SOME PROBLEMS RELATING TO ANAESTHETIC MANAGEMENT OF PHAEOCHROMOCYTOMA

By

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The fact that the hypertension resulting from phaeochromocytoma is amenable to surgical removal of the tumour and that the anaesthetic management is associated with formidable problems affecting the cardiovascular system, the subject deserves a close attention of the anaesthesiologist in all its aspects of its management.

The anaesthetic procedure is hazardous because extreme fluctuations in blood pressure and heart rate frequently occur during the procedure and may prove a serious threat to life. The vascular crisis is due to the excessive quantities of catecholamines circulating in the blood of these patients and during handling of the tumour there is further release of these hormones in the circulation, however when the veins draining the tumour are ligated a sudden fall in blood pressure occurs. The vascular system is adopted to a rich source of catecholamines which when suddenly withdrawn leads to hypotension and a shocked state.

The approach to deal with this crisis has changed considerably over the years as the understanding of the haemodynamic variations improved. It is intended to focus the attention on certain aspects of the anaesthetic management of this important surgical procedure in the light of the experience gained in dealing with the cases operated at the All India Institute of Medical Sciences Hospital, Delhi.

CLINICAL MATERIAL

Table No. 1 depicts informations about the 9 patients who had surgical removal of phaeochromocytoma in our hospital from the year 1958 to 1969. The age incidence was from 6 years to 47 years. There were 6 males and 3 females in the series. 6 had the tumour associated with right adrenal, 2 with left adrenal and in one case tumour was situated at the bifurcation of aorta. The maximum blood pressure ranged from 270/160 to 170/120 mm Hg. Phentolamine test was positive in all the cases. Other tests carried out in some patients were, estimation of urinary catecholamines and retroperitoneal pneumogram. These tests further helped in the diagnosis of these patients. There was no mortality in the series presented.

Choice of agents:

The anaesthetic management in phaeochromocytoma cases mainly depends on basic principles of a good sound anaesthetic technique which would avoid hypoxia and hypercarbia. There are theoretical objections to every agent that is required to be used. In this series 6 cases were conducted with thiopentone and suxamethonium induction, and ether was used to stabilize the patient after nitrous oxide and oxygen mixtures were used in combi-
### TABLE 1

**A twelve year survey of pre-operative status of 9 cases of phaeochromocytoma operated.**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Year</th>
<th>Age in years</th>
<th>Sex</th>
<th>Site</th>
<th>Pre-operative max. blood pressure</th>
<th>Phentolamine test</th>
<th>Other tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>1958</td>
<td>28</td>
<td>F</td>
<td>Rt adrenal</td>
<td>240/140 mm Hg</td>
<td>Positive</td>
<td>—</td>
</tr>
<tr>
<td>2.</td>
<td>1961</td>
<td>38</td>
<td>M</td>
<td>Rt adrenal</td>
<td>190/130 mm Hg</td>
<td>Positive</td>
<td>—</td>
</tr>
<tr>
<td>3.</td>
<td>1962</td>
<td>32</td>
<td>M</td>
<td>Bifurcation of aorta</td>
<td>170/120 mm Hg</td>
<td>Positive</td>
<td>Catecholamines 80 µg/100 ml of urine</td>
</tr>
<tr>
<td>4.</td>
<td>1962</td>
<td>37</td>
<td>M</td>
<td>Rt adrenal</td>
<td>220/130 mm Hg</td>
<td>Positive</td>
<td>552.5 µg in 24 hours of urine</td>
</tr>
<tr>
<td>5.</td>
<td>1964</td>
<td>47</td>
<td>M</td>
<td>Lt adrenal</td>
<td>200/130 mm Hg</td>
<td>Positive</td>
<td>Retroperitoneal pneumogram positive</td>
</tr>
<tr>
<td>6.</td>
<td>1965</td>
<td>6</td>
<td>M</td>
<td>Lt adrenal</td>
<td>270/160 mm Hg</td>
<td>Positive</td>
<td>—</td>
</tr>
<tr>
<td>7.</td>
<td>1966</td>
<td>39</td>
<td>F</td>
<td>Rt adrenal</td>
<td>210/120 mm Hg</td>
<td>Positive</td>
<td>Urinary catecholamines 610 µg in 24 hours</td>
</tr>
<tr>
<td>8.</td>
<td>1967</td>
<td>12</td>
<td>M</td>
<td>Rt adrenal</td>
<td>220/160 mm Hg</td>
<td>Positive</td>
<td>Retroperitoneal pneumogram positive</td>
</tr>
<tr>
<td>9.</td>
<td>1969</td>
<td>18</td>
<td>F</td>
<td>Rt adrenal</td>
<td>230/150 mm Hg</td>
<td>Positive</td>
<td>Urinary catecholamines 580 µg in 24 hours</td>
</tr>
</tbody>
</table>

