central dopaminergic systems. With Lysenyl, its known antiserotonin activity may also be involved.

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Ganglion blocking action of indomethacin

Hedqvist (1970) has shown that prostaglandins modulate adrenergic transmission. There are also several instances of changes in sympathetic activity when prostaglandin synthesis is inhibited by drugs such as indomethacin or aspirin. These include increased responses of the spleen to adrenergic nerve stimulation (Ferreira & Moncada, 1971) and increased concentrations of noradrenaline in the urine produced by an isolated kidney perfused with indomethacin (Junstad & Wennmalm, 1972). In view of these findings, we anticipated that the sympathetically mediated pressor reflex to carotid occlusion would be potentiated as a consequence of treatment with indomethacin, and we were surprised to find that the reflex was inhibited. We therefore attempted to discover why this happened, by studying the carotid occlusion response (COR) and the responses of the cat nictitating membrane simultaneously.

Arterial blood pressure was recorded from the femoral artery of cats under chloralose anaesthesia at 80 mg kg^{-1}. Indomethacin was infused through the left femoral vein, and the the right femoral vein was cannulated for injection of noradrenaline at 1–1·5 $\mu g\ kg^{-1}$.

The COR was obtained at 15 min intervals by occlusion of both carotid arteries for 20 s. Contractions of the nictitating membrane were produced by pre- and post-ganglionic stimulation of the superior cervical sympathetic trunk for 10 s using square pulses of 2 ms at 20 Hz.

Indomethacin was infused at 100 $\mu g\ kg^{-1}\ min^{-1}$ (i.v.). The infusion lasted 60 min (total dose 6 mg kg^{-1}) in those experiments which were designed to study changes in COR and blood pressure response to bolus injections of noradrenaline, whereas the infusion was stopped after 30 min (total dose 3 mg kg^{-1}) in those experiments in which nictitating membrane contractions were studied.

In each experiment the amount of indomethacin powder was calculated based on the weight of the animal (2–3·5 kg) and the solution was freshly prepared by dissolving the powder in absolute ethanol which was added dropwise (total amount 1·5–2 ml) and a few drops of 1 N NaOH. This was then diluted with normal saline to make up the volume to 50 ml and the pH was adjusted to 7·3 to 7·5 where necessary with hydrochloric acid.

Statistical analysis was done by employing Student's *t*-test.

There was a significant decrease of COR 30 to 45 min after starting the infusion of indomethacin. The mean data for 10 experiments showed that the change was highly significant ($P<0·01$). The control arterial pressor response due to carotid occlusion was 56·7 mm Hg s.d. 20·5 and after indomethacin the response was reduced to 23·9 mm Hg s.d. 10. The pressor response to injected noradrenaline did not change in the same way, indeed after indomethacin, it showed a tendency to increase—both in terms of rise in blood pressure as well as duration. The control response was 62 mm Hg s.d. 15·4 and that after indomethacin was 81 mm Hg s.d. 17·7. This fails to reach statistical significance in 10 experiments ($P>0·1$).

The contraction of the nictitating membrane produced by post-ganglionic stimulation was scarcely changed by infusion of indomethacin. By contrast, the contraction due to pre-ganglionic stimulation was reduced 20 min after starting the infusion, and sometimes completely abolished by 30 min, when the dose of indomethacin had reached 3 mg kg^{-1}. At this point the infusion was stopped. The response returned to control levels 30 min later.

The changes in the COR show that indomethacin diminishes the sensitivity of the reflex arc but give no indication of the site/sites of action of the drug.

The nictitating membrane responded normally to post-ganglionic sympathetic stimulation through the duration of infusion, showing that both the smooth muscle, the nerve endings, and the nerve trunk were unaffected by the drug. But the contractions due to pre-ganglionic stimulation diminished progressively and were finally abolished completely in some cases.

It is therefore evident that the cholinergic transmission in the superior cervical ganglion has been inhibited by indomethacin infusion, but the present study does not show whether this is the result of changes in the cholinergic nerve endings or the sympathetic cell bodies in the ganglion. The existence of sympathetic recurrent branches which hyperpolarize the ganglion cells and so limit the rate of firing (Goodman & Gilman, 1970) could account for a reduction in the contraction but not for total abolition as seen in this study. We have not measured changes in levels of prostaglandins. We are also aware that indomethacin has other actions on cells, but inhibition of transmission at autonomic ganglia, and possibly at synapses in the brainstem could have important consequences in man, and these effects of indomethacin therefore merit further study.

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