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

A.K. KELA, L. PRAKASAM REDDY AND D.P. THOMBRE

Departments of Pharmacology and Physiology,
Jawaharlal Institute of Post-graduate Medical Education and Research,
Pondicherry-605 006

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 consistant 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 roup: 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 and III), and augmented limb leads (aVR, aVL, aVF), as well as precordial leads (V_1, V_2, and V_4 to V_6) 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 interstital edema and haemorrhagic 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 consistant with those of Fraser *et al.* (7) and Beinfield 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 (V_1, V_2, and V_4 to V_6) leads in the control rats (Mean ± SEM)

ECG Waves	*I*	*II*	*III*	*aVR*	*aVL*	*aVF*	V_1	V_2	V_4	V_5	V_6
P	0.028 ± 0.002	0.0515 ± 0.0019	0.0428 ± 0.0022	0.0360 ± 0.0019	0.0235 ± 0.0019	0.048 ± 0.0028	0.032 ± 0.0025	0.0410 ± 0.0031	0.0380 ± 0.0025	0.0310 ± 0.0028	0.0204 ± 0.0015
Q	0.0472 ± 0.0085	——	——	0.2820 ± 0.0093	0.078 ± 0.0132	——	——	——	——	——	——
R	0.1953 ± 0.0204	0.3512 ± 0.0145	0.2868 ± 0.0139	——	0.1138 ± 0.0121	0.2885 ± 0.0137	0.1527 ± 0.0201	0.3100 ± 0.306	0.3427 ± 0.0295	0.2794 ± 0.0237	0.1721 ± 0.0190
S	0.0627 ± 0.0100	0.0400 ± 0.0073	0.1150 ± 0.0204	——	0.1411 ± 0.0038	0.0511 ± 0.0101	0.1100 ± 0.0166	0.1244 ± 0.0404	0.0480 ± 0.0074	0.0609 ± 0.0044	0.0433 ± 0.0084
T	0.0858 ± 0.0100	0.1258 ± 0.0083	0.0895 ± 0.0600	0.0900 ± 0.0060	0.0653 ± 0.0049	0.1022 ± 0.0050	0.1014 ± 0.0102	0.1550 ± 0.0137	0.132 ± 0.0107	0.1017 ± 0.0091	0.0615 ± 0.0062

TABLE II: 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.

Group	*Heart rate beats/min*	*P–R interval in sec*	*QRS complex in sec*	*Q–T interval in sec*
Control	421±8.97	0.0429±0.0005	0.0213±0.0017	0.0701±0.0006
Group I	419±17.5	0.0396±0.0008*	0.0224±0.0046	0.0724±0.0037
Group II	398±11.6	0.0416±0.0026	0.0246±0.0013***	0.0736±0.0039
Group III	421±17.7	0.0420±0.003	0.0260±0.0017***	0.0767±0.0047**
Group IV	439±26.9	0.0410±0.0015	0.0265±0.0017***	0.0777±0.001***

*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 (10,15). 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 Beinfield 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 ur 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).

