HYPERTENSIVE AND CATECHOLAMINE RESPONSE TO TRACHEAL INTUBATION IN PATIENTS WITH PREGNANCY-INDUCED HYPERTENSION

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An increase in arterial pressure is known to accompany laryngoscopy with or without tracheal intubation, and this response is accompanied by an increase in plasma noradrenaline concentration [1–3]. An exaggerated pressor response to tracheal intubation has been reported in hypertensive patients [4], but those treated with beta-adrenoceptor blocking drugs appear to respond in this respect similarly to normotensive subjects, whilst exhibiting greater increases in noradrenaline concentration [5].

Patients with severe pre-eclampsia or pregnancy-induced hypertension (PIH) also exhibit marked hypertensive responses to tracheal intubation, despite the use of vasodilator drugs [6, 7]. However, previous studies have not examined the response in normotensive parturients for comparison. Furthermore, the role of catecholamines in pre-eclampsia is uncertain, as plasma concentrations of noradrenaline have been reported to be lower than [8], higher than [9], or no different from [10] normotensive controls. Adrenaline concentrations are also inconsistent [10, 11].

In order to investigate further the hypertensive and catecholamine responses to tracheal intubation in PIH, we have measured these responses in an unselected group of parturients with PIH and compared them with those of normotensive controls.

SUMMARY

The pressor and catecholamine responses to laryngoscopy and intubation were studied in nine patients with pregnancy-induced hypertension (PIH) and in eight normotensive controls. Five of the PIH patients had received oral labetalol as antihypertensive therapy. Mean arterial pressure (MAP) increased significantly from the pre-induction value in all groups 1 min after intubation, and also at 3 min in those with PIH who had not received labetalol. Arterial pressure was significantly greater in both PIH groups than in the control group at all times. However, the percentage increase in MAP on intubation was significantly less in the labetalol treated group than in either the untreated or the control groups. There were no significant differences between the groups in plasma concentrations of either noradrenaline or adrenaline; noradrenaline concentration increased significantly after intubation only in the control group. Labetalol appears to confer some protection against the pressor response to intubation in parturients with PIH.

PATIENTS AND METHODS

We studied 10 patients with PIH, undergoing elective or emergency Caesarean section (group I) and 10 normotensive mothers undergoing elective Caesarean section under general anaesthesia (group II). PIH was defined as an arterial pressure greater than 140/90 mm Hg on two or more separate occasions appearing initially in the second or third trimesters. Informed consent was obtained from each patient for their inclusion in
the study, which was approved by the District Ethics Committee.

Each patient received premedication with 0.3-molar sodium citrate 30 ml, but no sedative agents were given, with the exception of antihypertensive or anticonvulsant therapy which had been prescribed. During pre-oxygenation in the operating theatre, an additional 18-gauge i.v. cannula was inserted under local anaesthesia into an antecubital vein on the arm contralateral to that with the existing i.v. infusion. An automatic arterial pressure cuff (Dinamap 845) was placed on the arm receiving the i.v. infusion, and the ECG was monitored. Heart rate and arterial pressure were recorded before induction and a 10-ml blood sample was withdrawn from the i.v. cannula.

Each group received the same anaesthetic technique: after full pre-oxygenation, standard rapid sequence induction of anaesthesia was commenced using thiopentone 4-5 mg kg\(^{-1}\) i.v., suxamethonium 1.5 mg kg\(^{-1}\) i.v. and application of cricoid pressure. Intubation of the trachea was accomplished as soon as neuromuscular block was achieved and anaesthesia was continued using 50 % nitrous oxide and 0.5 % halothane in oxygen. The lungs were ventilated using a Manley ventilator delivering a minute volume of 120 ml kg\(^{-1}\); in a pilot study this had been found to maintain \(P_{a_{\text{CO}_2}}\) in the range 3.5-4.5 kPa. Neuromuscular block was maintained with atracurium which was given before the effects of the suxamethonium had terminated in order to prevent coughing.

At 1, 3 and 5 min after intubation, 10-ml samples of blood were withdrawn from the i.v. cannula without the use of a tourniquet and placed in evacuated lithium-heparin tubes. Heart rate and arterial pressure were recorded at these times. In group II, surgery was delayed until completion of blood sampling, but in some patients in group I the urgency of the situation dictated that surgery commenced before the 5-min sample had been taken. Blood was centrifuged within 1 h at 4 °C and the separated plasma was stored at —70 °C until analysis for catecholamine concentration was carried out by High Pressure Liquid Chromatography as detailed elsewhere [2].