### TABLE 2

**Anaesthetic technique and control of blood pressure before removal of tumour.**

<table>
<thead>
<tr>
<th>Period</th>
<th>No. of cases</th>
<th>Induction</th>
<th>Relaxant</th>
<th>Maintenance</th>
<th>Control of blood pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1958—1965</td>
<td>6</td>
<td>Thiopentone Suxamethonium</td>
<td>d-tc</td>
<td>N₂O, O₂, ether</td>
<td>Regitine Arfonad in case No. 5.</td>
</tr>
<tr>
<td>1966—1969</td>
<td>3</td>
<td>Thiopentone Suxamethonium</td>
<td>d-tc</td>
<td>N₂O, O₂, halothane</td>
<td>Regitine occasionally</td>
</tr>
</tbody>
</table>
nation with d-tubocurarine as the muscle relaxant. In the last 3 cases, however, halothane was made use of, not only for anaesthetic purposes but also the judicious combination with d-tubocurarine helped to control blood pressure levels before the removal of the tumour. Ether is known to stimulate the release of catecholamines thus aggravating the peaks of blood pressure levels. This was required to be controlled by intermittent doses of phentolamine 1 to 5 mg intravenously. In case No. 5 trimetaphan (arfonad) drip was made use of for this purpose. Both phentolamine and trimetaphan gave rise to troublesome tachycardia. Judicious combination of d-tubocurarine and halothane is a useful adjunct to control the blood pressure by the anaesthetist. This method was used in the last three cases with a reasonable control on blood pressure levels; halothane in presence of excessive circulating catecholamines, is thought to be a significant disadvantage of the drug and some authors feel that the agent is contraindicated for fear of arrhythmias. In three cases where halothane was used in this series such arrhythmias were not noticed except in case No. 9 where supra-ventricular tachycardia was observed at one stage and this could be controlled by intra-venous administration of 3 ml of 2% lignocaine. It is considered that \( \beta \)-receptor antagonist drugs like propranolol could be helpful while dealing with the problems of arrhythmias in such situations. Cyclopropane has been used for the procedure but it obviously precludes the use of cautery during surgery and also stimulates secretion of adrenaline.

Theoretically again d-tubocurarine should be used with caution because of its property to release histamine which in its turn results in excessive secretions of catecholamines. This problem did not arise in any of the cases in this series.

**Control of fluctuations in blood pressure**

The difference in response to anaesthesia and surgery between patients with sustained hypertension and those with paroxysmal hypertension are impressively brought out by the figures of Mayo clinic. These figures suggest that patients with sustained hypertension are likely to present greater difficulties during anaesthesia than patients with paroxysmal hypertension. Sustained hypertension indicates that the phaeochromocytoma is secreting excessive catecholamines continuously with or without superimposed paroxysms of increased production. In paroxysmal hypertension, on the other hand, the tumour secretes large amounts of catecholamines only during paroxysms. In our series, as can be seen in table 3, 6 patients had paroxysmal type and 3 had sustained type of hypertension. The peak of pressure reached by the sustained group was

<table>
<thead>
<tr>
<th>Period</th>
<th>No of cases</th>
<th>Paroxysmal (P) Sustained (S)</th>
<th>Use of vasopressor after removal of tumour</th>
<th>Blood volume replacement on the day of operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1958—1965</td>
<td>6</td>
<td>4(P) &amp; 2(S)</td>
<td>Nor-adrenaline drip 2—4 days</td>
<td>Average 0.8 litres</td>
</tr>
<tr>
<td>1966—1969</td>
<td>3</td>
<td>2(P) &amp; 1(S)</td>
<td>nil</td>
<td>2.4 litres</td>
</tr>
</tbody>
</table>

**TABLE 3**

Use of Vasopressors and blood volume replacement

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more than the patients having paroxysmal hypertension.

