EFFECT OF TOTAL SYMPATHETIC BLOCKADE ON PLASMA RENIN ACTIVITY DURING SURGERY

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ABSTRACT

The interaction of sympathetic blockade and decreased mean arterial pressure on plasma renin activity during surgery was studied in dogs. Plasma renin activity was measured during lumbar laminectomy before and after sympathetic blockade produced by subarachnoid spinal anaesthesia. Plasma renin activity was significantly increased during laminectomy. Twenty minutes after sympathetic blockade there were marked decreases in mean arterial pressure and plasma renin activity; but with mean arterial pressure continuing to decline, plasma renin activity showed moderate increases at 50 minutes after sympathetic blockade. It is concluded that increases in plasma renin activity seen during surgical operations can be attenuated by sympathetic blockade produced by subarachnoid or epidural spinal anaesthesia, although decreases in mean arterial pressure resulting from the sympathetic blockade continue to provide a stimulus for renin secretion.

SYMPATHETIC STIMULATION of the kidneys either by infusion of catecholamines or electrical stimulation of the renal sympathetic nerves increases renin secretion¹ whereas renal sympathectomy decreases plasma renin activity.² Increase in plasma renin activity observed during surgery has been attributed to increased sympathetic activity.³ Subarachnoid (spinal) anaesthesia produces sympathetic blockade and, hence, would be expected to decrease plasma renin activity during surgery. But sympathetic blockade produced by spinal anaesthesia also decreases mean arterial pressure. Decreases in mean arterial pressure also result in increased plasma renin activity.⁴ Thus subarachnoid spinal anaesthesia would tend to have opposing effects on renin secretion during surgery. To study the interaction of sympathetic blockade and decreased mean arterial pressure on renin secretion during surgery, we measured plasma renin levels in dogs during lumbar laminectomy before and after producing a total sympathetic blockade by subarachnoid anaesthesia.

Materials and Methods

Ten adult mongrel dogs weighing 10 to 17 kg maintained on normal sodium diets were studied. Due to the diurnal variation in plasma renin activity,⁵ all experiments were performed between 11 a.m. and 3 p.m. A 16-gauge intravenous cannula was inserted percutaneously into a distal

forelimb vein and a blood sample was drawn for estimation of renin level during the awake state. Anaesthesia was induced with pentobarbitone 30 mg·kg⁻¹ intravenously. The trachea was intubated with a cuffed tube and the animals were ventilated mechanically to maintain arterial PCO₂ between 4.66 and 5.32 kPa (35 and 40 torr). Polyvinyl catheters were introduced into the right atrium and abdominal aorta through the femoral vessels and connected to Statham strain gauges. Arterial and central venous pressures were recorded continuously. With animals in the prone position, laminectomies of the fourth and fifth lumbar vertebrae were done and the dural sac was exposed. A 20-gauge teflon catheter was placed in the subarachnoid space through the dura mater. Cardiac output measurements were done in duplicate by the indicator dilution technique using indocyanine green. A sample of peripheral venous blood was drawn for estimation of renin level. Arterial and forelimb venous blood samples were analyzed for PO₂, PCO₂ and cH⁺ (pH) in six of the 10 animals to calculate arteriovenous oxygen content difference in the forelimb.

Total sympathetic blockade was produced by injecting 15 to 20 mg of tetracaine in 2 ml of 10 per cent dextrose in water into the subarachnoid space and placing the animals in 10- to 15-degree head down tilt for five to ten minutes. The animals were then returned to the neutral position. Cardiac output measurements and arterial and venous blood sampling for blood gas analysis and estimation of renin activity were done 20 and 50 minutes after injection of tetracaine. Renin activity was measured by radioimmunoassay as de-

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TABLE I
HAEMODYNAMIC VALUES AND PLASMA RENIN ACTIVITY (mean $\pm$ SE)

	N	Awake control	During Lumbar Laminectomy		
			Before sympathetic block	20 min after sympathetic block	50 min after sympathetic block
Mean arterial pressure (kPa)	10		18.9 $\pm$ 1.1	11.7 $\pm$ 0.5*	10.2 $\pm$ 0.4*
Cardiac output (l/min)	10		2.46 $\pm$ 0.27	1.56 $\pm$ 0.15*	1.46 $\pm$ 0.14*
Systemic vascular resistance (dyn $\cdot$ sec $\cdot$ cm ⁻⁵)	10		5216 $\pm$ 749	4912 $\pm$ 522	4608 $\pm$ 481
Forelimb arteriovenous oxygen content difference (ml of O ₂ /dl of blood)	6		3.14 $\pm$ 0.78	1.05 $\pm$ 0.36*	1.12 $\pm$ 0.29*
Plasma renin activity (ng/dl/3 hours)	10	536 $\pm$ 209	2530 $\pm$ 658†	1078 $\pm$ 203*†	1400 $\pm$ 383†

*P < 0.05 when compared to values during laminectomy before sympathetic block.

†P < 0.05 when compared to awake control values.

scribed by Haber, Koerner, Page, Kliman and Purnode⁶ and reported in nanograms of angiotensin per dl of plasma generated during a three-hour incubation period.⁶ Mean arterial pressure and cardiac output measurements during operation before and after sympathetic blockade were compared and plasma renin levels during operation before and after sympathetic blockade were compared with awake values and with each other, using Student's t-test for paired observations. Changes were considered significant when P < 0.05.