The data were analysed statistically using Student's paired \(t\) test and one-way ANOVA for

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**Table I. Description of patient groups**

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n)</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Mean (SEM) age (yr)</td>
<td>28 (2.5)</td>
<td>32 (1.0)</td>
</tr>
<tr>
<td>Mean (SEM) weight (kg)</td>
<td>74 (6.5)</td>
<td>72 (6.2)</td>
</tr>
<tr>
<td>Primip.</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Multip.</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Infant wt (mean) (g)</td>
<td>1963</td>
<td>3356</td>
</tr>
</tbody>
</table>

**Table II. Details of patients with PIH (group I).** *Severe PIH. CS = Caesarean section*

<table>
<thead>
<tr>
<th>No.</th>
<th>Age (yr)</th>
<th>Parity</th>
<th>Wt (kg)</th>
<th>Max. SAP/DAP before CS (mm Hg)</th>
<th>Proteinuria (g)</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1*</td>
<td>23</td>
<td>0</td>
<td>77</td>
<td>200/120</td>
<td>3+</td>
<td>Phenobarbitone, labetalol + hydralazine</td>
</tr>
<tr>
<td>2</td>
<td>38</td>
<td>2</td>
<td>102</td>
<td>150/100</td>
<td>—</td>
<td>None</td>
</tr>
<tr>
<td>3*</td>
<td>24</td>
<td>0</td>
<td>48</td>
<td>160/110</td>
<td>3+</td>
<td>Phenobarbitone</td>
</tr>
<tr>
<td>4</td>
<td>29</td>
<td>0</td>
<td>73</td>
<td>150/110</td>
<td>—</td>
<td>Phenobarbitone, labetalol + methyl dopa</td>
</tr>
<tr>
<td>6</td>
<td>26</td>
<td>0</td>
<td>77</td>
<td>150/100</td>
<td>1+</td>
<td>Phenobarbitone</td>
</tr>
<tr>
<td>10*</td>
<td>36</td>
<td>0</td>
<td>95</td>
<td>160/110</td>
<td>1+</td>
<td>None</td>
</tr>
<tr>
<td>11*</td>
<td>22</td>
<td>0</td>
<td>57</td>
<td>200/130</td>
<td>3+</td>
<td>Phenobarbitone, labetalol + hydralazine</td>
</tr>
<tr>
<td>17*</td>
<td>20</td>
<td>0</td>
<td>74</td>
<td>170/120</td>
<td>2+</td>
<td>Phenobarbitone, labetalol + hydralazine</td>
</tr>
<tr>
<td>18*</td>
<td>35</td>
<td>1</td>
<td>63</td>
<td>180/105</td>
<td>3+</td>
<td>Phenobarbitone, labetalol</td>
</tr>
</tbody>
</table>

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within group comparisons and unpaired t test for between group comparisons. \( P < 0.05 \) was considered to be significant.

RESULTS

Two patients in group II and one patient in group I were excluded because of incomplete data, leaving nine in group I and eight in group II. The demographic details of the patients are given in table I and details of individual patients in group I are given in table II. Five patients were classified as severely pre-eclamptic, that is, with an arterial pressure of 160/110 mm Hg or more on two separate occasions, proteinuria of > 5 g/24 h, or both [12]. Three patients were receiving anti-hypertensive treatment comprising labetalol 400 mg three times a day orally and hydralazine i.m.; one received labetalol only, and one labetalol and methyl dopa.

Patients in group I have been allocated to two subgroups on the basis of receiving labetalol (Ia) or not (Ib). In groups Ib and II SAP and DAP increased significantly from pre-induction values at 1 min; in group Ib they were increased also at 3 min. In group Ia, only DAP increased significantly at 1 min (fig. 1). Other values were not significantly different from baseline. However, arterial pressure was significantly higher at all times in both PIH groups than in the control group.

There was a 25% increase in MAP 1 min after intubation in groups Ib and II. However, patients receiving labetalol (group Ia) showed an increase of only 13%, which was significantly less than that of both the other groups (table III).

There were no significant differences in heart rate between labetalol-treated (Ia) and untreated (Ib) patients, therefore their results have been combined. The pre-induction value was signifi-

| Table III. Effect of labetalol on mean (SEM) MAP (mm Hg). A = Before induction; B = 1 min; C = 3 min; D = 5 min after intubation; ** Significant difference in % increase in MAP between groups Ia and Ib, and between Ia and II (\( P < 0.01 \)) |
|-----------------|----------------|----------------|----------------|
|                 | A              | B              | C              | D              |
| Group Ia (treated) | 119 (5.6)      | 135 (8.4)      | 118 (9.5)      | 117 (6.1)      |
| Group Ib (untreated) | 124 (3.5)      | 154 (4.6)**    | 139 (5.4)      | 126 (6.9)      |
| Group II         | 95 (3.8)       | 118 (3.8)      | 96 (3.8)       | 92 (5.5)       |

Fig. 1. Mean (SEM) systolic and diastolic arterial pressures in groups Ia (■), Ib (□) and II (□). *\( P < 0.02 \); **\( P < 0.01 \) within group comparison with baseline; †\( P < 0.05 \) groups Ia v. Ib.

