EFFECT OF EPIDURAL BLOCKADE ON THE PENTAZOCINE-INDUCED INCREASE IN PLASMA CATECHOLAMINES AND BLOOD PRESSURE

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SUMMARY
To elucidate the mechanism and site of action of pentazocine-induced sympathetic stimulation, plasma catecholamines were measured after intravenous pentazocine 1.2 mg/kg in 20 patients with epidural blockade extending to different levels. In patients with low epidural blockade (below T8) total plasma catecholamines increased during the 20-minute observation period to a maximum of about 40% 5 minutes after the injection of pentazocine. The increase in catecholamines comprised mainly noradrenaline and corresponded to the rise in blood pressure and heart rate. In patients with high epidural blockade (over T6) pentazocine caused a slight fall in catecholamine level. In these patients the pentazocine-induced rise in blood pressure was nearly abolished. It is considered that the site of pentazocine-induced sympathetic stimulation is central.

It is now established that intravenous injection of pentazocine causes a rise in blood pressure and heart rate (Keats and Telford, 1964; Tammisto et al., 1970). According to Keats and Telford this is caused by the sympathetic stimulation which in man is of central origin and a counterpart of the stimulation of the central nervous system which produces tremors and convulsions in animals (Harris and Pierson, 1964). Our earlier observation that both anaesthesia (Tammisto et al., 1970) and high epidural blockade (Tammisto and Kjellberg, unpublished) counteract the pressor response to pentazocine supports this assumption. Moreover, the recent finding that the increase in blood pressure after pentazocine was associated with clearly elevated plasma catecholamines indicates sympathetic stimulation (Tammisto et al., 1971). To elucidate further the mechanism of the sympathetic stimulation caused by pentazocine we measured plasma catecholamines, blood pressure and heart rate after intravenous pentazocine in patients with sympathetic blockade induced by epidural anaesthesia.

PATIENTS AND METHODS
Twenty male patients scheduled for elective surgery (mainly urological cases) received the same preanaesthetic medication of atropine 0.01 mg/kg and pethidine 1 mg/kg by intramuscular injection.

In the induction room, the largest accessible vein was cannulated and a slow infusion of balanced Ringer's solution (Fysiosol, Leiras Oy) was started. When cardiovascular stability had been achieved (three consecutive similar readings of blood pressure and heart rate) control blood samples were taken.

Epidural blockade was performed by the injection of 0.5% bupivacaine in half of the patients at the L1-L2 interspace to produce high blockade and in the other half at the L4-L5 interspace to produce low blockade. The volume of bupivacaine solution was calculated as described by Eriksson (1969) to achieve 20 segments in the high blockade and 10 segments in the lower blockade.

Half of the patients in each of the two groups received 0.5% bupivacaine as Marcain-adrenaline and the other half as Marcain-plain. Thereafter the intravenous drip was turned on and 10 ml/kg was infused in 30 min.

The blockade resulted in the division of the patients into three groups based upon the extent of epidural blockade. Tables I and II show their distribution between the three groups.

The level of extent of the blockade, as tested by pinprick and by thermal (+55°C) sensibility 30 min after the injection was higher than T6 in 8 patients and lower than T8 in the other 8 patients. In 4 patients the level of the block was from T6 to T8. At this time pentazocine 1.2 mg/kg was injected over 60 sec through the side arm of the drip.

Blood samples for measurements of catecholamines were collected from the cannulated antecubital...
TABLE I. Age, weight, height, haematocrit and serum creatinine distribution in the different epidural blockade groups. Means ± SE.

<table>
<thead>
<tr>
<th>Extent of epidural blockade</th>
<th>No. of patients</th>
<th>Age (yr)</th>
<th>Weight (kg)</th>
<th>Height (cm)</th>
<th>Haematocrit</th>
<th>Serum creatinine (µmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Above T6</td>
<td>8</td>
<td>55.5 ± 7.3</td>
<td>74.0 ± 5.7</td>
<td>171.6 ± 2.9</td>
<td>0.45 ± 0.05</td>
<td>110.6 ± 12.8</td>
</tr>
<tr>
<td>Below T8</td>
<td>8</td>
<td>58.6 ± 8.4</td>
<td>76.2 ± 3.7</td>
<td>171.0 ± 2.2</td>
<td>0.41 ± 0.01</td>
<td>94.4 ± 4.7</td>
</tr>
<tr>
<td>T6-T8</td>
<td>4</td>
<td>69.8 ± 2.6</td>
<td>78.0 ± 3.4</td>
<td>170.3 ± 1.7</td>
<td>0.37 ± 0.04</td>
<td>118.5 ± 19.9</td>
</tr>
</tbody>
</table>

TABLE II. Preoperative systolic and diastolic blood pressure, heart rates and plasma catecholamines (CA) in the different epidural blockade groups. Means ± SE (NA = noradrenaline; A = adrenaline).

