E.C.G. FINDINGS IN NORMAL RATS AND AFTER ADMINISTRATION OF
ISOPROTERENOL

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Summary: Electrocardiograms of normal rats were studied and compared with those of the rats receiving parenteral IPT. The rat E.C.G. resembles essentially human E.C.G. IPT administration brought about E.C.G. changes suggesting myocardial infarction. Appearance of Q wave in aVL was a consistent feature of E.C.G. after 24 hr of IPT injection. With additional doses of IPT the ECG in these rats showed a well marked Q wave and increase in the amplitudes of R and T waves in limb and increase in the amplitudes of R and T waves in limb and chest leads.

Key words: isoproterenol myocardial infarction electrocardiogram

INTRODUCTION

Isoproterenol (IPT) administration is an important experimental tool to produce consistent myocardial infarction (MI) in animals (15), as surgical methods are found to be disappointing because of the difficulty in achieving standard myocardial infarcts (1,6,12).

Though a number of workers (5,13,14) have reported changes in electrocardiograms (ECG) in clinical studies during administration of IPT, there are few reports of such studies in animals (9). The present work was, therefore, undertaken to study ECG in normal rats and ECG changes after administration of IPT.

MATERIALS AND METHODS

Healthy adult albino rats of either sex and weighing between 100-180 g were used in this study.

Control group: ECG were recorded from 42 rats for control studies.

Experimental group: IPT sulphate (Burroughs Wellcome & Co., India) in dose of 100 mg/kg was administered subcutaneously (SC) to each animal in this group and if the study was continued for more than 24 hr the same dose was repeated at 24 hr intervals.

Groups of 5 rats each were utilized to study effects of IPT by recording ECG 24, 48,72 and 96 hr (Group I, II, III and IV) after administration of first dose. The later three groups received additional doses of IPT.
Electrocardiography: Under light ether anaesthesia, electrodes constructed from 26 gauge hypodermic needles were placed subcutaneously in the gently extended limbs of the supine animal. Standard leads (I, II, III), and augmented limb leads (aVR, aVL, aVF), as well as precordial leads (V1, V2, and V4 to V6) were used to record ECG at paper speed of 100 mm per sec on a Grass Polygraph. For precordial leads, electrodes were placed SC on chest sites corresponding to the positions in a human subject. Sensitivity was adjusted to provide a deflection of 20 mm for 1 mV standard square wave. ECG was also recorded in prone position of the animal using limb leads only.

At the end of the study, the animal was sacrificed. The heart was excised and examined for any macroscopic changes and later processed histologically.

ECG of the rat recorded in dorsal position was not significantly different from that recorded in the ventral position (2). On the other hand the supine position facilitated the recordings from the precordial leads; needed for our present study. Hence, the results of this work include the recordings taken from the animals in supine position only.

RESULTS

Amplitudes of the waves recorded with various leads in control rats are shown in Table I.

The changes seen in the heart rates, P.R. interval, QRS complex and Q.T. interval following IPT administration are given in Table II.

Histological findings revealed interstitial edema and hemorrhagic necrosis resulting in separation of myocardial fibres. Inflammatory cells were also seen.

DISCUSSION

Normal ECG of the rat resembles in essential detail that of man (Fig.1). Heart rates of the control rats in our study are (421 ± 8.97) comparable to the values reported by Hill et al. (9) but are slightly higher than those reported by Fraser et al. (7).

An upright P wave is present in all leads except in aVR and aVL where it is inverted. Similar pattern was observed by Benifield and Lehr (4). P-R interval (Table II) in this study does not show any relation with the heart rates, these observations are in consistent with those of Fraser et al. (7) and Benifield and Lehr (4).
TABLE I: The amplitudes (mV) of various E.C.G. waves recorded with limb (I, II, III and aVR, aVL and aVF) and chest (V1, V2, and V4 to V6) leads in the control rats (Mean ± SEM).

<table>
<thead>
<tr>
<th>ECG Waves</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>aVR</th>
<th>aVL</th>
<th>aVF</th>
<th>V1</th>
<th>V2</th>
<th>V3</th>
<th>V4</th>
<th>V5</th>
<th>V6</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>0.028 ± 0.002</td>
<td>0.0515 ± 0.0019</td>
<td>0.0428 ± 0.0022</td>
<td>0.0360 ± 0.0019</td>
<td>0.0235 ± 0.0019</td>
<td>0.048 ± 0.0028</td>
<td>0.032 ± 0.0025</td>
<td>0.0410 ± 0.0031</td>
<td>0.0380 ± 0.0025</td>
<td>0.0310 ± 0.0028</td>
<td>0.0204 ± 0.0028</td>
<td></td>
</tr>
<tr>
<td>Q</td>
<td>0.0472 ± 0.0085</td>
<td>— — ± 0.0093</td>
<td>0.2820 ± 0.0132</td>
<td>0.078 ± — —</td>
<td>0.0008</td>
<td>— —</td>
<td>0.0008</td>
<td>— —</td>
<td>0.0008</td>
<td>— —</td>
<td>0.0008</td>
<td>— —</td>
</tr>
<tr>
<td>R</td>
<td>0.1953 ± 0.0204</td>
<td>0.3612 ± 0.0146</td>
<td>0.2868 ± 0.0139</td>
<td>0.1139 ± 0.0121</td>
<td>0.2886 ± 0.0137</td>
<td>0.1527 ± 0.0201</td>
<td>0.3100 ± 0.303</td>
<td>0.3427 ± 0.0295</td>
<td>0.2794 ± 0.0237</td>
<td>0.1721 ± 0.0190</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>0.0627 ± 0.0100</td>
<td>0.0400 ± 0.0073</td>
<td>0.1150 ± 0.0204</td>
<td>0.1411 ± 0.0038</td>
<td>0.0611 ± 0.0101</td>
<td>0.1100 ± 0.0166</td>
<td>0.1244 ± 0.0166</td>
<td>0.0480 ± 0.0004</td>
<td>0.0809 ± 0.0044</td>
<td>0.0433 ± 0.0084</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T</td>
<td>0.0852 ± 0.0100</td>
<td>0.1258 ± 0.0083</td>
<td>0.0999 ± 0.0060</td>
<td>0.0900 ± 0.0060</td>
<td>0.0853 ± 0.0049</td>
<td>0.1022 ± 0.0050</td>
<td>0.1014 ± 0.0102</td>
<td>0.1560 ± 0.0137</td>
<td>0.1320 ± 0.0107</td>
<td>0.1017 ± 0.0091</td>
<td>0.0615 ± 0.0062</td>
<td></td>
</tr>
</tbody>
</table>
Isoproterenol and ECG Changes

