Do nitric oxide and prostaglandins protect the renal medullary circulation from ischaemia during renal nerve stimulation?

N.W. Rajapakse[1], G.A. Eppel[1], K.M. Denton[1], S.C. Malpas[2] and R.G. Evans[1], [1]Department of Physiology, Monash University, Melbourne, Australia and [2]Department of Physiology, University of Auckland, Auckland, New Zealand.

Renal medullary blood flow (MBF) is less sensitive than cortical blood flow (CBF) to sympathetic activation (Guild *et al.*, 2002), in part because of a counter regulatory vasodilator role of nitric oxide (NO) (Eppel *et al.*, in press). Thus, blockade of NO-synthase in anaesthetised rabbits enhances responses of total renal blood flow (RBF), CBF, and particularly MBF, to renal nerve stimulation (RNS) (Eppel *et al.*, in press). However, other mechanisms must also be involved, because even after NO-synthase blockade, RNS still reduces CBF more than MBF.

In the present study we tested whether prostaglandins contribute to the relative insensitivity of MBF to renal sympathetic drive in pentobarbitone (90-150 mg + 30-50 mg h^{-1}) anaesthetised rabbits. We also tested the effects of NO-synthase inhibition on regional kidney blood flow responses to RNS in rabbits pre-treated with a cyclooxygenase inhibitor.

A transonic flow probe was used to measure RBF and laser-Doppler flow probes were used to measure CBF and MBF. Responses to RNS were tested before and after intravenous ibuprofen (12.5 mg/kg plus 12.5 mg/kg/h; n = 18) or its vehicle (n = 6). In ibuprofen-treated rabbits, responses were then tested after N^G-nitro-L-arginine (L-NNA; 20 mg/kg + 5 mg/kg/h; n=6), L-NNA + glyceryl trinitrate (GTN; 8 - 22 μg/kg/min; n = 6) or vehicle (n = 6).

Ibuprofen but not its vehicle reduced basal RBF, CBF and MBF. Subsequent treatment with L-NNA, but not L-NNA + GTN or vehicle, increased mean arterial pressure and reduced RBF and MBF. RNS (0.75 – 6 Hz) caused stimulus-dependent reductions in RBF (85 ± 4% at 6 Hz) and CBF (87 ± 3% at 6 Hz) more than MBF (36 ± 14% at 6 Hz) in vehicle-treated rabbits. Ibuprofen did not significantly affect responses of RBF, CBF or MBF to RNS. L-NNA, but not vehicle or L-NNA + GTN, significantly enhanced RNS-induced reductions in RBF ($P \leq 0.001$) and CBF ($P = 0.02$) but not MBF ($P = 0.8$).

We conclude that cyclooxygenase products have little net impact on regional kidney blood flow responses to RNS. Our finding that NOS blockade did not affect responses of MBF to RNS after cyclooxygenase blockade contrast with our previous findings in rabbits with intact cyclooxygenase activity (Eppel *et al.*, in press). This may reflect interactions between nitric oxide and vasoconstrictor prostaglandins in modulating responses of MBF to RNS. This notion is consistent with previous studies of isolated perfused kidneys, in which NO blockade enhances vasoconstrictor responses to noradrenaline under control conditions, but not after cyclooxygenase blockade (Zhang & Sassard, 1993).

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