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Signal Averaged ECG Parameters following Administration of Sotalol in Patients with Arrhythmogenic Right Ventricular Cardiomyopathy

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ABSTRACT

Background: Sotalol is the most effective anti-arrhythmic drug in patients with Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC).

Objective: This retrospective study aimed to evaluate the effect of sotalol on Signal Averaged ECG (SAECG) parameters in patients with ARVC.

Methods: This retrospective study was performed on 11 ARVC patients who were recruited from the cardiology clinic. SAECG was performed in all patients at baseline and six weeks after treatment with sotalol. To assess the effects of sotalol on SAECG, the three following parameters were taken into account: 1) filtered QRS duration, 2) duration of terminal QRS < 40 μv, and 3) Root Mean Square (RMS) voltage of terminal 40 ms. Patients with coronary artery disease, dilative or hypertrophic cardiomyopathy, congenital heart disease, and significant valvular heart disease were excluded from the study.

Results: In total, 11 patients with confirmed ARVC were included. The mean age of the participants was 28 ± 11 years and all patients were male. History of syncope was reported in four patients, ventricular tachycardia in three patients, positive family history of cardiac disorders in two patients, and Epsilone wave in four patients. Besides, Implantable Cardioverter Defibrillators (ICDs) were implanted in five patients. No significant change was detected in the filtered QRS duration following the use of sotalol (P = 0.542). However, a significant reduction was observed in the Low Amplitude Signal (LAS) duration below 40 μv (P = 0.002). Additionally, a significant increase was found in the RMS voltage in the last 40 ms of the QRS (P = 0.043).

Conclusion: Sotalol decreased the duration of terminal QRS < 40 μv. Because of this valuable effect, sotalol should be considered as the first-line therapy for treating ARVC patients.

1. Background

Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC), a right ventricular and occasionally with a simultaneous left ventricular disorder, is characterized by progressive fibro-fatty replacement of the myocardium. This could lead to ventricular tachycardia, which predisposes patients to sudden cardiac death (1, 2). In the recent years, the genes overexpressed in ARVC have been identified via application of advanced genetic testing, indicating strong genetic sources for ARVC (3). Diagnosis of ARVC is based on family history, abnormal electrocardiogram, clinical manifestation, genetic testing, and findings on cardiac Magnetic Resonance Imaging (MRI) and ventricular angiography (4-6). The main pharmacological options are antiarrhythmic agents to prevent life-threatening symptomatic ventricular arrhythmias as well as to improve patients' quality of life (7). However, a few randomized trials have been conducted on such therapeutic strategies in ARVC. Moreover, several antiarrhythmic medications have been used with various agents, including sodium channel blockers, beta-blockers, nitrates, antianginal and class III antiarrhythmic drugs such as amiodarone, and combination therapy (8). Sotalol, a nonselective beta-adrenergic receptor blocker, has been shown to be the most effective anti-arrhythmic drug with approximately a treatment response rate of 68% in patients suffering from ARVC (9). Class I and III antiarrhythmic drugs achieved 18% and 26%

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efficacy, respectively (10, 11). Overall, Sotalol has been deemed to be not only the most effective drug, but also the safest one in the treatment of ARVC-associated arrhythmias (12). However, some studies have reported a lower rate of clinically relevant arrhythmias following the use of sotalol compared to other anti-arrhythmic medications such as amiodarone (13, 14).

2. Objectives

Hence, the present retrospective study aims to evaluate the effect of sotalol on Signal Averaged ECG (SAECG) parameters in patients with ARVC.

3. Patients and Methods

This retrospective study was performed on 11 confirmed ARVC patients who were recruited from a cardiology clinic in Shiraz University of Medical Sciences. The patients' data, including age, gender, cardiac risk factors, family history of sudden death, left ventricular ejection fraction, right ventricular function, previous history of ventricular arrhythmia, aborted sudden cardiac death, syncope, left ventricle involvement, and clinical findings, were collected from their medical records. The patients with coronary artery disease, dilative or hypertrophic cardiomyopathy, congenital heart disease, and significant valvular heart disease were excluded from the study. The participants were treated with sotalol at a dose of 80 mg twice a day. The dose was decreased to 40 mg twice daily if the patient was intolerant to the higher dose. SAECG was done in all patients at baseline and six weeks later. SAECG was recorded by Cardioscan Resting 12-lead during the sinus rhythm with bipolar X, Y, and Z leads. The QRS complexes were amplified, digitized, and averaged (100 - 200 beats/min). In each assessment, the three following parameters were computed: (1) duration of the filtered QRS complex (fQRSd), (2) Root Mean Square (RMS) of amplitude in the terminal 40 ms (RMS40), and (3) duration of Low Amplitude Signal (LAS40). Abnormalities were detected if the filtered QRS complex was more than 114 ms, the square of the terminal signal was lower than 20 μV, or LAS was longer than 38 ms. The patients were considered as having Late Potentials (LPs) if they had abnormalities in at least two SAECG indices.

