

ELECTROCARDIOGRAPHIC CHANGES UNDER THERAPY WITH Ro 1-9334, A SYNTHETIC RACEMIC 2-DEHYDROEMETINE

Antonio GONZÁLEZ DE COSSÍO

SUMMARY

The effects of Ro 1-9334 (2-dehydroemetine) on the electrocardiogram were studied in 14 patients.

No changes of P, P-R, QRS or AQRS were observed. QT was prolonged in 4 patients. T diminished its voltage in 6 patients and showed an inversion in 2. ST revealed no changes.

These electrocardiographic changes are considerably less frequent and of shorter duration than those provoked by emetine.

INTRODUCTION

Emetine hydrochloride has been established for a long time as the most specific treatment for intestinal and extra-intestinal amebiasis. However, the risks entailed by its high toxicity have limited its use for some years past and forced the investigators to search for new substances with equivalent efficacy but without the side-effects of emetine.

During the chemical research which led to the total industrial synthesis of emetine¹, several substances exhibiting experimental anti-schistosomic and marked antiamebic activity, and less toxicity than emetine were discovered². Ro 1-9334^{*}, 2-dehydroemetine, was chosen from these substances for investigation in humans. The first results obtained seem to confirm its therapeutic effect in amebiasis³ and schistosomiasis⁴.

The aim of our work was to determine whether, and how important, the electrocar-

diographic changes appear under treatment with Ro 1-9334, and to compare them with the changes caused by emetine which have been repeatedly described in the medical literature by other authors and ourselves^{2, 3, 4, 5, 7}.

MATERIAL AND METHODS

We studied 14 patients with amebic liver abscess. The total doses administered over 10 days varied from 0.01 to 0.02 g/kg body-weight with an average of 0.018 g/kg. The daily doses varied from 0.02 g to 0.08 g. The therapy was given by subcutaneous injection.

As explained in a previous paper³ the electrocardiograms were taken repeatedly and regularly, before, during and after the treatment. The tracings included the three standard leads, the augmented unipolar limb leads, and six precordial V leads.

Department of Electrocardiography, Hospital de Enfermedades de la Nutrición, México City.

* Synthesized by F. Hoffmann-La Roche & Co., Basle, Switzerland.

RESULTS

P showed no modification.

P-R remained within normal limits.

QRS and AQRS showed no alteration.

QT was slightly prolonged in 4 cases.

T voltage diminished in 6 cases and an inversion was observed in 2 of them (V_1 and V_3).

ST showed no change.

TABLE I

	No. of cases		Changes appeared after administration of Ro 1-9334 in following doses (mg/kg)
	No.	%	
QT prolongation	4	33	0.02
ST elevation	—	—	
T lower voltage	6	50	0.02
T inversion	2	16	0.02

These changes disappeared between 10 and 15 days after discontinuation of the treat-

ment. Figures 1-6 show some of the curves observed.

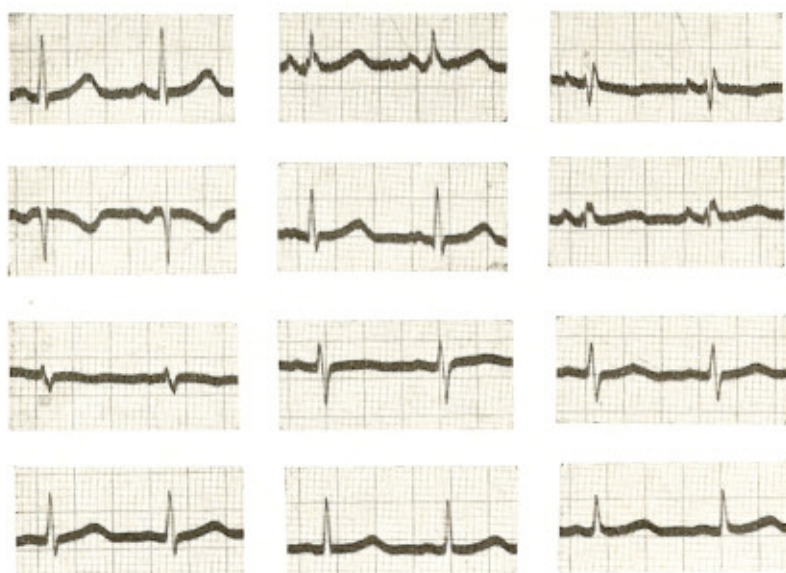


Fig. 1 — D.H.R. 1st April, 1959. Control tracing.

