

It is likely that the clinical anti-plaque activity reported for this toothpaste (Saxton 1986; Saxton et al 1987) is due to the retention of triclosan and zinc at specific sites of activity in the mouth.

In conclusion, about one quarter of the triclosan and zinc present in an anti-plaque toothpaste is retained in the mouth. Both these antibacterials are present in saliva for at least 2 h after brushing.

I wish to thank Miss K. A. Dundon for technical assistance, Mr N. Whitehead for zinc analyses and Mr E. Huntington for statistical help.

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Communicated October 7, 1986
- © 1987 J. Pharm. Pharmacol.

Antiarrhythmic effect of desethylamiodarone in conscious rats

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The effect of desethylamiodarone, a metabolite of amiodarone, was studied in the early phase of arrhythmias induced by coronary artery ligation in conscious rats. Desethylamiodarone pretreatment improved survival without altering the occurrence of different types of arrhythmias during the first 20 min after coronary ligation. It was concluded that desethylamiodarone may contribute to the antiarrhythmic effect seen after chronic amiodarone treatment.

Amiodarone is effective in the treatment of cardiac arrhythmias especially after chronic administration. It is also more effective against experimental arrhythmias in dog (Patterson et al 1983) and rat (Varró & Rabloczky 1986) after chronic, compared with acute treatments. During chronic treatment, the metabolite, desethylamiodarone, appears in plasma and accumulates in cardiac muscle (Plomp et al 1985). Electrophysiological studies indicate that desethylamiodarone delayed repolarization of cardiac muscle both in-situ (Nattel 1986) and in-vitro (Yabek et al 1986). However, no data are available so far about the antiarrhythmic effect of desethylamiodarone even though it is likely that the effects of desethylamiodarone contribute to the strong antiarrhythmic efficacy of the chronic amiodarone

administration. We describe here the antiarrhythmic action of desethylamiodarone in conscious rats.

Methods

The method of Leprán et al (1983) was used. Young male rats, 200-250 g, were anaesthetized by ether inhalation.

After thoracotomy, a loose loop of thread was placed around the descending branch of the left coronary artery. The end of the loop was exteriorized through a polyethylene tube. Thereafter, the chest was closed. Artificial ventilation was not needed during the entire surgical manoeuvre. The ends of the thread were hidden subcutaneously. Seven to ten days after that operation, the thread was exteriorized under light ether anaesthesia and the loop tightened, thereby producing acute myocardial ischaemia. ECG recordings were taken by a bipolar thoracic lead both before and continuously for 20 min after ligation (Medicor ER 362). The occurrence of several types of arrhythmias and the survival ratio were determined.

The post-ligation arrhythmias were categorized as ventricular extrasystole (single, double or triple premature beats), bradycardia (heart rate lower than 200 beats min⁻¹, typical signs of A-V block), ventricular fibrillation (very high frequency potentials with irregular amplitudes) as was suggested by Leprán et al (1983).

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The hearts of animals that survived the first 24 h were stained with nitrotetrazolium blue solution according to Leprán et al (1983). Thereby, we were able to demonstrate the infarction that developed. The cases ($n = 7$) where infarction did not appear were excluded

Table 1. Effect of intraperitoneal desethylamiodarone treatment in the early phase (first 20 min) of arrhythmias induced by coronary ligation in conscious rats.

Parameters	Control n = 32 (%)	Polyethylene glycol n = 32 (%)	Desethyl- amiodarone n = 34 (%)
Survival	4/32 (12.5)	6/32 (18.7)	14/34* (41.2)
Fatal bradyarrhythmia	4/32 (12.5)	4/32 (12.5)	6/34 (17.6)
Extrasystoles	26/32 (81.2)	27/32 (84.4)	28/34 (82.3)
Ventricular tachycardia	24/32 (75.0)	22/32 (68.7)	19/34 (55.9)
Ventricular fibrillation	24/32 (75.0)	23/32 (71.9)	20/34 (58.7)
Survival rate of ventricular fibrillation	0/24 (0.0)	1/23 (4.3)	6/20 (30.0)

n = number of animals.
* = statistically significant ($P < 0.01$) differences from the control calculated by the Chi-square test.

from the evaluation as unsuccessful surgeries. Animals were given desethylamiodarone HCl (Sanofi-Labaz) 50 mg kg⁻¹ intraperitoneally 30 min before the ligation in a volume of 1 mL kg⁻¹ dissolved in polyethylene glycol. The latter is known to change repolarization in cardiac muscle (Northover 1984), and so 30 animals were treated with 1 mL kg⁻¹ polyethylene glycol alone to act as solvent control. In addition, a control group of rats received physiological saline solution intraperitoneally. Statistical analysis of the results were performed with the Chi-square test.

Results

Results are summarized in Table 1. Desethylamiodarone pretreatment significantly improved the survival during the early phase of arrhythmias compared with the control and polyethylene glycol pretreated groups. Fatal bradyarrhythmia due to complete A-V block caused the death of 4 animals in the control, 4 in the polyethylene glycol-, and 6 in the desethylamiodarone-treated groups. Arrhythmias developed in all animals within 20 min of the ligation. There was no statistical difference between groups in the occurrence of severe

types of arrhythmias i.e. extrasystoles, ventricular tachycardias and ventricular fibrillation. It is noteworthy that desethylamiodarone pretreatment improved the chances of survival from ventricular fibrillation compared with control, or polyethylene glycol-treated animals.

Discussion

The present results show that desethylamiodarone pretreatment improved the survival in the acute phase of arrhythmias caused by coronary ligation in conscious rats. As far as we know this is the first evidence that desethylamiodarone exerts antiarrhythmic effects *in vivo*.

The electrophysiological effects of desethylamiodarone are very similar to those of amiodarone (Yabek et al 1986; Nattel 1986). Moreover in this study antiarrhythmic effects were produced by a dose of desethylamiodarone comparable with that of amiodarone we have already reported (Varró & Rablóczyk 1986) to be effective in the present model. During chronic amiodarone administration, desethylamiodarone accumulates in cardiac tissue in concentrations that may even be higher than those of amiodarone itself (Nattel 1986). Although the antiarrhythmic effect of desethylamiodarone needs to be examined in other species, including man, we assume that it contributes to the antiarrhythmic effect seen after chronic amiodarone administration.

Our results also indicate that polyethylene glycol, which is used as a solvent in Cordarone injections (Labaz) did not influence the coronary ligation-induced arrhythmias in conscious rats. Thus while polyethylene glycol may alter the electrophysiological properties of cardiac muscle, it is unlikely to contribute to the antiarrhythmic efficacy of Cordarone injections.

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