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Lösemi Hastalarında Kemoterapötiklerin Frontal QRS-T Açısı Üzerine Etkisi

The effect of Chemotherapeutics on Frontal QRS-T Angle in Patients with Leukemia

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ÖZ

GİRİŞ ve AMAÇ: *Bazı kemoterapötikler özelikle de antrasiklinlerin kalbe zararlı etkileri olabilir. Biz bu çalışmamız da lösemi hastalarında kemoterapötiklerin frontal QRS-T açısı üzerine etkisini değerlendirmeyi amaçladık.*

YÖNTEM ve GEREÇLER: *Toplam 39 antrasiklin alan lösemi hastası bu retrospektif çalışmada yer aldı. Bütün hastalara antrasiklin öncesi ve sonrası 12 lead elektrokardiografi (EKG) ve ekokardiyografi çekilenler çalışmaya dahil edildi.14 hasta doxorubicin, 25 hasta da idarubicin alıyordu. Bütün hastaların. QT interval, QTc interval, Tp-e interval, Tp-e/QT, Tp-e/QTc ve frontal QRS-T açıları 12 lead EKG üzerinden hesaplandı*

BULGULAR: *Çalışmamız toplam 39 hastadan (%23 kadın) oluşmaktadır. Hastaların ortalama yaşı 40 ±15 di. QT interval (360 ± 32 vs. 368 ± 27.1, P = 0.161), QTc interval (400 ± 6.4 vs. 404 ± 20, P = 0.276), Tp-e interval (80.17 ± 14.2 vs. 84.3 ± 13 P = 0.248). Daha da önemlisi frontal QRS-T angle (17.5 ±17 vs. 16.5 ±14, P = 0.692) değerinin kemoterapi öncesi ve sonrası arasında fark izlenmedi. Ek olarak Tp-e/QT (0.22 ± 0.04 vs. 0.23 ± 0.04, P = 0.543) and Tp-e/QTc (0.20 ± 0.03 vs. 0.20 ± 0.04, P = 0.313) değeride kemoterapi sonrası değişmedi. Alt grup analizinde de benzer sonuçlar elde ettik.*

TARTIŞMA ve SONUÇ: *Hem doxorubicin hem de epirubicin temelli kemoterapi erken fazda düşük doz kullanıldığından dolayı EKG parametrelerini değiştirmedi. Antrasiklinleri güvenli bir biçimde lösemi hastalarına kullanabiliriz.*

Anahtar Kelimeler: *Antrasiklin, frontal ORS-T açısı, kemoterapötikler*

ABSTRACT

INTRODUCTION: *Some of the chemotherapeutics can inflict the cardiac damage, especially anthracyclines. In our study we evaluate to effect of anthracyclines on frontal QRS-T angle in patients with leukemia.*

METHODS: *A total of 39 leukemia patients who take anthracyclines were included in this retrospective study. All patients underwent 12-lead surface electrocardiograms (ECGs) and echocardiography just before and after the anthracyclines. 14 patients were taken doxorubicin and 25 patients were taken idarubicin. QT interval, QTc interval, Tp-e interval, Tp-e/QT, Tp-e/QTc and frontal QRS-T angle were calculated from 12-lead ECGs.*

RESULTS: *In all, 39 patients(23% females) were enrolled in our study. Mean age of patients is 40 ±15 years. QT interval (360 ± 32 vs. 368 ± 27.1, P = 0.161), QTc interval (400 ± 6.4 vs. 404 ± 20, P = 0.276), Tp-e interval (80.17 ± 14.2 vs. 84.3 ± 13 P = 0.248). More importantly, frontal QRS-T angle (17.5 ±17 vs. 16.5 ±14, P = 0.692) was not significantly before and after chemotherapy. In addition, Tp-e/QT (0.22 ± 0.04 vs. 0.23 ± 0.04, P = 0.543) and Tp-e/QTc (0.20 ± 0.03 vs. 0.20 ± 0.04, P = 0.313) were not significantly changed after chemotherapy. When we made subgroup analysis we found same results.*

DISCUSSION AND CONCLUSION: *Both doxorubicin and epirubicin-based chemotherapy did not change the ECG parameter in early phase because of the lower dose. They can be used safely in patient with leukemia.*

Keywords: *Anthracyclines, chemotherapeutics, frontal QRS-,, T angle*

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INTRODUCTION

Cancer treatments are cytotoxic chemotherapies and they have been related to the myocyte damage, heart failure, pericardial disease, hypertension, myocardial ischemia, cardiac arrhythmias, and vasospasm (1-2) . Especially anthracyclines are used in many kind of cancers. They have many cardiotoxic side effects. In addition, cardiotoxicity is a feared side effect of anthracyclines. Cardiotoxicity determines survival of patients with cancer and oncological prognosis (3-4).

Myocardial repolarization is at first evaluated with QT interval then another parameters using like as Tp-e interval and frontal QRS-T angle (5-6) . Both of them were associated with ventricular arrhythmias and cardiovascular mortality (7-11).