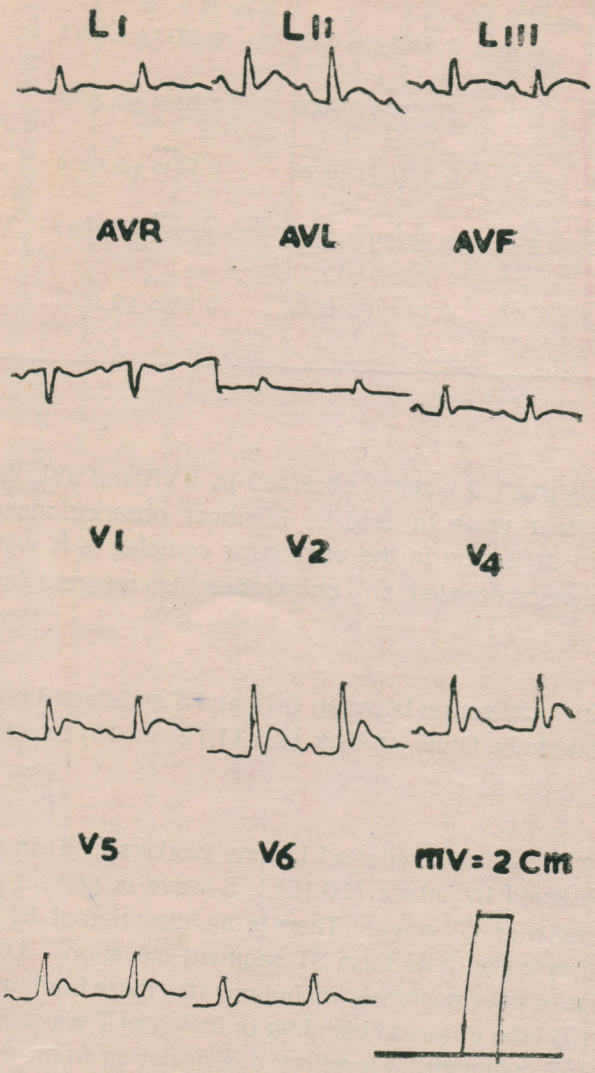

Fig. 1 : Electrocardiographic records of control rats. Leads II, V_1, V_2 & V_4 show "false" elevation of ST segment.

In the experimental groups subjected to additional doses of IPT, presence of a well

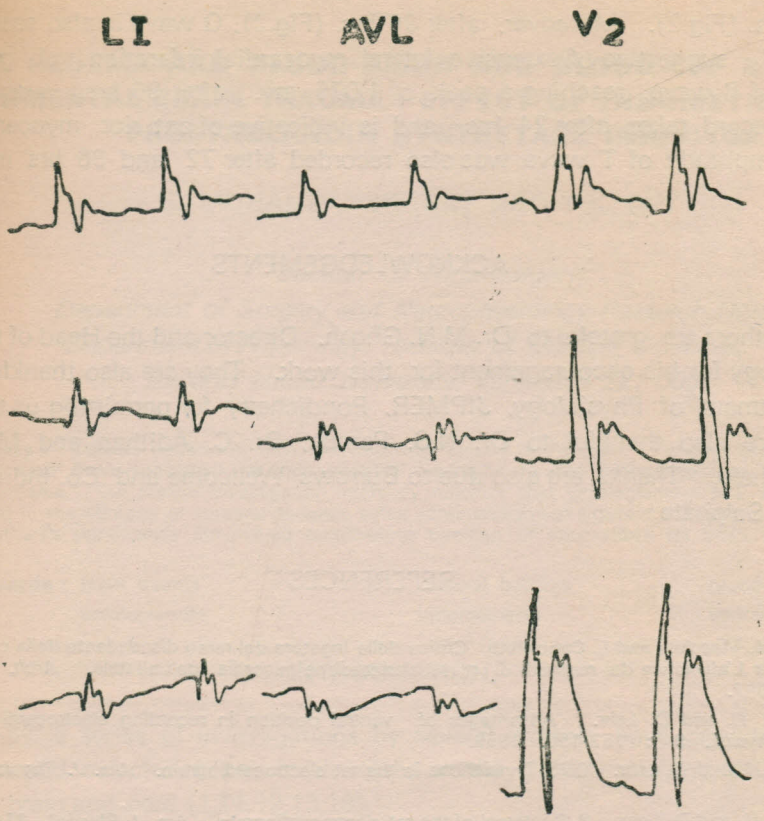

Fig. 2 : ECG records of the experimental rats. Gradual increase in amplitudes of Q in L1 and AVL and R and T waves in V_2 seen 24 hr (upper tracing), 48 hr (middle tracing) and 72 hr (lower tracing) after IPT.

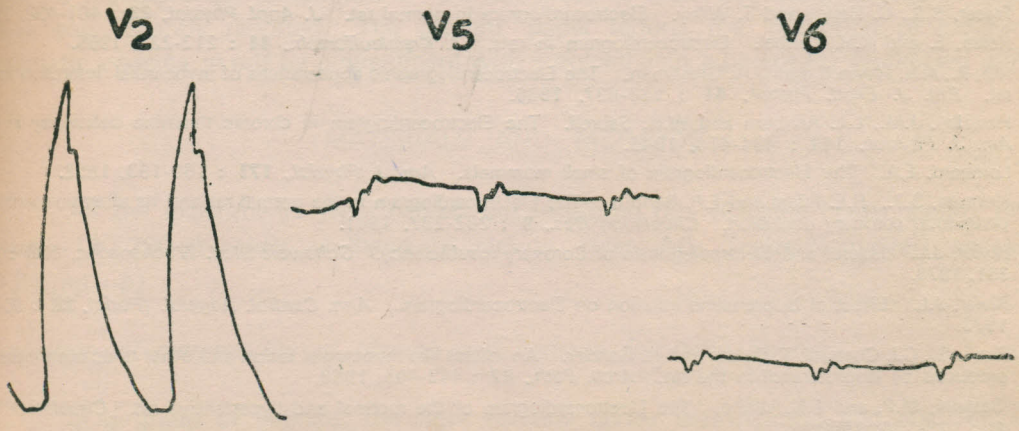

Fig. 3 : ECG record of experimental rat after 96 hr of IPT. 'R' wave in V_2 shows high amplitude. Notch on the downstroke of 'R' and 'T' is due to 50 cycle filter. 'Q' wave is seen in V_5 and V_6.

