is oxidative stress. Oxidative stress resulted from as an imbalance between free radicals and the capacity of protective antioxidant systems has gained a lot of attention as pathologic factor for several diseases including cardiovascular diseases to preeclampsia [1].

There are various studies suggesting that oxidative stress, which occurs with the disorder of the balance between oxidant substances, which may lead to cell or tissue damage and antioxidants, has a significant role in preeclampsia occurrence [14-18].

It is pointed out in some studies that psychological stress may lead to oxidative stress [19-21]. Under psychological stress, the balance between oxidant and antioxidant defence systems are disturbed, which leads to oxidative damage and influences tissue function [21].

As pointed out in the literature, it is thought that oxidative stress and psychological stress are effective on preeclampsia occurrence. It is stated that planned training given to patients significantly reduce stress levels [5,22-24]. In the light of these results, it is thought that planned training given to women with preeclamptic pregnancy may have a positive effect on stress, anxiety and by extension on oxidative stress and on oxidative stress treatment as well. This research has been carried out in the light of these results in order to study the effects of planned training given to women with preeclamptic pregnancy on stress-anxiety levels and oxidative stress levels.

Materials and methods

This research has been done experimentally with the aim of studying the effects of planned training given to women with preeclamptic pregnancy on stress-anxiety and oxidative stress levels.

Study population

The universe of the research was the patients being treated with a diagnosis of preeclampsia in the Gynecology and Obstetrics Clinics of Research and Application Hospital of one university. Preeclamptic patients being treated in the hospital were included in the research sample. Subjects matching the criteria were selected through purposeful sampling.

In the study, 28 preeclamptic patients matching the sampling criteria were taken as the experimental group and 22 other preeclamptic patients who also match the sampling criteria constituted the control group. A sample size was estimated using power analysis based on and α level 0.05, power of 0.99, assumed effect size was 0.53 for the sample size estimation.

In 2014, the International Society for the Study of Hypertension in Pregnancy (ISSHP) revised the definition of preeclampsia as a combination of hypertension developing at or after the 20th week of gestation and one or more of the following conditions: 1) proteinuria, 2–1) renal insufficiency, 2–2) liver involvement, 2–3) neurological complications, 2–4) hematological complications, and 3) uteroplacental dysfunction. According to these changes, pregnant women with chronic hypertension will be diagnosed as having preeclampsia superimposed on chronic hypertension if they present with one or more of the following conditions: proteinuria, renal insufficiency, liver involvement, neurological complications, hematological complications, or uteroplacental dysfunction [25].

Mild to moderate high blood pressure (140-159 mm Hg systolic or 90-159 mm Hg diastolic measured on two occasions at least four hours apart) warrants close evaluation and monitoring. The experimental and the control group were chosen randomly. Women being treated with a diagnosis of preeclampsia in clinic of the constituted the experimental and the control group. They were patients with mild preeclampsia, after the 20th week of their pregnancies, non-smokers with no chronic systemic disease (hypertension, diabetes, and gestational diabetes mellitus, trophoblastic) and were receiving the same type of treatment.

Patients who did not meet the inclusion criteria were excluded from the study (case and control groups). All the pregnant women included in the study both from the experimental and control group received similar treatments according to our department protocol. The decision for hospitalization based on the presence of severe features of preeclampsia and was also made based on maternal and fetal status. Since receiving antihypertensive drugs do not improve neonatal outcomes, we did not start anti-hypertensive therapy for mild preeclamptic patients. We prescribed antihypertensive drugs when patients

blood pressure was above 150/100 mmhg. Alpha metil-dopa was the first-line antihypertensive drug for long-term therapy. We added nifedipin for uncontrolled patients with severe features of preeclampsia, the labour induction was employed. Magnesium sulphate prophylaxis for eclamptic seizure was started before delivery and postpartum 24-hour period.

Data collection

The scale and the survey form created by the researchers in accordance with the literature were employed as the data collection tool. The State-Trait Anxiety Inventory (STAI) consists a 40-item scale, using a 1-4 Likert scoring for each item. The scale can be used to measure both trait anxiety and state anxiety as it consists two 20-item separate sub-scales (STAI-T State-Trait Anxiety Inventory-Traite and STAI-S State-Trait Anxiety Inventory-State, respectively). STAI scores range from 20 to 80 with higher scores indicating higher levels of anxiety.

The survey form included sociodemographic data and obstetric stories related to the women, questions concerning their awareness of the disease and a daily observation form containing such vital findings as blood pressure etc. The survey form and the inventory were conducted through face-to-face interviews.