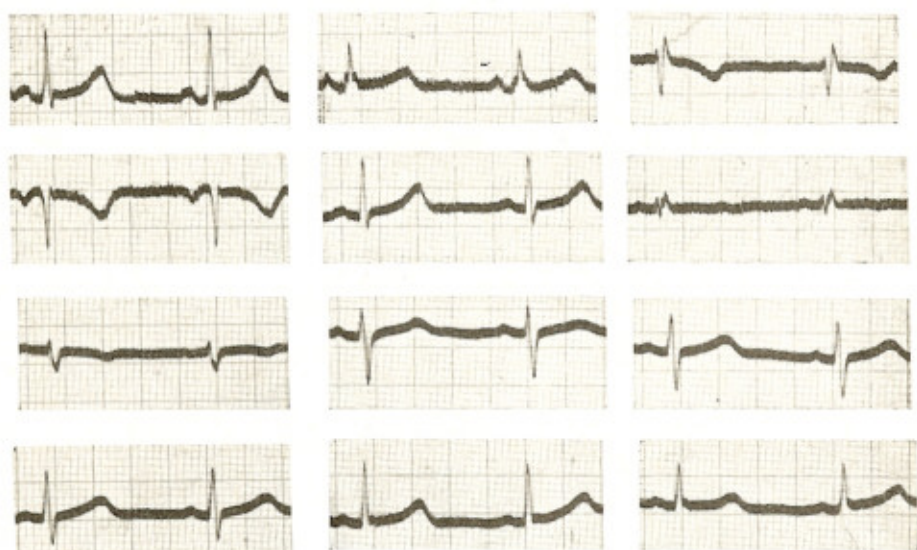


Fig. 2 — D.H.R. 10th April, 1959. 0.05 g were injected daily with a total dose of 0.50 g. A slight prolongation of QT is observed. Q-T VM: +0.06".

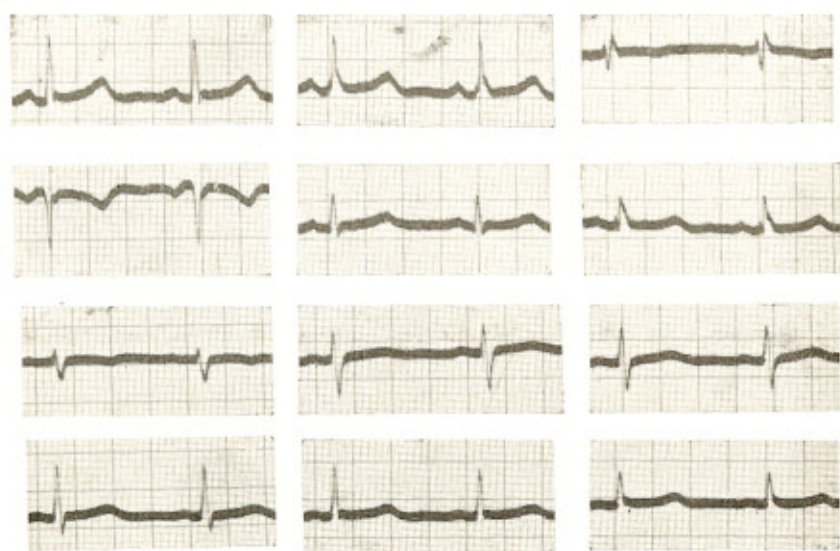
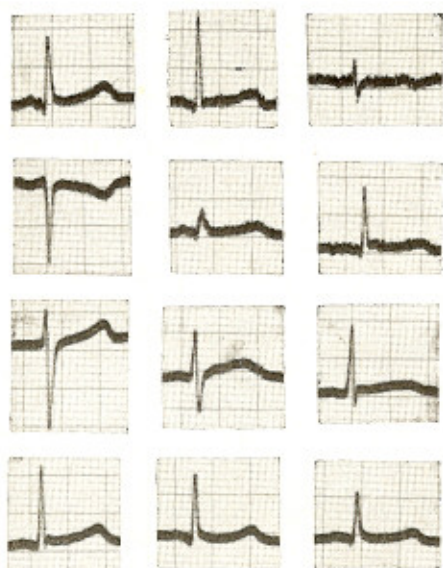


Fig. 3 — D.H.R. 25th April, 1959. Tracing is normal.