Heart rate, P-R interval, QRS complex and Q-T interval in control and experimental animals 24, 48, 72 and 96 hr. (Group I, II, III & IV) after administration of IPT. Values are mean ± SEM.

<table>
<thead>
<tr>
<th>Group</th>
<th>Heart rate</th>
<th>P-R interval</th>
<th>QRS complex</th>
<th>Q-T interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>beats/min</td>
<td>in sec</td>
<td>in sec</td>
<td>in sec</td>
</tr>
<tr>
<td>Control</td>
<td>421 ± 8.97</td>
<td>0.0429 ± 0.0006</td>
<td>0.0213 ± 0.0017</td>
<td>0.0701 ± 0.0005</td>
</tr>
<tr>
<td>Group I</td>
<td>419 ± 17.5</td>
<td>0.0396 ± 0.0008</td>
<td>0.0224 ± 0.0046</td>
<td>0.0724 ± 0.0037</td>
</tr>
<tr>
<td>Group II</td>
<td>398 ± 11.6</td>
<td>0.0416 ± 0.0026</td>
<td>0.0246 ± 0.0013</td>
<td>0.0739 ± 0.0039</td>
</tr>
<tr>
<td>Group III</td>
<td>421 ± 17.7</td>
<td>0.0420 ± 0.0003</td>
<td>0.0260 ± 0.0017</td>
<td>0.0767 ± 0.0047</td>
</tr>
<tr>
<td>Group IV</td>
<td>439 ± 26.9</td>
<td>0.0410 ± 0.0015</td>
<td>0.0265 ± 0.0017</td>
<td>0.0777 ± 0.0001</td>
</tr>
</tbody>
</table>

*P 0.05  **P 0.01  ***P 0.001

In control animals small Q wave is observed in aVR and aVL, but occasionally it is present as an insignificant wave in lead I. Identical observations are reported by Hill and Fraser (7,9). Main deflection in the ventricular complex is R wave in all leads. In aVR, a late R wave is always recorded, an observation also reported by Samphi and White (16).

'N' wave, a positive deflection between QRS and T and described in rat ECG by Heise (8) is not observed in this study. Other studies (7,9,11,12 and 16) too do not confirm Heise's findings.

QRS pattern resembles that reported by few workers (7,8) in their rats but differs slightly from those observed by others (10,16). S-wave is present in all leads and T is inscribed in direct continuity of S' wave. There is an elevation of ST segment as observed by others (9,15) and they called it as false ST segment elevation. Lombard (11) has also reported similar findings in small mammals including rats, these findings were also confirmed by Bainfield and Lehr (3) who observed blending or fusing of T wave with the QRS complex and absence of a true ST segment. However, this deviation from the human ECG could not be explained. Some of the leads display that the T wave component starts before the down stroke of R reaches the base line. No double peak of T wave is found in our series as reported by Hill et al. (9). Q-T interval is also close to the values of other workers (9, 10,11).
After 24 hr. of IPT injection, heart rate did not differ from that of the control, whereas there was an increase in QRS and Q-T intervals associated with decrease in P-R interval. This stage was marked by appearance of small Q wave in aVL. These changes suggest the onset of ischaemia (Fig.2).

Fig. 1: Electrocardiographic records of control rats. Leads II, V₁, V₂ & V₆ show “false” elevation of ST segment.

In the experimental groups subjected to additional doses of IPT, presence of a wall...
from that of the control, whereas with decrease in P-R interval.

These changes suggest the presence of IPT. 

Fig. 2: ECG records of the experimental rats. Gradual increase in amplitudes of Q in L1 and AVL and R and T waves in V2 seen 24 hr (upper tracing), 48 hr (middle tracing) and 72 hr (lower tracing) after IPT.

Fig. 3: ECG record of experimental rat after 96 hr of IPT. ‘R’ wave in V2 shows high amplitude. Notch on the downstroke of ‘R’ and ‘T’ is due to 50 cycle filter. ‘Q’ wave is seen in V5 and V6.
marked Q wave was a consistent feature in Lead I, aVR and aVL obtained at the end of 72 and 96 hrs. (Fig.2). Moreover, after 96 hrs. (Fig.3), Q wave is also seen in precordial leads V4, V5, V6, suggestive of extensive lateral myocardial infarction. A gradual increase in amplitude of R wave, reaching a peak of 1.075 mv. after 96 hrs. was noticed in V1 and V2 of all record taken after 24 hrs and is indicative of anterion myocardial infarction. Increase in amplitude of T wave was also recorded after 72 and 96 hrs in all precordial leads.

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REFERENCES