RESEARCH ARTICLE

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Effect of Magnesium Sulfate on QT Dispersion in Severe Preeclampsia

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Objective: The study aimed to calculate the QT distance on ECG in patients with severe preeclampsia and to investigate the effect of magnesium sulfate given in treatment on QT dispersion (QTd).

Materials and Methods: Thirty pregnant women with severe preeclampsia as study group and 30 pregnant women of similar age and gestational age without any systemic diseases and pregnancy-related complications as control group were included in the study. Standard 12-channel ECGs of all patients were recorded. Corrected QT (QTc) interval was calculated.

Results: The QTc dispersion of severe preeclamptic patients was 49.35±3.33 msec. The QTc dispersion of the control group was 31.39±0.91 msec. There was a statistically significant difference between the preeclampsia and control groups ($p<0.001$). The QTc dispersion decreased by 33.43±1.13 msec in severely preeclamptic pregnant women after magnesium sulfate ($p<0.001$).

Conclusions: Severe preeclampsia significantly increases QTc dispersion. Administration of magnesium sulfate in treatment positively affects QTd.

Key Words: *Electrocardiography, magnesium sulfate, severe preeclampsia*

Şiddetli Preeklampside Magnezyum Sülfatın QT Dispersiyonu Üzerine Etkisi

Amaç: Şiddetli Preeklampsili hastalarda EKG deki QT mesafesini hesaplamak ve tedavide verilen magnezyum sülfatın QT dispersiyonu (QTD) üzerine etkisini araştırmaktır.

Gereç ve Yöntem: Şiddetli preeklampsi olan 30 gebe ve benzer yaş aralığı ve gebelik haftasında olan, herhangi bir sistemik hastalık ve gebelikle ilişkili komplikasyonların görülmediği 30 gebe kontrol grubu olarak çalışmaya alındı. Tüm olguların 12 kanallı EKG leri çekildi, kaydedildi. Düzeltilmiş QT (QTc) aralığı hesaplandı.

Bulgular: Şiddetli preeklemtik olguların QTc dispersiyonu 49.35±3.33 msn olarak ölçüldü. Kontrol grubunun QTc dispersiyonu 31.39±0.91msn olarak ölçüldü. Preeklampsi ve kontrol grubu arasında anlamlı istatiksel fark izlendi. ($p<0.001$). Magnezyum sülfat sonrası şiddetli preeklemtik gebelerde QTc dispersiyonu 33.43±1.13 msn geriledi ($p<0.001$).

Sonuç: Şiddetli preeklemsi QTc dispersiyonunu belirgin olarak artırmaktadır. Tedavide Magnesium Sülfat verilmesi QT dispersiyonunu olumlu olarak etkilemektedir.

Anahtar Kelimeler**:** *Elektrokardiyografi, magnezyum sülfat, şiddetli preeklampsi*

Introduction

Preeclampsia is a syndrome that affects approximately 3%–5% of pregnant women and is characterized by multisystem involvement (1). However, its physiopathology has not been clearly elucidated. Preeclampsia usually occurs after the 20th week of pregnancy and manifests itself in the form of hypertension and increased protein excretion in the urine (1,2). Preeclampsia may cause intrauterine growth retardation (IUGG), oligohydramnios, abruption of placenta, premature labor, and maternal and fetal death (3,5). QT dispersion (QTd) is found by measuring the difference between the longest QT interval and the shortest QT interval on electrocardiography (6). QTd indicates changes in myocardial repolarization. Increased QTd indicates impaired ventricular homogeneity. This may lead to life-threatening ventricular rhythm disturbances and sudden death (6-8). Magnesium sulfate is an ideal drug for the prevention and treatment of eclampsia and its use is recommended by the World Health Organization (9-10).

QTd in severely preeclamptic pregnant women that were administered magnesium sulfate has not been previously studied. The aim of this study was to investigate the effect of magnesium sulfate on QTd in preeclamptic pregnant women.