<table>
<thead>
<tr>
<th>Extent of epidural blockade</th>
<th>No. of patients</th>
<th>Blood pressure (mm Hg)</th>
<th>Heart rate (min)</th>
<th>Catecholamines (µg/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Syst.</td>
<td>Diast.</td>
<td></td>
</tr>
<tr>
<td>Above T6</td>
<td>8</td>
<td>158.1 ± 10.1</td>
<td>93.8 ± 7.2</td>
<td>82.8 ± 5.4</td>
</tr>
<tr>
<td>Below T8</td>
<td>8</td>
<td>153.1 ± 7.8</td>
<td>87.5 ± 4.9</td>
<td>82.3 ± 7.0</td>
</tr>
<tr>
<td>T6-T8</td>
<td>4</td>
<td>173.8 ± 19.1</td>
<td>85.0 ± 15.7</td>
<td>88.5 ± 12.4</td>
</tr>
</tbody>
</table>

results

Blood pressure and heart rate.

Effect of blockade. Based on the extent of the blockade the results were examined in three groups. The characteristics of the patients before the institution of the blockade are shown in tables I and II. After institution of the blockade, systolic blood pressure fell similarly with high and intermediate blockade whereas only a negligible fall was found with low blockade (fig. 1). With high or intermediate blockade, systolic blood pressure stabilized at a level about 30 mm Hg below the preanaesthetic pressure before pentazocine injection. The changes with low blockade differed significantly (P < 0.05) from those with high or intermediate blockade throughout the whole observation period except at 5 min. The changes in diastolic pressure after the blockade followed the same pattern as those in systolic pressure.

![Fig. 1. Changes in arterial systolic and diastolic pressure, and heart rate in the three different blockade groups. The arrow refers to the time point of pentazocine injection. Mean values ± SE.](image)
but were less marked and were not significantly different in the three groups. The increase in heart rate (fig. 1) was more marked in low and intermediate blockade groups but without there being a statistically significant difference between the groups (P>0.05). In all groups the heart rate then fell, gradually returning to the preanaesthetic level before pentazocine injection.

Effect of pentazocine injection. Since the blood pressure and plasma catecholamines after institution of blockade were similar in the bupivacaine-adrenaline and bupivacaine-plain groups these results have been considered together. Also the distribution of the two types of bupivacaine solutions was the same in the groups with different extent of epidural blockade. The mean rise in systolic blood pressure following pentazocine in the low epidural group reached its maximum (23.1 ± 5.3 SE mm Hg from the prepentazocine level) 10 min after the injection and was sustained at this level throughout the whole observation period. In the high blockade group a minor increase (6.3 ± 4.2 SE mm Hg) 10 min after the injection was observed. The results between high and low blockade groups differed significantly (P<0.01) at 5 and (P<0.05) at 10 min. The rise in systolic blood pressure in the intermediate group was of the same order as that in the low blockade group and also differed significantly (P<0.05) from the corresponding response in the high blockade group at 5 and 10 min. In the intermediate group the systolic pressure, however, did not reach the initial preanaesthetic level. The changes in diastolic blood pressure and heart rate followed the same pattern as the systolic pressure but were less marked and without statistically significant differences between the groups.

Plasma catecholamines.

Effect of blockade. In the high epidural blockade group the level of total plasma catecholamines (fig. 2) tended to increase following the institution of the block. This increase in total catecholamines was mainly due to increase of noradrenaline level. In the low and intermediate blockade groups this tendency was not observed. In the low blockade group, however, an increase in plasma catecholamines at 30 min was measured which was due to increase in the level of adrenaline. No statistically significant differences between these changes were found.

Effect of pentazocine injection. Pentazocine administration increased the total plasma catecholamine level (fig. 2), with a maximum rise of 0.46 ± 0.26 SE µg/l. (40% from the preinjection level) 5 min after the injection in the low blockade group, and 0.31 ± 0.07 SE µg/l. at 15 min in the intermediate group. In the high blockade group there was tendency for the levels to fall, by -0.14 ± 0.16 SE µg/l. at 5 min, and -0.16 ± 0.09 SE µg/l. at 15 min.

The pentazocine-induced increase in catecholamine comprised mainly noradrenaline in low and intermediate groups. The mean increase of noradrenaline was 0.25 ± 0.17 µg/l. at its maximum 5 min after injection in the low blockade group, and thus about 53% of the preinjection level of 0.47 ± 0.12 SE µg/l. A similar increase 0.24 ± 0.09 SE µg/l. was measured in the intermediate blockade group. After pentazocine in the high blockade group the noradrenaline and adrenaline levels showed a slight tendency to fall, whereas the adrenaline levels in the low and intermediate blockade groups remained unchanged. The statistical significance of these changes could not be ascertained.
DISCUSSION

The blood pressure response to intravenously administered pentazocine has previously been attributed to sympathetic stimulation of central origin (Keats and Telford, 1964). This is in keeping with the finding that the pressor response is associated with an increase in plasma catecholamine levels (Tammisto et al., 1971) and that the pressor response is counteracted by general anaesthesia and epidural blockade (Tammisto, 1971).