Implementation of training-questionnaire-scale

State-trait anxiety inventory and survey form were applied to each of the women in both the experimental and control group. A planned training program concerning the disease and the personal care was given to the women in the experimental group. This planned patient training was about weight and edema control, nutrition, signs of hypertension and eclampsia, stress coping methods and fetal health evaluation. Following the training, a booklet containing a summary of the training program was given to each woman. The training was given three day after the initial questionnaire and inventory was performed. The laboratory evaluations and state-trait anxiety inventory were applied both before and after the training (three day after the training).

No training was given to the control group. Questionnaire, scale application and laboratory evaluation for the control group were performed only once. This condition and the fact that the control group was used is an important indicator for the effectiveness of the training activity.

Total antioxidant status (TAS)-Total oxidant status (TOS) analyses

In the experimental group, the laboratory analyses were done one day before and at least three day after the training. And in the control group, the laboratory analyses were done only once. On the same day, the blood samples were stored in the deep freeze at -80 °C and kept until the blood analysis day.

A fully automatic method developed by Erel, TAS test is a method that measures the total antioxidant capacity of the body against strong free radicals. Fe2+ –o-dianisidine complex creates OH radical by forming a Fenton type reaction with hydrogen peroxide. The result is given by spectrophotometrically measuring this reaction in the automatic analyzer. Trolox, a water-soluble analogue of traditionally used vitamin E, was used as a standard and the results were expressed as mmol Trolox Equiv./L [26]. TOS measurement is a fully automatic colorimetric method again developed by Erel. Oxidants existing in the sample oxidize the ferrous ion-o-dianisidine complex to ferric ion. Glycerol molecules in the medium speed up this reaction approximately tripling it. Ferric ions creates a colored complex with "xylenol orange" in an acidic medium. Color intensity, which is related to the quantity of oxidants present in the sample is measured spectrophotometrically. Spectrophotometric analyses were performed with a Perkin Elmer brand spectrophotometer (UV/Vis spectrophotometer model lambda 20–USA) [27].

Oxidative stress index (OSI) was calculated according to the ratio of the TOS to TAS levels.

$$\text{Oxidative stress index (OSI)} = \frac{\text{TOS (μmol } H_2O_2 \text{ equivalent/L)}}{\text{TAS (μmol Trolox equivalent/L)}} \times 100$$

Data analysis

In the analysis of the data, numeric values, number and percentage distribution, arithmetic means, standard deviations, independent sample T-tests, and paired sample t-tests were used.

Results

The average age of the experimental group and the control group are 29.72 ± 4.26 and 30.50 ± 4.27 respectively; the average pregnancy number of the experimental group and the control

group are 1.66 ± 0.97 and 2.91 ± 2.15 respectively. According to pre-pregnancy BMI, the experimental and the control groups are in the over-weights group.

While 50% of the experimental group and 41.7% of the control group in the 28th to 32th gestational week; 41.7% of the experimental group and 22.2% of the control group have had preeclampsia in their previous pregnancies. 50% of the experimental and the control group have indicated eating mainly fruit and vegetables (**Table 1**).

There is no statistically significant difference between the experimental and the control groups regarding the systolic (t = 0.196 P = 0.85) and the diastolic (t = 0.226 P = 0.38) average blood pressure comparisons. The average systolic, diastolic, and mean arterial BP, the birth of weeks and birth weight of the experimental group and the control group were indicated **Table 2**.

There is no statistically significant difference between the TOS (μmol H_2O_2 equivalent/L) (t = -0.33 P = 0.74) and the TAS (mmol trolox equ./L) (t = -1.22 P = 0.57) measurements of the preintervention experimental and control groups (**Table 3**).

In the experimental group, there is a statistically significant difference between the TAS (μmol Trolox equivalent/L) (t = -9.71 P = 0.00) and the TOS (lmol H_2O_2 equ./L) (t = 6.56 P = 0.00) measurements before and after the training (**Table 4**). After the training, while the oxidant level decreases, the antioxidant level increases. A statistically significant difference was determined between the OSI value of the control group (0.010) and that of the experimental group (0.009) (t = 4.56, P = 0.04).

There is no statistically significant difference between the State (t = -0.05 P = 0.06) and the Trait (t = 0.14 P = 0.14) Anxiety Inventory of the pre-training experimental and control groups.

Discussion

In this experimental study, the planned training given to the pregnant women with preeclampsia in the experimental group, has decreased the TOS levels of the pregnant women in the experimental group significantly and increased the TAS levels significantly as against the control group. At the same time, a significant decrease has been determined in the pre and post-training state anxiety levels of the women. This positive effect towards this important and dangerous disorder in pregnancy is important in terms of preventing complications. It is important that this study is the first in literature evaluating oxidative stress markers after training.