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Materials and Methods

In this retrospective study, after obtaining the Ethics Committee approval of our University, 60 pregnant women who were followed up and treated in our gynecology and obstetrics clinic between 2019 and 2020 were included. Thirty pregnant women with severe preeclampsia who were followed up and treated, along with 30 healthy pregnant women of similar gestational age in the third trimester of pregnancy without any chronic disease and pregnancy-related complications were included. A signed informed consent form was obtained from all the patients.

The patients with at least one of the symptoms of a systolic blood pressure >160 mm Hg, diastolic blood pressure >110 mm Hg; thrombocytopenia (<100000/microliter); impaired liver function (increase of liver transaminases [ALT and AST] up to twice the normal concentration, abdominal pain); progressive renal failure (creatinine concentration >1.2 mg/dL or doubling of serum creatinine concentration in the absence of another renal disease); pulmonary edema; brain and visual symptoms were included in the severe preeclampsia group (1, 11). Routine blood biochemical samples (glucose, renal function tests, liver function tests, and electrolytes etc.) were measured with Siemens ADVIA 2400 analyzer (Siemens Healthineers, Berlin, Germany) using appropriate methods.

$MgSO_4$ treatment protocol in severe pre-eclampsia: $MgSO_4$ infusion was administered to pregnant women diagnosed with severe preeclampsia according to the intravenous treatment protocol of Zuspan regimen (12) with a loading dose of 4–6 g given intravenously for over 15 minutes followed by a dose of 1–2 g/hour. Normal serum magnesium level in pregnancy is 1.5–2.5 mg/dL. Therapeutic serum magnesium level in severe preeclampsia is 4.3–8.4 mg/dL. When the serum level is >9 mg/dL, there is a risk of magnesium toxicity (13). Because of the risk of magnesium toxicity, blood magnesium level, hourly patella reflex, respiratory rate, and urine output were monitored.

QT Measurement: Standard 12-lead ECGs (25 mm/sec, 10 mm/mV) of the pregnant women included in the study were obtained before $MgSO_4$ treatment and during $MgSO_4$ maintenance infusion. The interval from the beginning of the QRS complex to the end of the T wave was calculated as the QT interval. No measurements were taken at the leads where the end of the T wave was uncertain. Bazett formula (QT [ms]/RR [sec]1/2) was used for heart rate-corrected QT (QTc) measurement (7). QTd was defined as the difference between the longest and shortest QT intervals in one of the 12 leads. Corrected QT dispersion (QTcD) was measured in a minimum of eight leads, four of which had to be precordial leads. ECGs scanned at high resolution were transferred to a computer and measured.

Exclusion criteria were determined as having a twin pregnancy, intrauterine fetal mortality, thyroid dysfunction, diabetes, and diagnosed heart disease.

Statistics: Statistical analyses were performed using the SPSS 21.0 package (Chicago, Illinois, USA). The data were calculated as “mean±standard deviation. Normal distribution test used. The t-test was used to compare the data and $p<0.05$ was considered significant.

Results

The mean age of the patients included in the study was 28±6.2 years and the mean gestational age was 37.4±1.3 weeks. There was no significant difference between the groups in terms of age and gestational week. The routine evaluation of ECGs in both groups was mostly non-pathologic and there was no significant difference between the two groups in terms of pathologic findings considered. There was no history of arrhythmia in both groups and no rhythm disturbances were encountered during follow-ups. In the preeclamptic patients, the longest QTc duration was 446.20±24.82 msec, the shortest QTc duration was 396.85±21.49 msec, and QTcD was 49.35±3.33 msec. In the control group, the longest QTc duration was 423.24±34.82 msec, the shortest QTc duration was 391.85±33.89 msec, and QTcD was 31.39±0.91 msec. There was a statistically significant difference between the two groups in terms of QTc and QTcD ($p<.001$). In the preeclamptic pregnant women who received magnesium sulfate, the maximum QTc duration was 429.28±22.62 msec, the minimum QTc duration was 395.85±21.49 msec, and QTcD was 33.43±1.13 msec ($p<0.001$). QTcD was shorter in patients receiving $MgSO_4$ treatment.