In the present study the pressor response to pentazocine was almost completely blocked by high epidural blockade, while the response under low epidural blockade was similar to that obtained in healthy unanaesthetized patients (Tammisto et al., 1970, 1971). The results further suggested that the pentazocine-induced increase in plasma catecholamine levels is prevented by a high epidural blockade.

The interpretation of the results is, however, hampered by the changes caused by the institution of epidural blockade. Thus the blood pressure at the time of the pentazocine injection was at a significantly lower level after high epidural blockade than after a low blockade. This different reference level, however, does not explain the abolished pressor response, since in the intermediate group the pressor response was elicited despite a lowering of blood pressure after institution of blockade. Epidural blockade seemed to affect the level of catecholamines also and curiously a tendency to elevated noradrenaline levels was seen after high blockade. If this finding is confirmed then it must represent a compensatory overactivity of the still functioning sympathetic nervous system above the blockade.

After low blockade the level of catecholamines was above the preanaesthetic level at the time of the pentazocine injection. Here the increase, however, was due to adrenaline. Though this isolated increase was not statistically significant it might partly explain the fact that the elevation of plasma catecholamines after low blockade was 40% and was of noradrenaline only, compared to the 100% increase comprising both noradrenaline and adrenaline previously found in unanaesthetized patients (Tammisto et al., 1971).

Despite the limitations discussed there is strong evidence that in addition to the pentazocine-induced pressor response the associated increase in plasma catecholamines is also prevented by a high epidural blockade. These findings, therefore, suggest that the pressor response to pentazocine is due to sympathetic stimulation at central sites.

ACKNOWLEDGEMENTS

This study was supported financially by the National Research Council for Medical Sciences and the Paulo Foundation, Finland.

REFERENCES


EFFET DU BLOQUAGE EPIDURAL SUR L'AUGMENTATION SOUS L'INFLUENCE DE PENTAZOCINE DES CATECHOLAMINES DU PLAAS ET DE LA PRESSION SANGUINE

SOONMAIRE

Afin d'éclaircir le mécanisme et le lieu d'action de la stimulation sympathique sous l'influence de pentazocine, les catécholamines ont été mesurées dans le plasma après pentazocine i.v. 1,2 mg/kg chez vingt patients avec blocage epidural atteignant divers niveaux. Le taux total des catécholamines plasmatiques augmenta chez les patients avec blocage epidural bas (inférieur à T8) pendant les 20 minutes d'observation et atteigna un maximum d'environ 40%, 5 minutes après l'injection de pentazocine. L'augmentation des catécholamines impliqua surtout la noradrenaline et correspondit à l'élévation de la pression sanguine et de la fréquence cardiaque. Pentazocine causa une légère réduction du taux des catécholamines chez les patients avec blocage epidural haut (au-dessus de T6). Chez ces malades l'élévation de la pression sanguine, causée par pentazocine, était quasi complètement abolie. Il est cru que le lieu de la stimulation sympathique causée par pentazocine est central.

WIRKUNG EINER EPIDURALEN BLOCKADE AUF DEN PENTAZOCINE-INDUZIERTEN ANSTIEG DER PLASMAKATECHOLAMINE UND DES BLUTDRUCKES

ZUSAMMENFASSUNG

Um den Mechanismus und den Wirkungsort der pentazocine-induzierten sympathischen Reizung zu erhehlen, wurden die Plasmakatecholamine nach intravenöser Verabreichung von Pentazocine 1,2 mg/kg an 20 Patienten mit epiduraler Blockade verschiedener Höhen gemessen. Bei Patienten mit tiefer epiduraler Blockade (unter T8) stieg das gesamte Plasmakatecholaminkonzentration im Verlauf von 20 Minuten Beobachtungszeit 5 Minuten nach der Injektion von Pentazocine bis zu einem Maximum von etwa 40%.