Previous studies have consistently shown an association between QTc and chemotherapies (12-13). However, there are not enough available data regarding the association between frontal QRS-T angle (fQRS) and anthracyclines. Therefore, we want to evaluate association between frontal QRS-T angle and anthracyclines , which is an indicator of ventricular arrhythmia risk.

MATERIALS AND METHODS

A total of 39 leukemia patients who take anthracyclines were included in this retrospective study between 2019-2020 years. 14 patients were taken doxorubicin and 25 patients were taken idarubicin. Idarubicin administration was given 20 mg per day for 3 days. Doxorubicin administration was given total 120 mg for all patients. All patients underwent 12-lead surface electrocardiograms (ECGs) and echocardiography just before chemotherapy and after the end of chemotherapy day . QT interval, QTc interval, Tp-e interval, Tp-e/QT, Tp-e/QTc and frontal QRS-T angle were calculated from 12-lead ECGs. Laboratory and hematological parameters of leukemia patients are impaired because of the leukemia and chemotherapy. Therefore, we determined the dyslipidemia by asking whether they were using anti-hyperlipidemic drugs. In addition , we determined smoking status by asking patients.

Patients showed no signs of infection. Patients with coronary artery disease, previous myocardial infarction, left ventricular dysfunction, or left ventricular hypertrophy on echocardiography were excluded. In addition, patients with uncontrolled hypertension, renal dysfunction, connective tissue diseases or thyroid function disorders were not included. The study has been carried out according to the principles of the Declaration of Helsinki and its protocol was approved by local ethical committee.

Electrocardiographic Examination

Electrocardiographic (ECG) measurements of QT and Tp-e intervals were performed manually by two different cardiologists, using calipers and a magnifying glass to decrease measurement errors. The cardiologists were blinded to the echocardiographic measurements of the study population. Subjects with U waves on their ECGs were excluded from the study. The average value of three examinations was calculated for each lead. The QT interval was measured from the beginning of the QRS complex to the end of the T wave, and corrected for heart rate using the Bazett formula (14). The QTd was defined as the difference between the maximum (QTmax) and minimum QT (QTmin) intervals of the 12 leads. The difference between the corrected QTmax (cQTmax) and corrected QTmin (cQTmin) was defined as corrected QTd (cQTd) (15). The Tp-e was measured in each precordial lead and obtained from the difference between QT interval and QT peak interval; measured from the beginning of the QRS until the peak of the T-wave (Figure 1). In case of negative or biphasic T waves, QT peak was measured to the nadir of the T-wave. T waves smaller than 1.5 mm in amplitude were not measured. The reported Tp-e value was the maximum obtained by two observers in all precordial leads (16). The frontal QRS-T angle was measured as the absolute value of the difference between QRS and T wave axes (frontal QRS-T angle = |QRS axis–T axis|). An example of the measurement of frontal QRS-T angle from the automatic report of surface ECG is demonstrated in Figure 2.

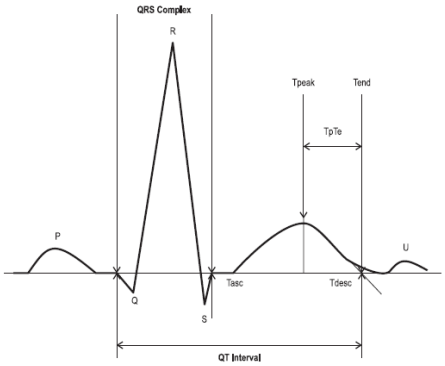

Figure 1. Electrocardiographic parameters measured when assessing the QT interval and Tp-e interval.

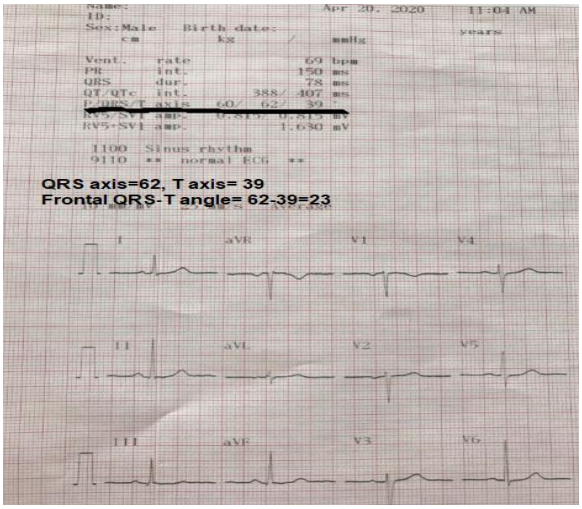

Figure 2. An example of the measurement of frontal QRS-T angle from automatic report of 12-lead surface electrocardiography.

Statistical analysis

Data are analyzed using SPSS version 17 software (SPSS Inc, Chicago, Illinois, USA). To determine whether data fits to normal distribution, Shapiro-Wilk test was executed. Continuous variables are presented as mean standard deviation, and qualitative variables are presented by percentage . Changes of ECG parameters were tested by paired samples t-test for normally distributed data and two related samples test (Wilcoxon Signed Rank test) for non-normally distributed data. All p values were two-tailed and values less than 0.05 were considered to indicate statistical significance.

