EXPERIMENTAL STUDIES ON ANTIDYSRHYTHMIC DRUGS WITH SPECIAL REFERENCE TO ANALGESICS

Studies on the effects of analgesic and other antidysrhythmic agents on general haemodynamics and arrhythmias induced in anaesthetized cats and isolated guinea-pig myocardial tissues

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ABSTRACT

Meptazinol, a new analgesic drug, has been studied experimentally *in vivo* and *in vitro* for antidysrhythmic activity in comparison with known clinically active antidysrhythmic drugs, analgesics and the new antihypertensive agent indoramin.

Four *in vivo* dysrhythmia inducing techniques were evaluated in cats, namely, (1) ouabain, (2) hypothermia, (3) indirect electrical stimulation of the left ventricle, using pentobarbitone anaesthetized cats, and (4) adrenaline induced dysrhythmia were produced by using halothane/oxygen anaesthetized cats. Detailed descriptions have been given of the effects of the various dysrhythmic conditions on the general haemodynamics of the animals used. For each of the techniques used, drugs were classified as "markedly active" only if the dysrhythmia was reversed for a 30 minute period or longer without accompanying overt depression of cardiovascular function. Meptazinol was moderately active against ouabain-, adrenaline- and electrically-induced dysrhythmias and markedly active in hypothermia. In *in vitro* studies meptazinol showed a "middle-range" potency in increasing the effective refractory period of guinea-pig atrial and ventricular preparations.

An overall assessment of meptazinol therefore showed this drug to be moderately active as an antidysrhythmic agent. The additional finding that it did not exacerbate the severe circulatory dysfunction caused by the various experimental dysrhythmic procedures lends weight to the belief that it may be used safely as a parenteral analgesic.

Considering the value of the various experimental procedures in a drug evaluation programme, the electrically-induced ventricular fibrillation technique was regarded as the most useful of the four *in vivo* methods studied for the routine screening of novel antidysrhythmic drugs in cats. This contention is supported by the ease with which the preparation could be set up, its good haemodynamic viability and dysrhythmia reproducibility, and its consequent simulation of the human diseased state.