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EFFECT OF INDORAMIN ON HUMAN SPERM MOTILITY

Indoramin, a selective α_1 -adrenoceptor antagonist, is an effective anti-hypertensive drug in man. Animal studies have also demonstrated anti-histamine, anti-5-hydroxytryptamine and myocardial membrane stabilising properties (Alps *et al.*, 1970, 1972; Archibald, 1981). Electrophysiological studies of the effects of indoramin on canine isolated myocardial strips, indicated a statistically significant ($P = < 0.001$) decrease in $V_{\max}$ of depolarization with concentrations achieved in man after therapeutic doses (Coltart *et al.*, 1971).

Human sperm motility is a potential model to study pharmacological and toxicological effects of drugs (Hong *et al.*, 1981b, 1981c). Propranolol, lignocaine and other membrane stabilizing drugs have been shown to inhibit sperm motility (Hong, 1982; Hong & Turner, 1982). The effect of indoramin on this experimental model was therefore studied.

Fresh samples of human semen were collected from either healthy volunteers or patients attending the seminology laboratory at our hospital. The method of Hong *et al.* (1981a) was followed to study human sperm motility. Only samples with sperm counts higher than $15 \times 10^6 \text{ ml}^{-1}$ and more than 20% of progressive forward moving sperms were used. Indoramin maleate was freshly dissolved in a mixture of 5% ethanol and phosphate buffered saline at a pH of 6.0. The maleate was used because of the relative insolubility of the hydrochloride salt. Sperm motility was measured using the ability of forward moving sperms to cross a $5 \mu\text{m}$ pore nucleopore membrane during 2 h incubation time at 37°C . The transmembrane migration ratio (TMMR) was compared with a semen buffer mixture which was used as control at the same pH. The use of

5% ethanol as a solvent has already been demonstrated not to interfere in the basal motility values (Hong *et al.*, 1981c). Six samples were tested for each concentration of drug.

Figure 1 shows the log concentration response curve for indoramin and its inhibition of human sperm motility. A concentration of 4 mM decreased sperm motility to 50% of the control value. This compares

Figure 1 Log concentration-response curve for the inhibition of human sperm motility by indoramin. The motility of sperms in semen-buffer mixture was used as control. All points are mean $\pm$ s.e. mean of six samples.

with EC₅₀ values of 0.8 mM for propranolol and 16 mM for lignocaine (Hong, 1982), and suggests that indoramin possesses marked membrane stabilising properties in man, which are consistent with its myocardial effects in animal studies. Their clinical relevance, however, awaits the results of further investigation.

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β -ADRENOCEPTOR BLOCKERS REDUCE BLOOD PRESSURE IN NORMAL SUBJECTS

It was astonishing to see in a recent paper (Fuller & Vallance, 1982) the statement that no placebo controlled trials have been published demonstrating a fall in blood pressure produced by β -adrenoceptor blocking drugs, in normal subjects. Several such trials have been published from this and other departments, one of the earliest being by Ogle & Turner (1974) which demonstrated a significant fall in both systolic (Figure 1) and diastolic pressures after single oral doses of oxprenolol 160 mg and propranolol 160 mg compared with placebo under double-blind conditions in eight normal subjects.

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Figure 1 Systolic blood pressure
● = placebo; ○ = propranolol 160 mg; ▲ = oxprenolol 160 mg. * = $P < 0.01$ when compared with placebo. SE = standard error of the differences between means.

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