Fig. 2. Mean (SEM) heart rates in groups I (---) and II (----). *\( P < 0.05 \) within group comparison with baseline; **\( P < 0.01 \) between groups.
Before induction

FIG. 3. Mean (SEM) noradrenaline concentrations in groups I (□) and II (■). *P < 0.05 within group comparison with baseline.

significantly higher in group II, but thereafter there were no differences. Within both groups I and II, values at 1 and 3 but not 5 min after tracheal intubation were significantly higher than before induction (fig. 2).

At 1 min after intubation there was a 28% increase in plasma concentration of noradrenaline in group II, which was significant compared with baseline (fig. 3). There was a 33% increase in noradrenaline concentration after 1 min in group I patients, but this was not significant. There were no significant differences between the groups in noradrenaline concentration at any study point, no significant changes in plasma concentration of adrenaline in each group and no differences between groups.

DISCUSSION

Although previous studies have described the cardiovascular changes during general anaesthesia in patients with pre-eclampsia [6, 7] they have not included a group of normotensive parturients for comparison. We have demonstrated that the percentage increase in MAP after intubation was similar in healthy parturients and in patients with PIH untreated with labetalol, although the absolute values were obviously higher in the latter patients. The actual (as opposed to percentage) increase in MAP in group II closely resembled that reported by Millar-Forbes and Dally [13] for a similar induction technique in gynaecological patients.

The increase in MAP on intubation in group Ib (30 mm Hg) was less than that reported by Hodgkinson, Husain and Hayashi (45 mm Hg) [6], and by Connell, Dalgleish and Downing (43 mm Hg) [7]. However, these workers used direct intra-arterial monitoring and reported increases from post-induction values and not pre-induction as in this study, and this may explain the discrepancy. We did not feel it justified to wait for an indirect reading of arterial pressure between induction and intubation and it is also possible that transient pressure peaks were missed using an oscillotonometric method.

Two other differences between this and Connell’s study make comparison difficult: the previous study included only severely affected patients, whereas only six of the nine patients in group I of our study were in this category, and our patients with PIH were mostly primiparous and of average age 28 yr, compared with more multiparous and a younger mean age (23.6 yr) in Connell’s study.

Patients in group Ia who had received oral labetalol as antihypertensive treatment showed a significantly reduced pressor response compared with both untreated hypertensives and normotensive controls. The fact that most of this group were also in a severe category of PIH/pre-eclampsia makes this observation striking.

Labetalol, a mixed alpha and beta-adrenergic blocking agent, has become popular with obstetricians for the treatment of PIH and is now the first-line treatment in our unit. Pure beta-blocking drugs, for example metoprolol, given orally have been shown to attenuate hypertensive responses in non-pregnant patients undergoing general anaesthesia [14]. More recently, one oral dose of labetalol has been shown also to be effective [15]. In contrast, i.v. practolol given immediately before intubation seems to be ineffective, at least in normotensive subjects [16]. It is interesting to note that 60% of patients in Connell’s series had received i.v. practolol, with obviously ineffective results [7].

Labetalol did not always prevent peaks of arterial pressure; one patient in group Ia had an
SAP greater than 200 mm Hg. An alternative or additional approach might be to use a rapidly acting potent opioid as part of the induction sequence; fentanyl has been found effective in this respect in severe pre-eclampsia [17].

Plasma concentrations of noradrenaline increased significantly 1 min after tracheal intubation in group II, and this has been found to occur in most studies of non-pregnant subjects. Shnider and colleagues [18] reported a 21% increase in plasma concentration of noradrenaline following intubation in normotensive parturients having Caesarean section. This is comparable to our finding (28%), but, to our knowledge, catecholamine concentrations have not been reported previously in relation to tracheal intubation in pre-eclampsia. Although the increase in the PIH group was not significant because of large variability, it is likely that more patients would have yielded a significant result.

In conclusion, our results indicate that there was no quantitative difference in the pressor or catecholamine response to intubation experienced by normotensive and untreated hypertensive parturients, although the number of patients studied was relatively small. Our findings do not support the concept of vascular hyperactivity to pressor agents in pre-eclampsia which has been propounded [19]. However, the potential clinical effect of a surge in arterial pressure is much greater if the basal value is higher, as it is more likely to exceed the upper limit of cerebral autoregulation.

In view of the high proportion of deaths caused by cerebral haemorrhage and oedema in hypertensive diseases of pregnancy [20] and the known morbidity from intubation [21], it seems prudent to attempt to limit the maximum MAP after intubation to 130 mm Hg, the upper limit of autoregulation in man [22]. Labetalol given orally may be a useful agent to help attenuate hypertensive responses to airway manipulation, but its use requires more careful evaluation in a larger number of patients.

REFERENCES