RESULTS

The time interval between administration of pentobarbitone and completion of laminectomy ranged between 60 and 90 minutes in all dogs.

Arteriovenous oxygen content difference in the forelimb measured in six of the ten dogs showed consistent significant decreases, confirming total sympathetic blockade. In the remaining four dogs, arteriovenous oxygen content difference in the forelimb was not measured due to technical problems, but the haemodynamic response to injection of tetracaine into the subarachnoid space was similar to the other six dogs.

Mean arterial pressure and cardiac output were decreased significantly at 20 and 50 minutes following sympathetic blockade and systemic vascular resistance showed only insignificant decreases. Plasma renin activity during laminectomy, before sympathetic blockade, was increased significantly when compared to awake control values. Twenty minutes after induction of sympathetic blockade there was a significant 57 per

cent drop in plasma renin activity, but this value was still significantly higher than awake control values. With mean arterial pressure continuing to fall at 50 minutes following sympathetic blockade, plasma renin activity increased moderately so that the difference when compared to values during operation before sympathetic blockade was no longer significant. However, plasma renin activity at 50 minutes after sympathetic blockade was significantly higher when compared to awake control values. Results are summarized in Table I.

DISCUSSION

Increase in plasma renin activity occurs after administration of pentobarbitone with peak levels being observed at 30 minutes. Sixty minutes after administration of pentobarbitone plasma renin activity returns to control levels.^{6,7} Thus the markedly increased plasma renin activity that we observed in samples drawn during laminectomy 60 to 90 minutes after administration of pentobarbitone probably reflects increased sympathetic activity due to stress of surgery. Such increases during operation have been documented in animals⁸ and in man.³

To confirm total sympathetic blockade, we measured arteriovenous oxygen content difference in the forelimb in six of ten dogs. As a result of arteriolar dilatation produced by sympathetic blockade anatomical arteriovenous shunts open up, leading to a decrease in arteriovenous oxygen content difference.⁹ We consistently observed decreased arteriovenous oxygen content difference in the forelimb 20 and 50 minutes after injection of tetracaine into the subarachnoid space,

confirming total sympathetic blockade at both time intervals.

Marked decrease in plasma renin activity that we observed 20 minutes after sympathetic blockade provides further evidence that the increase in plasma renin activity during surgery is due to sympathetic stimulation. Although plasma renin activity decreased significantly 20 minutes following sympathetic blockade it did not return to awake control values. This can be explained by the fact that the half-time of the disappearance of renin activity in plasma of dogs is 10 to 30 minutes.¹⁰ Moreover, it has been noted that decreases in mean arterial pressure stimulate renin secretion even in non-secreting denervated kidneys.⁴ Thus, the decrease in mean arterial pressure that we observed after sympathetic blockade probably prevented plasma renin activity from returning to awake control values. Furthermore evidence of this is provided by the finding that at 50 minutes following sympathetic blockade, with mean arterial pressure that we observed did not plasma renin activity showed moderate increases when compared to activity 20 minutes after sympathetic blockade. However, it appears that decreases in mean arterial pressure are not as profound a stimulus for renin release as sympathetic stimulation, since the 40 to 50 per cent decrease in mean arterial pressure that we observed did not restore plasma renin activity to levels seen during operation before sympathetic blockade.

It is generally accepted that systemic vascular resistance is decreased during sympathetic blockade produced by subarachnoid spinal anaesthesia;¹¹ but we observed only insignificant decreases in systemic vascular resistance after sympathetic blockade and others have reported similar findings before.^{12,13} This could be partly due to continuing renin release by the kidneys in response to decreased mean arterial pressure.

In conclusion, we observed that the increase in plasma renin activity occurring during surgical operations could be partly prevented by sympathetic blockade produced by subarachnoid spinal anaesthesia. However, decreases in mean arterial pressure produced by the sympathetic blockade continue to provide a stimulus for renin release, though not as strong a stimulus as the increased sympathetic activity seen during surgery. It has been recently reported that subarachnoid anaesthesia and subsequent surgical operation produced no changes in plasma aldosterone concentrations and renin activity in man.¹⁴ Hence, if untoward effects of increased

plasma renin activity such as increased sodium retention are to be prevented or minimized in surgical patients, sympathetic blockade could be induced. For operations on the lower extremities and abdomen, sympathetic blockade could best be achieved along with analgesia by subarachnoid or epidural anaesthesia techniques.

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RÉSUMÉ

Les interactions d'un bloc sympathique et d'une diminution de la pression artérielle moyenne sur l'activité plasmatique de la rénine ont fait l'objet de cette étude effectuée chez le chien. A cette fin, l'activité de la rénine plasmatique a été mesurée au cours de laminectomies lombaires avant et après production d'un blocage sympathique par de rachi-anesthésie. On a observé une augmentation significative de l'activité de la rénine au cours des laminectomies. Des diminutions marquées de cette activité et de la pression artérielle moyenne étaient notées 20 minutes après le bloc sympathique. La pression artérielle moyenne continuait à décroître alors que l'activité de la rénine était légèrement augmentée 50 minutes après le bloc. Il est conclu que l'augmentation de l'activité plasmatique de la rénine observée au cours d'interventions chirurgicales peut être atténuée par un blocage sympathique (anesthésie rachidienne ou péridurale) bien que la diminution de la pression artérielle moyenne produite par le bloc sympathique contribue à stimuler la sécrétion de rénine.