To assess the effect of sotalol on SAECG parameters, the three following parameters were taken into account: 1) filtered QRS duration in ms, 2) duration of the terminal QRS < 40 μV in ms, and 3) RMS voltage of the terminal 40 ms in μV.

3.1. Statistical Analysis

All statistical analyses were performed using the Statistical Package for Social Sciences, version 16.0 (SPSS Inc., Chicago, IL, USA). SAECG parameters were presented as mean ± standard deviation and were compared before and after the intervention using paired t-test. On the other hand, categorical variables were displayed as proportions. In addition, changes in the proportion of patients exhibiting LPs between baseline and six weeks were investigated using McNemar test. P-values less than 0.05 were considered to be statistically significant.

4. Results

In total, 11 patients with confirmed ARVC were included. The mean age of the participants was 28 ± 11 years and all patients were male. History of syncope was reported in four patients, ventricular tachycardia in three patients, positive family history of cardiac disorders in two patients, and Epsilone wave in four patients. Besides, Implantable Cardioverter Defibrillators (ICDs) were implanted in five patients. As shown in Table 1, no significant change was observed in the filtered QRS duration following the use of sotalol (P = 0.542). However, a significant decrease was detected in LAS (P = 0.002) and a significant increase was found in RMS-40 (P = 0.043).

5. Discussion

SAECG documents the delayed depolarization of myocardial areas with slow conduction, which can trigger monomorphic ventricular tachycardia. The present study revealed the significant effect of sotalol on some SAECG parameters. In a similar study by Freedman et al. (15), the duration of signal-averaged QRS became shorter in cases with no inducible tachycardia during therapy, while it became longer in those with inducible tachycardia. In other words, sotalol could alter QRS and LPs durations as measured by SAECG, implying the slowing of conduction and possibility of interference with this agent's antiarrhythmic efficacy. In another study conducted by Stafford et al. (16) among patients with paroxysmal atrial fibrillation, the administration of sotalol caused a decrease in high-frequency P-wave energy without any effects on the duration of P wave. Contrarily, some studies could not show any changes in time- and frequency-domain parameters of SAECG in patients with ischemic heart disease. The present study revealed that sotalol could decrease the duration of terminal QRS < 40 μV. This was a valuable and interesting result, introducing sotalol as an appropriate pharmacological intervention in ARVC patients. There are significant heterogeneities among the studies reporting the effects of sotalol as a non-selective beta-blocker with anti-arrhythmic efficacies. Several reports have supported the clinical benefits of sotalol therapy in ARVC cases, while some others have indicated that sotalol could not be a therapeutic choice in ARVC cases. Wichter et al. (17) proved sotalol to be a highly effective agent compared to other drugs, including class Ia, Ib, and Ic agents, beta-blockers,

Table 1. SAECG Parameters following Sotalol Administration

SAECG Parameter	Baseline	After Sotalol Therapy	P
fQRSD (ms)	118.36 ± 2.420	118.00 ± 3.521	0.542
LAS (ms)	41.73 ± 4.496	35.36 ± 3.042	0.002
RMS-40 (μv)	20.36 ± 3.325	26.18 ± 6.997	0.043

Abbreviations: fQRSD, filtered QRS duration; LAS, low amplitude signal duration below 40 μV; RMS-40, root mean square voltage in the last 40 ms of the QRS

amiodarone, and verapamil, in cases with inducible and non-inducible ventricular tachycardia. Marcus et al. (18) reported that there was no acceptable follow-up and assessment of the efficacy and safety of antiarrhythmic drugs after discharge from the hospital, which could massively affect true findings. They also believed that evaluation of ventricular arrhythmias was incomplete in the previous reports and that administration of sotalol as the first-line therapy for preventing or treating ventricular arrhythmias could not be acceptable in ARVC patients. They reported that the average length of ventricular arrhythmias was lower in patients with sotalol therapy compared to those who had undergone intervention without sotalol. Furthermore, they indicated that the administration of a high dose of sotalol could induce inappropriate events and adjustment of the dosage could surely affect the clinical outcomes and present advantages and disadvantages.

5.1. Conclusion

Sotalol decreased the duration of terminal QRS < 40 μV. Because of this valuable effect, sotalol should be considered as the first-line therapy for treating ARVC patients.

5.2. Clinical Trial Registration Code

This was a retrospective research.

5.3. Ethical Approval

This study was approved by the Ethics Committee of the University (IR.SUMS.MED.REC.1396.71).

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Authors' Contribution

Study concept and design: A.A.; Acquisition of data: A.A., M.H., and Z.M.; Critical revision of the manuscript for important intellectual content: A.A. and V.J.

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