

LETTER TO THE EDITOR

ARGININE VASOPRESSIN POTENTIATES METHYLDOPA INDUCED HYPOTENSION IN ANESTHETIZED WISTAR RATS

Sir,

(Received on January 7, 1992)

Arginine vasopressin (AVP) plays an important role in cardiovascular regulation through several mechanisms (1). Methyldopa reduces blood pressure by a centrally mediated effect on the sympathetic nervous system through its action on alpha receptors (2). The relationship between central alpha2 receptors and vasopressin release has been reported (3).

In this study we have tried to ascertain the effect of AVP on the hypotensive action of methyldopa in anesthetized Wistar rats.

Albino Wistar rats (either sex, 225 to 250 g) were anesthetized with Sodium pentobarbitone (50 mg/kg, i.p.). Blood pressure was measured with a pressure transducer (T301) on a INCO polygraph through a polypropylene cannula placed in the carotid artery. A polypropylene cannula introduced in the jugular vein was used for the infusion of drugs.

After 20 min period of baseline recording ( $98.12 \pm 2.48$  mm of Hg), two different doses of methyldopa (5 mg/kg and 10 mg/kg) administered with an interval of 15 min in between each dose produced fall in blood pressure to  $76.18 \pm 1.18$  and  $68.89 \pm 0.87$  mm of Hg respectively ( $P < 0.01$ ). 10 min after methyldopa, AVP (4 I.U./kg) produced a rise in the blood pressure to  $183 \pm 3.52$  mm of Hg ( $P < 0.001$ ) which slowly returned to the basal level approximately 15 min after the injection. Administration of methyldopa after AVP resulted in a potentiated hypotensive response and blood pressure fell to  $62.73 \pm 1.78$  and  $54.37 \pm 2.37$  mm of Hg ( $P < 0.001$ ), (Fig. 1).

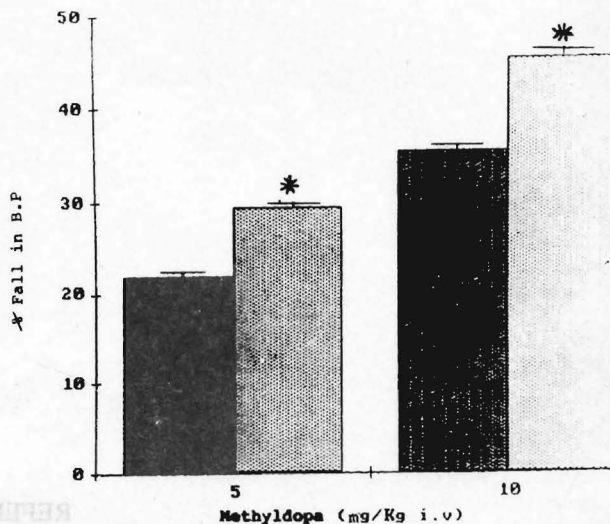


Fig. 1 : Fall in blood pressure produced by methyldopa (5 and 10 mg/kg) before and after AVP (4I U/kg), n = 8, values are Mean  $\pm$  SEM; \* $P < 0.001$  (paired Mann Whitney U test).

Methyldopa produces hypotension by decreasing sympathetic outflow possibly mediated by central alpha2 receptors (2). Since central alpha2 adrenergic system control vasopressin release (3), it is possible that a feed back mechanism exists between vasopressin and the central alpha2 adrenergic system. In our study AVP (4 I.U./kg) produced a pressor response, and only after the blood pressure returned to basal level, methyldopa was injected resulting in a potentiated hypotensive response, thus it seems unlikely that enhancement of baroreflex sensitivity caused by prior injection of AVP could be responsible

for the potentiation of blood pressure lowering action of methyldopa. The interaction between AVP and methyldopa resulting in potentiated hypotensive response may be due to the interplay

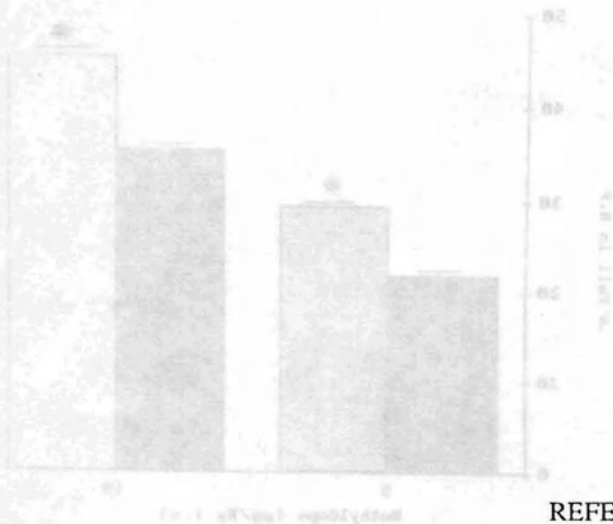
between central alpha2 adrenergic and vasopressinergic systems. Further studies are being conducted to elucidate the exact mechanism involved in this interaction.

MANOJ G. TYAGI\*, MOHAMMED A. KAMDOD,  
JEYASEELAN, L\* AND PAUL M. STEPHEN

\*Department of Pharmacology,  
Jawaharlal Institute of Postgraduate  
Medical Education and Research,  
Pondicherry - 605 006

and

Department of Pharmacology and  
\*Department of Biostatistics,  
Christian Medical College,  
Vellore - 632 002



#### REFERENCES

- Share L. Role of vasopressin in cardiovascular regulation. *Physiol Rev* 1988; 68: 1248-1284.
- Henning M. Alpha methyldopa and related compounds. In Van Zweiten PA, Ed. Handbook of hypertension, Elsevier, Amsterdam, 1984; 154-193.
- Brooks DP, Share L, Crofton JF. Central adrenergic control of vasopressin release. *Neuroendocrinology*, 1986; 42: 416-420.

\*Corresponding Author