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**EFECTO DEL BLOQUEO EPIDURAL SOBRE EL AUMENTO DE LAS CATECOLAMINAS PLASMICAS Y PRESSION ARTERIAL INDUCIDOS POR LA PENTAZOCINA**

**RESUMEN**

Con el fin de dilucidar el mecanismo y lugar de acción de la estimulación simpática inducida por pentazocina, se determinaron las catecolaminas plasmáticas tras la administración por vía endovenosa de 1.2 mg de pentazocina/kg de peso corporal, en 20 pacientes con bloqueos epidurales de distinto nivel. En pacientes con bloqueo epidural bajo (por debajo de T8), las catecolaminas plasmáticas totales aumentaron durante los 20 minutos que duró el periodo de observación hasta un máximo de aproximadamente el 40% 5 minutos después de la inyección de pentazocina. El aumento en las catecolaminas se compuso principalmente de noradrenalin y se correspondió con un aumento de la presión arterial y de la frecuencia cardíaca. En pacientes con bloqueos epidurales altos (por encima de T6) la pentazocina dio lugar a un ligero descenso en los niveles de catecolaminas. En estos pacientes la elevación de la presión arterial inducida por la pentazocina fue abolida casi por completo. Consideramos que la ligera estimulación simpática inducida por la pentazocina es central.

**CORRESPONDENCE**

**THE RISK OF ASPIRATION IN PRESENCE OF CUFFED ENDOTRACHEAL TUBES**

Sir,—In the second edition of his classic book *Endotracheal Anaesthesia* (University of Wisconsin Press, p. 98), Dr Noel Gillespie says: "An endotracheal cuff should lie just below the vocal cords; if it lies more deeply in the trachea foreign fluids can accumulate above it, and be aspirated into the respiratory tree when the cuff is deflated prior to extubation."

He also says (p. 10): "George Bernard Shaw has drawn attention to the frequency with which a given idea recurs in the history of Medicine. Usually those who 're-discover' the idea do so in perfectly good faith, unaware that similar work has been done before" (*The Doctor's Dilemma, Act I*).

C. J. COGHLAN
Nakuru

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**ENDOTRACHEAL INTUBATION IN THE RAT**

Sir,—I was interested to read the paper by Drs Proctor and Fernando (*Brit. J. Anaesth.* (1973), 45, 139).

Several years ago, while working in the Department of Surgery, Manchester University, Mr Hugh Bailie and I were faced with the same problem. However, before we had mastered the technique of orotracheal intubation we discovered that blind nasal intubation could easily and regularly be achieved using a medium or large Braunula without needle (I have forgotten the exact size). It seems that the airway must virtually be a straight line, as we discovered that blind nasal intubation could easily and regularly be achieved using a medium or large Braunula. When we had mastered the technique of blind nasal intubation we were faced with the same problem. However, before we had mastered the technique of orotracheal intubation we discovered that blind nasal intubation could easily and regularly be achieved using a medium or large Braunula without needle (I have forgotten the exact size). It seems that the airway must virtually be a straight line, as we encountered no difficulty whatever.

As we were using this for resuscitation, I have no information as to how it stands up to prolonged IPPV.

D. J. F. MACDONALD
Glasgow

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**PROLONGED NEUROMUSCULAR BLOCKADE**

Sir,—Dr Hall and his colleagues describe an interesting case of prolonged neuromuscular blockade following tubocurarine, lignocaine and gentamicin (*Brit. J. Anaesth.* (1972), 44, 1729).

However, they do not discuss the possible contribution made by the preoperative and postoperative therapy to this patient's stormy postoperative course.

It would appear that, with a blood urea in excess of 120 mg/100 ml, the patient was receiving 4 g/day of cephaloridine accompanied by 160 mg/day of furosemide. In patients whose blood urea is elevated between 110 and 160 mg/100 ml, the serum half-life of cephaloridine is prolonged to 5–10 hours and the maximum daily dose should not exceed 1 g (Foord, 1970). The addition of furosemide enhances the nephrotoxicity of cephaloridine (Dodds and Foord, 1970).

The subsequent renal failure seen in this patient should serve as a salutary reminder of the dangers of high-dose intravenous cephaloridine in patients with inadequate renal function, particularly when large doses of furosemide are being prescribed concurrently.

ALASTAIR J. J. WOOD
MARGARET WOOD
Dundee

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**REFERENCES**


Sir,—Dr A. J. J. Wood and Dr M. Wood are quite correct in their point about high dosage of cephaloridine, and we are now much more aware of the dangers of this drug, particularly when used with diuretics.

We do not, however, agree with their suggestion that this antibiotic was responsible for the renal failure in our patient, for the following reasons:

1 The blood urea postoperatively fell as a result of improved cardiac performance, even though the daily 4 g dosage of cephaloridine was continued.

2 On the 11th postoperative day when the blood urea began to rise steeply, cephaloridine had already been discontinued in favour of gentamicin, because of the isolation of the gram-negative organisms from the sputum.

3 After surgery furosemide was only used in infrequent "stat" dosage.

We therefore feel that the renal failure that followed was much more likely due to gram-negative bacteremia rather than to any nephrotoxic effect of the cephaloridine.

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