marked Q wave was a consistant feature in Lead I, aVR and aVL obtained at the end of 48 72 and 96 hrs. (Fig.2). Moreover, after 96 hrs. (Fig.3), Q wave is also seen in precordia leads V_4, V_5, V_6, suggestive of extensive lateral myocardial infarction. A gradual increas in amplitude of R wave, reaching a peak of 1.075 mv. after 96 hrs. was noticed in V and V_2 of all record taken after 24 hrs and is indicative of ant rior myocardial infarctio Increase in amplitude of T wave was also recorded after 72 and 96 hrs in all precordia leads.

ACKNOWLEDGEMENTS

The authors are grateful to Dr. M.N. Ghosh, Director and the Head of the Departmen of Pharmacology for his encouragement for this work. They are also thankful to the Hea of the Department of Physiology, JIPMER, Pondicherry for permitting us to carry out thi work. We are also thankful to Dr. N.S. Parmar, Dr. C. Adithan and Mr. Ramalingam for their kind help. Thanks are also due to Burrows Wellcome and Co. India for supply o Isoproterenol Sulphate.

REFERENCES

1. Allegra, G., M. Macchini and L. Cancellotti. Critica della legatura del ramo discendente della coronaria. Sinistra quale test per L'efficience dei methodi di revascolarizzazione micordia sperimentale. *Arch. Chir Torace.*, **11** : 299-304, 1957.
2. Beinfield, W. H. and D. Lehr. Advantages of ventral position in recording electrocardiograms of the rat. *J. Appl. Physiol.*, **9** : 153-156, 1956.
3. Beinfield, W.H. and D. Lehr. QRS-T variations in the rat electrocardiogram. *Am. J. Physiol.*, **214** : 197-204, 1968.
4. Beinfield, W.H. and D. Lehr. P-R interval of the rat electrocardiogram. *Am. J. Physiol.*, **214** : 205-211, 1968.
5. Berger, H.J. Isoprenaline and Electrocardiographic findings. *Ann. Intern., Med.*, **84** : 221, 1976.
6. Fox, J.R. Jr. and F.A. Hughes, Jr. Experimental protection of dog heart against coronary artery ligation. *South M.J.*, **48** : 599-602, 1955.
7. Fraser, R.S., C. Harley and T. Wiley. Electrocardiogram in normal rat. *J. Appl. Physiol.*, **23** : 401-402, 1967.
8. Heise, E. and K.H. Kimbel. Electrocardiogram in rats. *Z. Kreislaufforsch.*, **44** : 212-221, 1955.
9. Hill, R., A.N. Howard and G.A. Greshman, The Electrocardiographic appearances of myocardial infarction in the rat. *Brit. J. Exptl. Pathol.*, **41** : 633-637, 1966.
10. Huncley, J.M., L.L. Ashburn and W.H. Sebrell. The Electrocardiogram in chronic thiamino deficiency in rats. *Am. J. Physiol.*, **144** : 404-414, 1945.
11. Lombard, E.A. The Electrocardiogram of small mammals. *Am. J. Physiol.*, **171** : 189-193, 1952.
12. Norman, S.J., R.E. Priest and E.P. Benditt. The Electrocardiogram in the normal rat and its alteration with experimental coronary occlusion. *Circulation Res.*, **9** : 282-287, 1961.
13. Rivier, J.L. Isuprel and Electrodiagnosis of Coronary insufficiency. *Scheweiz Med. Wochenschr.*, **103** : 348-351, 1973.
14. Rivier, J.L. Effect of Isoprenaline infusion on Electrocardiogram. *Ann. Cardiol. Angeiol. (Paris)*, **22** : 95-100, 1973.
15. Rona, G., C.I. Chappel, T. Balazs and R. Gandry. An infarct like myocardial lesion and other toxic manifestations produced by Isoproterenol in the rat. *Arch. Path.*, **67** : 443-455, 1959.
16. Samphi, M.P. and F.N. White. The Electrocardiogram of the rnormal and hypertensive rat. *Circulation Res.*, **8** : 129-134, 1960.