RESULTS

In all, 39 patients (23% females) were enrolled in our study. Mean age of patients is 40 ±15 years. Baseline clinical, demographic and echocardiographic parameters of the study participants are listed in Table 1.

Table 1. Baseline characteristics and echocardiographic parameters of the study population

Age, years	40 ±15
Gender, female/male	9/30
BMI, kg/m2	25.7 ±1,6
Dyslipidemia, n (%)	12(30)
Hypertension, n (%)	9(23)
Smokers, n (%)	10(25)
LVEDD, mm	47.4 ± 1.8
LVESD, mm	30.4 ± 1.6
LA, mm	35.2 ± 2.2
IVS, mm	9.9 ± 0.9
PW, mm	8.8 ± 0.6
LVEF, %	56.1 ± 1.4

BMI: Body mass index; IVS: Interventricular septum; LA: Left atrium; LVEDD: Left ventricular end-diastolic diameter; LVEF: Left ventricular ejection fraction; LVESD: Left ventricular end-systolic diameter; PW: Posterior wall;

The ECG parameters of the groups are shown in Table 2. Heart rate was different between the two groups (85.4 ± 16.9 vs 81.6 ± 13.6 p=0.177) but ıt was not statistically significant. QT interval (360 ± 32 vs. 368 ± 27.1, P = 0.161), QTc interval (400 ± 6.4 vs. 404 ± 20, P = 0.276), Tp-e interval (80.17 ± 14.2 vs. 84.3 ± 13 P = 0.248). More importantly, frontal QRS-T angle (17.5 ±17 vs. 16.5 ±14, P = 0.692) was not significantly before and after chemotherapy. In addition , Tp-e/QT (0.22 ± 0.04 vs. 0.23 ± 0.04, P = 0.543) and Tp-e/QTc (0.20 ± 0.03 vs. 0.20 ± 0.04, P = 0.313) were not significantly changed after chemotherapy. When we made subgroup analysis we found same results.

Table 2 .Electrocardiographic parameters of the study population

Variable	Before Chemotherapies	After Chemotherapies	p value
HR, (beat/min)	85.4 ± 16.9	81.6 ± 13.6	0.177
QT, (ms)	360 ± 32	368 ± 27.1	0.161
cQT, (ms)	400 ± 6.4	404 ± 20	0.276
Tp-e, (ms)	80.17 ± 14.2	84.3 ± 13	0.248
Tp-e/QT	0.22 ± 0.04	0.23 ± 0.04	0.543
Tp-e/QTc	0.20 ± 0.03	0.20 ± 0.04	0.313
F QRS	17.5 ±17	16.5 ±14	0.692

HR: Heart rate; cQT: Corrected QT ; Tp-e: Transmural dispersion of repolarization; cTp-e: Corrected transmural dispersion of repolarization; F QRS: frontal QRS angel

DISCUSSION

We found that anthracyclines-based chemotherapy did not change the ECG parameters in early phase of cancer treatment. We used both former ECG parameter like as QTc and new parameters such as Tpe and fQRS. All of them shows that we can use lower dose of epuribicin and doxorubicin safely.

However previous studies show that QT interval and doxorubicin-induced cardiotoxicity have a relationship. Especially , doxorubicin effects on heart rate and QRS complex duration. In addition, doxorubicin has been extend the QT-interval (17–22). On the other hand ,this effect of doxorubicin is dose-dependent and QT interval has been reported as the earliest abnormality because of the periodic ECG measurement (17,20). In addition, doxorubicin has been shown to increase susceptibility to arrhythmias (23). However our study is a retrospective and they didn't measure periodic ECG so we may not have detected abnormalities.

Epirubicin, idarubicin, and mitoxantrone are analogs of anthracyclines that are less cardiotoxic than conventional anthracyclines. Epirubicin cardiotoxicity occurs after higher doses of doxorubicin(24-25). New guidelines recommend that the total cumulative dose of anthracyclines limit is 450–550 mg/ml (26-27). In our study lower dose chemotherapies were given patients. Therefore we didn't find any changes at ECG parameters. When we made subgroup analysis we didn't find significant changes between the idarubicin and doxorubicin.

Abnormalities in this measure indicate altered ventricular repolarization, possibly related to underlying structural and functional myocardial changes. For this reason, we used not only one parameter. We use whole ventricular repolarization parameters like as Tpe, fQRS. For instance, abnormal QRS-T angle predicts future cardiovascular disease events and all-cause mortality (28-31). It is very important for leukemia patients survival. On the other hand , patients were young and they have a few risk factor so we may not find any ECG changes.

Limitations of the Study

We recognize that our study has limitations that warrant consideration. First, it was conducted at a single centre. Second, the sample size of the study was relatively small and follow up was not long enough to detect any ventricular arrhythmias in patients with anthracyclines treatment. Thirdly, this study may provide knowledge that can be used in large prospective studies.

CONCLUSION

Both doxorubicin and epirubicin-based chemotherapy did not change the ECG parameter in early phase because of the lower dose. They can be used safely.

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