Beta receptor adrenergic blocking agents produce a fall of systemic arterial blood pressure which has been attributed to interference with the function of sympathetic nerves to the heart (1). While pronethalol and propranolol are known to have a peripheral vasodilator component of action which contributes to their hypotensive effect (2, 3), it has not been determined if the more recently synthesized beta blockers viz., MJ-1999 [dl 4-(2-isopropylamino-1-hydroxyethyl) methanesulfonanilide hydrochloride] and Ko-592 [1-(3-methylphenox)-2-hydroxy-3-isopropyl aminopropane hydrochloride] have similar actions. Hence the peripheral vascular actions of these beta blockers have been investigated and compared with propranolol.

In 12 mongrel dogs anaesthetized with pentobarbital sodium (30 mg/kg i.v.), right femoral artery was perfused at a constant rate with a Rotor pump by deriving animal’s own arterial blood from left femoral artery.
A tube with a side-arm was interposed between the pump and the right femoral artery for recording the perfusion pressure on a kymograph. Systemic arterial blood pressure was recorded from the proximal limb of the right femoral artery.

Propranolol, MJ-1999 and Kō-592 were used as hydrochloride salts in doses of 50 µg/kg. Adrenaline hydrochloride (1 µg/kg) and isoproterenol sulphate (1 µg/kg) were given before and 10 minutes after a beta blocker in order to investigate the modification of their responses by the drugs under study. All injections were made directly into the perfused right femoral artery.

It was observed that the beta blockers produced a fall of perfusion pressure. This hypotensive effect varied between 11.7 and 21.6% with propranolol, between 1.3% and 9.7% with MJ-1999 and between 10.1% and 16.1% with Kō-592.

Changes in perfusion pressure in individual experiments produced by adrenaline and isoproterenol and their modification by various beta blocking agents are illustrated graphically in Fig. 1. After a beta blocking drug, the vasodepressor effects of isoproterenol and adrenaline were reduced or abolished. The pressor response to adrenaline was decreased in 9 experiments, increased in one instance and remained unaltered in 2 dogs.

Since femoral vascular bed has been perfused at a constant rate, changes in the perfusion pressure reflect the local vascular effects of intra-arterially administered drugs. As the above results indicate, propranolol, MJ-1999 and Kō-592 in doses of 50 µg/kg produce vascular beta receptor blockade since the vasodilator effects of adrenaline and isoproterenol are reduced or abolished. Beta receptor blockade in the blood vessels is anticipated to cause vasoconstriction. However, in almost all the experiments, propranolol, MJ-1999 and Kō-592 in beta receptor blocking doses produce a decrease in perfusion pressure. It means that these drugs exert a direct vasodilator effect which is independent of their beta receptor blocking property.

Decrease in vasopressor effect of adrenaline observed in many experiments cannot be explained on the basis of beta receptor blockade in the myocardium since cardiac influence on femoral vascular bed has been eliminated by perfusion of the artery at a constant rate. It may be due to alpha receptor blocking property of these drugs as has also been reported previously.


REFERENCES