There is no statistically significant difference between the TOS (lmol H_2O_2 equ./L), and the TAS (mmol trolox equ./L) levels of the pre-application (training) experimental and control groups. However, in the experimental group, there is a statistically significant difference between the TAS (mmol trolox equ./L) and the TOS (lmol H_2O_2 equ./L) levels before and after the training. After the training, while the oxidant level decreases, the antioxidant level increases. It is observed that the training given has positive effects on the TOS and the TAS levels. The initiatives taken helped to reduce the level of OSI. Although the etiology of preeclampsia is not yet fully understood, there are some studies in the literature showing that oxidative stress plays a role in its pathophysiology [1,28-30]. Markers of lipid peroxidation have been noted to be increased in the plasma of women with preeclampsia [31]. Antioxidants, such as caroteinoids, tocopherols, and ascorbic acid, due to their capacity for scavenging free radicals and their function as inhibitors of reactive oxygen species, are lower in women with preeclampsia [32]. There are various studies concerning the oxidative stress characterized by the failure of the balance between the substances that cause potential cell or tissue damage and the antioxidant substances that has prophylactic effects on these has a crucial role in occurrence of preeclampsia [14,15,33,34].

The effects of stress on relevant risk factors for these diseases immunosuppression, oxidative stress, and elevations in blood pressure and blood lipids are also well documented. Two recent human studies have also demonstrated enhanced production of reactive oxygen species (ROS), including lipid peroxides, during periods of psychological stress [35,36]. Psychological events such as high stress levels, anxiety or depression may directly or indirectly affect pregnancy and may thus lead to preeclampsia It is well established that acute stress elevates blood pressure [34]. Some studies demonstrated that changes of nervous, endocrine, and immune systems were founded in pregnant women encountering stress, which may involve in the development of gestational hypertension and preeclampsia [4,37-39]. In our study too, there is a statistically significant difference in the experimental group between the pre and post-training state anxiety inventories. A decrease in the post-training state anxiety levels has been determined. Similarly, in the study performed by Işık), Erer and Akan the difference between the anxiety levels of the pregnant women with preeclampsia before and after the training of disorder and caring, has been found to be statistically significant ($P < 0.05$). In consequence of the training, knowledge points of the pregnant women with preeclampsia have increased and their state anxiety levels have decreased [20]. Mental intervention and health education are helpful for patients with mild preeclampsia to release the anxiety and improve the clinical outcome and prognosis [22]. Health professionals have

key roles in facilitating preeclamptic women's adjustment to the hospital environment, establishing communication with the family and putting them in touch with people who can give them information [40]. As pointed out in the studies, when information and counsel about their disorder is given to inpatient women who are in the hospital for preeclampsia treatment, their anxiety levels decrease. And according to our research results, the decrease in their anxiety levels has created a positive effect by decreasing their oxidative stress levels. By looking at the information that the oxidative stress levels are efficient in the formation of the disorder, it can be thought that it could have a positive effect on the treatment, too.

There is no statistically significant difference between the experimental and the control groups regarding the systolic and the diastolic average blood pressure comparisons. A difference, although not statistically significant, was found between the systolic blood pressures and diastolic blood pressures both in the control and the experimental groups. There is not a statistically significant difference between the groups with regard to delivery week and birth weight. Because the interventions performed during the study were short-termed, it is thought that they may not have been effective on long term results (blood pressure, delivery week, birth weight). In a similar study on pregnant women, it was determined that social support and planned education were not effective on similar variables [5].

A limitation of the study is that it was performed in a small sample group due to the limitedness of time and facilities. For the future, studies with high power and a large sample size are required. It can be a restriction for the study that the drugs partaking in preeclampsia treatment are in different doses for the patients.

Conclusions

This article will help obstetrician and nurses to evaluate the mental stresses that can affect preeclampsia to identify the risk factors for these conditions, and to determine possible measures to prevent these conditions. Besides the care and the treatment given to the patients with preeclampsia, providing disease information training and psychological support is thought to create a positive development in the treatment of the disorder. Since, as in our research findings, it will affect treatment results positively, routinely providing the patients with information about the disorder and giving them support is recommended. In addition, in the light of the findings obtained, those women with a high anxiety level may be determined during the prenatal period inspections and the essential interventions may be performed by the medical professionals.

For future studies, it can be recommended in terms of supporting the findings that this study be repeated on a larger sample group. If the interventions performed are sustained until the patients are discharged from the hospital, it is thought that this will have a positive effect on the variables such as the newborn's weight, the delivery week etc.

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