PLASMA ADRENALINE AND NORADRENALINE LEVELS DURING HAEMORRHAGE INDUCED AFTER CHLORPROMAZINE INJECTION

BY

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It has been reported that chlorpromazine protects against irreversible haemorrhagic shock (Overton and DeBakey, 1956; Spurr et al., 1956) when administered before but not after the induction by haemorrhage of hypotension (Gowdey et al., 1957). It has been claimed that chlorpromazine exerts a beneficial effect in these and other conditions of "sympathetic irritation" because of a central sympathetic inhibitory action (for a review of the literature see Hopkin, 1955; Hopkin and Brown, 1958). This implies that chlorpromazine has an "automatic stabilizing" effect of value in the anaesthetized or shocked patient. However, it will be recalled that Holzbauer and Vogt (1954) found that chlorpromazine did not inhibit the stimulation of sympathetic centres (i.e. did not prevent depletion of hypothalamic noradrenaline) induced in cats by morphine injection or by the stress of surgery.

We have previously reported on the plasma and urinary adrenaline and noradrenaline levels during progressive haemorrhage in dogs (Millar and Benfey, 1958). It appeared to be of interest to measure plasma catechol amine levels during haemorrhage induced following chlorpromazine administration.

METHOD

Five dogs were used. Each dog was lightly anaesthetized with thiopentone, the groin infiltrated with a few millilitres of 1 per cent lignocaine solution, and the femoral artery cannulated to allow withdrawal of blood samples and direct measurement of arterial blood pressure by means of a Statham strain gauge and Sanborn recorder. After withdrawal of a blood sample (Sample 1, 40 ml) 5-10 mg/kg of chlorpromazine was injected slowly intravenously. One hour later, a second blood sample (Sample 2, 40 ml) was taken to determine any effect of chlorpromazine on circulating adrenaline and noradrenaline levels. Every 15 minutes thereafter, 10 ml/kg blood samples were withdrawn until circulatory collapse occurred.

Plasma was immediately separated from blood samples by centrifuging, and assays of plasma adrenaline and noradrenaline completed within 24 hours. The chemical method of estimation as originally described (Millar and Benfey, 1958) has been modified for these and other studies and is included elsewhere (Millar et al., 1959). The data refer to μg of free base per litre of plasma, and are uncorrected for losses in recovery up to 30 per cent.

RESULTS

Table I shows that there was no significant change in arterial adrenaline and noradrenaline concentrations 1 hour after injection of chlorpromazine, 5-10 mg/kg. When graded haemorrhage was induced (starting 75 minutes after chlorpromazine injection) circulating adrenaline levels increased progressively with each sample withdrawal. Increases in plasma noradrenaline were more moderate and occurred to a marked degree only in the later stages of haemorrhagic hypo-
Table I

Plasma adrenaline (A) and noradrenaline (N) concentration (µg/litre) before and after chlorpromazine (5–10 mg/kg), and during haemorrhagic hypotension.

<table>
<thead>
<tr>
<th>Study No.</th>
<th>Chlorpromazine Before</th>
<th>After '60 min</th>
<th>Graded haemorrhage (each sample 10 ml/kg)</th>
<th>B.P.*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>N</td>
<td>75 min</td>
<td>90 min</td>
</tr>
<tr>
<td>1</td>
<td>0.2</td>
<td>0.1</td>
<td>0.0</td>
<td>0.1</td>
</tr>
<tr>
<td>2</td>
<td>0.4</td>
<td>0.6</td>
<td>0.3</td>
<td>0.5</td>
</tr>
<tr>
<td>3</td>
<td>0.4</td>
<td>0.2</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>4</td>
<td>0.0</td>
<td>0.2</td>
<td>0.0</td>
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<tr>
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<td>0.0</td>
<td>0.0</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Means</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>B.P.*</td>
<td>107</td>
<td>103</td>
<td>105</td>
<td>84</td>
</tr>
</tbody>
</table>

*Mean arterial blood pressure before and after withdrawal of each blood sample.

Studies 1 and 2, chlorpromazine 5 mg/kg; studies 3–5, chlorpromazine 10 mg/kg.

Fig. 1

Mean plasma adrenaline and noradrenaline concentrations, with average mean arterial blood pressure, in five dogs before and after intravenous chlorpromazine, and during graded haemorrhage induced subsequently.
FIG. 2
Mean plasma adrenaline and noradrenaline concentrations, with average mean arterial blood pressure in eight dogs subjected to graded haemorrhagic hypotension.

Discussion and Summary
These data fail to demonstrate significant depression, by chlorpromazine, of the rise in circulating catechol amine levels which accompanies progressive haemorrhagic hypotension. This is evident from a comparison of figures 1 and 2. Figure 2 is reprinted from our previous paper (Millar and Benfey, 1958) and shows the catechol amine levels attained during haemorrhagic hypotension in dogs which have not been given chlorpromazine.

In contrast to the potent anti-adrenergic compound dibenzyline (Millar et al., 1959) chlorpromazine injection per se does not appear to alter arterial adrenaline and noradrenaline concentrations, nor does it limit the blood volume which can be withdrawn prior to circulatory failure.

It is concluded that chlorpromazine does not reduce the sensitivity of dogs to autonomic stimulation induced by circulatory stress. The central component of the sympathetic nervous system appears to be fully reactive following intravenous injection of chlorpromazine.
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REFERENCES


