ASSESSMENT OF DIFFERENT ADMINISTRATION SCHEDULES OF SOTALOL BY ELECTROCARDIOGRAPHY

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Abstract

In this study we examined the effects of dosage and timing of sotalol treatment (prescribed for preventing fibrillation) on the occurrence of arrhythmias in an 82-year old man. We recorded and analysed ECG data obtained over a 7-day period in relation to sotalol dosage and timing. Our result showed that, in the absence of treatment, the heart rate tended to increase, the number of ventricular premature beats (VPCs) was higher and the number of atrial premature beats (APCs) was lower.

Key words

Arrhythmia, Atrial fibrillation, Sotalol treatment

INTRODUCTION

The ambulatory monitoring of blood pressure and heart rate is very important for treatment evaluation. Usually, it is carried out only for short spans, i.e., 24 or 48 hours (1). The recommended use of ambulatory monitoring for 7 days as a minimum (2) stems from several objectives.

First, the desirability of improving both the precision and accuracy of the daily mean value of blood pressure is a concern, as is the need to assess the extent of day-to-day variability in the circadian characteristics of blood pressure and heart rate, preferably in association with a diary to determine which, if any, activities or other life events may adversely influence the blood pressure pattern. There are two other concerns of even greater importance. One is the possibility to assess the patient’s response to treatment on an individual basis once a longitudinal record is available. The other is the availability of a chronodiagnosis, i.e., the first step in chronotherapy (timed treatment) (2).

The scheduling of sotalol is discussed separately in terms of putative effects on blood pressure (BP). Longitudinal BP monitoring has suggested that twice
daily treatment with sotalol may be associated with an increased circadian amplitude of BP beyond a threshold value, above which the risk of adverse vascular events (cerebral ischemic events and nephropathy in particular) has increased with statistical significance (9).

This study was designed to examine the effects of dosage and timing of sotalol treatment (prescribed for preventing fibrillation) in an 82-year old man. The effect evaluation was based ECG records over 7-days of monitoring and their analysis for the presence of ventricular (VPC) and atrial premature (APC) beats.

**CASE REPORT AND METHODS**

An 82-year old man with a history of coronary artery disease was prescribed sotalol (Betapace; 80mg) treatment, twice a day (morning and evening) after a second quadruple coronary artery bypass grafting. For 11 days, he monitored his electrocardiogram by a two-channel ECG recorder (Fukuda Denshi, Tokyo, Japan), while also monitoring his blood pressure (BP). The data were analysed using the Fukuda Denshi system that included an interval counter of R-R intervals and a built-in A/D converter (interval resolution, 8 ms). For each ~24-hour monitoring tape, the total number of heart beats was counted and minimal and maximal heart rates were determined. The average number of VPCs and APCs per hour were also determined and compared with the treatment schedule: at first 6 days sotalol was taken in a single tablet in the morning, for next 3 days it was administered twice a day (morning and evening) and, on the last two days, there was no treatment. The recorded values were evaluated by one-way analyses of variance (ANOVA) and expressed as means± SD.

**RESULTS**

The effects of sotalol treatment on cardiovascular parameters are shown in Table 1. There were no significant differences between the two treatments but, in the absence of treatment, the heart rate tended to increase, the number of VPCs was higher while that of APCs was lower.

The differences in VPCs were of borderline statistical significance (F=4.009; P=0.062).

<table>
<thead>
<tr>
<th>Treatment Schedule</th>
<th>One tablet (morning)</th>
<th>Sotalol treatment (morning, evening)</th>
<th>No treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (HR)</td>
<td>63.7 ± 1.4</td>
<td>59.4 ± 0.8</td>
<td>66.1 ± 6.4</td>
</tr>
<tr>
<td>Minimal HR</td>
<td>45.8 ± 1.0</td>
<td>43.7 ± 1.2</td>
<td>50.0 ± 5.0</td>
</tr>
<tr>
<td>Maximal HR</td>
<td>111.7 ± 3.1</td>
<td>102.3 ± 4.3</td>
<td>110.5 ± 6.5</td>
</tr>
<tr>
<td>VPCs</td>
<td>49.9 ± 3.6</td>
<td>31.7 ± 1.4</td>
<td>80.7 ± 35.2</td>
</tr>
<tr>
<td>VPCs</td>
<td>131.5 ± 25.1</td>
<td>159.9 ± 13.1</td>
<td>78.1 ± 40.3</td>
</tr>
</tbody>
</table>

VPCs , ventricular premature beats; VPCs , atrial premature beats

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DISCUSSION

It appears that the difference between any treatment and no treatment is larger than the difference between treatment with two doses and that with a single dose. When data on treatment were pooled and compared with the data after no treatment, the difference in terms of VPCs was statistically significant (F=5.630; P=0.042). Also in the absence of treatment, the Lown index dropped to 4B from a value of 3 on all the other days. Although the results presented herein are based only on a single patient, they suggest the merit of conducting prospective studies involving long-term follow-ups to evaluate morbidity and mortality outcomes in relation to one-daily or two-daily treatment with sotalol.

Considering the extent of hour-to-hour and day-to-day variability in blood pressure (3–5), around-the-clock monitoring for 7 days has been recommended in order to detect blood pressure overswinging or circadian hyper-amplitude-tension (CHAT) and to reduce the number of false positive and false negative diagnoses (6, 7). St. Anna Hospital (Brno, Czech Republic), Tokyo Women’s Medical University, and the city of Urausu, Hokkaido, Japan, along with the Halberg Center at the University of Minnesota in Minneapolis, are currently offering 7-day/24-hour screening schemes to interested parties. Reports of the results of analyses of the data prompted by such projects are facilitated by the integration of different procedural steps in an updated sphygmochron (8).

The main issue is not whether sotalol treatment is indicated, but rather what are the relative risks firstly of suppressing fewer undesirable arrhythmias by reducing treatment with two daily doses to a single morning tablet and, secondly, of iatrogenic CHAT (circadian hyper-amplitude-tension, i.e., an excessive circadian blood pressure amplitude). Answers to both questions will require studies of longer monitoring spans and analyses based on a denser assessment before they can be called chronobiologic N-of-1 trials.

Acknowledgement

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Stanovení různých režimů dávkování sotalolu podle elektrokardiografie

Souhrn

V této práci jsme sledovali účinky léčby sotalololem v závislosti na různých režimech dávkování na výskyt arytmii u 82-letého muže. Zaznamenávali jsme po dobu sedmi dnů EKG křivky, které jsme analyzovali vztahem k účinku léčby sotalololem, podávaným v určitých dávkách a časových intervalech. Naše výsledky ukázaly, že bez léčby srdeční frekvence měla tendenci se zvýšit, počet komorových extrasystol (VPCs) byl vyšší, a počet síťových extrasystol (APCs) byl nižší.

References