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Twelve-Month Report

DEPRESSION OF CARDIAC CONDUCTION BY PROPOXYPHENE AND NORPROPOXYPHENE

The following abstract is a preliminary report of conduction depression produced by propoxyphene and norpropoxyphene. A complete presentation of this data will be submitted in a manuscript that is now being prepared.

PHARMACOLOGY

DEPRESSION OF CARDIAC CONDUCTION BY PROPOXYPHENE AND NORPROPOXYPHENE. Donald R. Holland* and Mitchell I. Steinberg. The Lilly Research Laboratories, Indianapolis, Ind. 46206

The centrally acting analgesic, d-propoxyphene (P), and its N-demethyl metabolite, d-norpropoxyphene (NP), are potent local anesthetics. Since local anesthetics depress cardiac conduction, we studied the effects of these agents on conduction in the canine heart both in vivo and in vitro. When P was infused intravenously into conscious dogs at doses of 2.1 to 21 μmole/kg (0.8 to 8 mg/kg), the P-R interval was prolonged in a concentration dependent manner. A 30% prolongation of the interval was observed at 21 μmole/kg. Norpropoxyphene (21 μmole/kg. i.v.), prolonged the P-R interval 17%. His bundle electrograms were recorded in pentobarbital anesthetized dogs pretreated with propranolol and atropine to block neurogenic influences. Intravenous administration of either P or NP prolonged conduction times in the AV node and infra-His conduction system. AV nodal conduction was prolonged 10% by P and NP at doses of 3.3 ± 0.5 μmole/kg and 6.5 ± 1.2 μmole/kg, respectively. Infra-His conduction was prolonged 10% by P and NP at doses of 17.1 ± 1.2 μmole/kg and 7.5 ± 2.8 μmole/kg, respectively. In isolated canine Purkinje fibers superfused in vitro, both agents depressed the maximum rate of rise of phase 0 of the action potential ($\dot{V}_{max}$) and shortened action potential duration. The concentrations that produced a 50% decrease in $\dot{V}_{max}$ were 2.5×10^{-5} M with P and 1.2×10^{-5} M with NP. Thus P and NP, like other local anesthetics, depress cardiac conduction in the canine heart, in vivo and in vitro.

Donald R. Holland, Ph.D.
Associate Sr. Pharmacologist
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