Table 1. Preeclamptic and healthy pregnants datas

	Preeclamptic patients (n:30)	Healthy pregnant (n:30)	p value
Abnormal ECG findings	None	None	>0.05
QTcD duration	49.35±3.33	31.39±0.91	<0.001
Arrhytmia history	None	None	>0.05

Discussion

In this study, we found that preeclampsia increased QTcD, which indicates regional heterogeneity in myocardial repolarization, while magnesium administered in treatment significantly decreased QTc dispersion. The autonomic, hemodynamic, and hormonal changes that occur during pregnancy, especially the increase in blood volume and the increase in estrogen hormone levels, may trigger arrhythmias by stretching the myocardium and increasing sympathetic tone (14-17). These physiopathological changes may contribute to the occurrence of cardiac arrhythmias by directly affecting myocardial repolarization (17). In addition, many studies have shown the presence of various steroidal sex hormone receptors in the heart. The effect of hormonal changes during pregnancy on the heart suggests that pregnancy may contribute to the proarrhythmic effect of pregnancy (16, 17). QT and QTc, which indicate cardiac repolarization, are longer in

women compared to men in adulthood (18). Therefore, women are more prone to arrhythmogenic conditions, especially torsades de pointes (19). These sex differences are thought to be caused by the effect of sex hormones, especially androgens, on ventricular repolarization. Moreover, virilized women exhibited QTc intervals similar to those of healthy men, while castrated men had QTc intervals similar to normal women (20). These results explain why the repolarization time in women is longer. For this reason, female sex is an independent risk factor in terms of syncope and "torsade de pointes" in patients with hereditary long QT syndrome (14). It is possible that preeclampsia has a significant effect on ventricular repolarization. However, a previous prospective study showed a markedly longer QTc interval in women who developed eclampsia (21). The heterogeneity of the ventricular repolarization phase underlies the electrophysiological changes that occur during preeclampsia, even in the absence of symptoms. Previous studies have focused on the effect of preeclampsia on heart rate variability and have shown a state of sympathetic hyperactivity, especially before the onset of symptoms (22). Electrophysiologic cardiac changes may result from increased hemodynamic stress on the cardiovascular system due to elevated systolic blood pressure. However, high levels of circulating mediators may also have a specific role during preeclampsia (23). In this study, both QT and QTc intervals were longer in preeclamptic women than in the control group. Magnesium sulfate is an ideal drug for the prevention and treatment of eclampsia (11, 14). To the best of our knowledge, this is the first study to investigate the effect of magnesium sulfate given during preeclampsia on QTcD. Serum magnesium and potassium levels may affect QTcD, but no electrolyte imbalance was observed between the groups in our study. Some studies have reported conflicting results of magnesium sulfate on QTcD. Nakaigawa et al. (24) and Grin J et al. (25) claimed that magnesium sulfate affects cardiac repolarization by causing hypokalemia. In our study, hypokalemia was not observed in patients that were administered magnesium sulfate.

Gurfinkel et al. (26) reported that magnesium sulfate improved myocardial heterogeneity and prevented proarrhythmia. Changing ECG parameters such as QTc and QTcD with treatment will have a positive effect on placental blood flow in preeclamptic women and prevent maternal and fetal complications.

As a result, preeclampsia causes alteration of ventricular repolarization as evidenced by prolongation of ECG parameters such as QT and QTcD. Preeclampsia appears to be the only determinant of increased QTcD. Although these changes are mostly asymptomatic, clinical assessment of ventricular repolarization in preeclamptic women can be performed simply with a non-invasive 12-lead ECG. In these cases, magnesium sulfate corrects ventricular repolarization abnormalities and improves placental blood flow.

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