*Fig. 4 — J.S.V. 12th August, 1959.
Control tracing.*

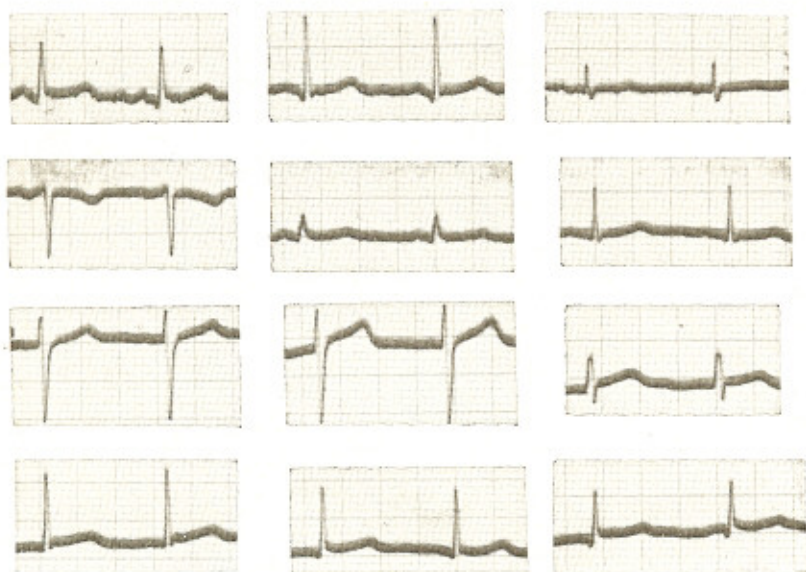


Fig. 5 — J.S.V. — 18th August, 1959. Total dose of 0.48 g injected in doses of 0.08 g for a period of 6 days. No changes were observed.

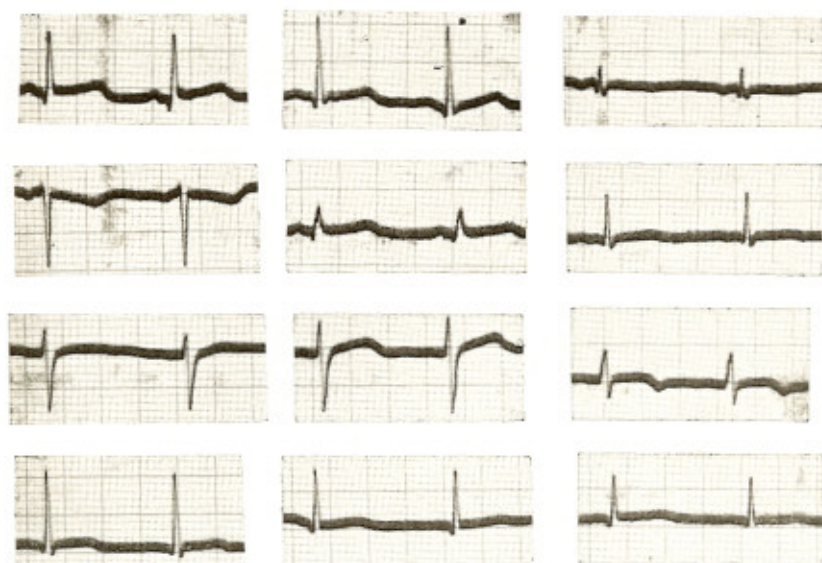


Fig. 6 — J.S.V. 25 August, 1959. Total doses of 0.72 g had been injected. A diminution of the T-voltage in $V_1, V_2, V_3, V_4, V_5, V_6$ and an inversion of T in V_2 were observed.

COMMENTS

There is no doubt that the effects of this new drug on electrocardiograms are definitely less intensive and of shorter duration than those provoked by emetine^{2, 3, 7}. This can be appreciated in Table II which compares the percentage of cases which showed electrocardiographic changes after use of emetine² and 2-dehydroemetine.

TABLE II

	Ro 1-9334	Emetine
	(%)	(%)
QT prolongation ..	33	90
ST elevation	—	45
T inversion	16	100

The longest time taken for the changes effected by Ro 1-9334 to disappear was 15 days and for emetine 40-50 days³.

RESUMO

Alterações electrocardiográficas por efeito de terapêutica com Ro 1-9334, 2-dehidroemetina racêmica sintética.

Foram estudados os efeitos de Ro 1-9334 (2-hidroemetina) sobre o electrocardiograma de 14 pacientes.

Não foram observadas alterações de P, P-R, QRS ou AQRS; QT apresentava-se maior em 4 pacientes; T diminuiu de voltagem em 6 pacientes e apresentou inversão em 2 deles. Não houve alteração de ST.

Estas alterações electrocardiográficas são consideravelmente menos freqüentes e de menor duração do que aquelas provocadas pela emetina.

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