The crisis of hypertension and hypotension presents in a dramatic manner during the anaesthetic procedure for the removal of this tumour.

A patient suffering from this disease can tolerate the hypertensive episodes better than someone who never before was exposed to rise of blood pressure of the magnitude because long before coming for operations the system of the patient is used to higher levels of blood pressure either continuously or in paroxysms. Still, the marked hypertensive crisis during surgery should be under control.

Regitine (phenolamine), the α-receptor blocking agent, has been described as the drug of choice to control the hypertensive crisis in these cases. The drug is administered in 1 to 5 mg doses intravenously depending on the severity of hypertension. Phentolamine was used to control the hypertensive crisis in all the cases in the first group of 6 cases except in one, where trimetaphan drip 0.2% strength was utilised to control the rise of blood pressure. However the tachycardia resulting from the use of phentolamine was alarming. In the second group of 3 cases this drug was used only occasionally and halothane concentrations were adjusted with advantage to control the hypertensive episodes during the anaesthetic procedure. Although β-receptor antagonist drug was not used in the present series this could be considered as an useful adjunct to avoid arrhythmias occurring during the anaesthetic procedure. It must be emphasised at this stage that hypoxia and hypercarbia are avoidable factors which are likely to initiate a hypertensive crisis.

**Hypotensive Crisis**

In the first six cases, the hypotensive crisis have been dealt with by administration of nor-adrenaline infusion in the period following removal of tumour. The period varied from 2 to 4 days. Although there was no mortality, the patient's condition was considered precarious during this period followed by the difficult period of weaning the patient off the infusion.

A better physiological approach based on the changes in the blood volume was utilized in the last 3 cases with gratifying results. The excessive catecholamines circulating in the blood stream results in a contracted blood volume in these patients, and when the excessive catecholamine secretions are withdrawn from circulation as a result of the removal of the tumour, there is suddenly a relative hypovolaemia resulting in hypotensive crisis. In patient Nos. 7 and 8 blood was transfused at a rapid rate at this stage till the systolic blood pressure level of 100 mm Hg. was reached. The transfusions were adjusted to maintain this level. In the last case pre-operative blood volume measurement was carried out with the Risa method using volumetron. The predicted blood volume was calculated on the weight basis and the deficit of 0.7 litres was quickly injected in the form of blood and Ringer's lactate solution as soon as the veins from the tumour were ligated and the tumour was removed. In these 3 cases on an average of 2.4 L of blood and Ringer's lactate solution were administered on the day of operation as compared with the first 6 cases where only 0.8 litres consisting of blood and 5% glucose solution were given in the first 24 hours. In these last 3 cases where blood volume replacement was carried out, nor-adrenaline infusion was not found necessary to maintain the blood pressure level and the patients’ condition was judged as satisfactory during the immediate post-operative period. It was observed that the post-operative course of these patients was smoother.

Thus the severe post-removal hypotension can be explained by the loss of arteriolar tone
and dilatation of the vascular bed resulting from withdrawal of the catecholamine. In these circumstances a rapid transfusion of blood or volume expander seems to be a logical step to raise the arterial pressure and central venous pressure.

In general, the disease causes important changes in the patient’s haemodynamics. Some degree of vasoconstriction seems to persist whether hypertension is sustained or appears in paroxysms. The contraction of the total circulating blood volume commonly found, may be regarded as a compensatory reaction to persistent vasoconstriction. Continuous monitoring of the arterial blood pressure and venous pressure seems to be a very useful guide for the rapid transfusion to replenish the blood volume after the removal of the tumour. In centres where facilities for measurement of the blood volume are available, the knowledge of the blood volume deficit in these patients could further help in the rapid replacement. It should, however, be noted that the preoperative measurement must be based on determination of both the plasma volume and the cell volume and provision is made to over-transfuse the patient beyond the loss of blood at surgery by an amount equal to the difference between measured pre-operative values and the predicted blood volume.

The difficulty about preoperative estimation of blood volume and thus ascertaining the deficit is that the pre-operative blood volume is significantly contracted in sustained hypertensive group of patients and it may be normal in a paroxysmal type of patient. It is difficult to come to any conclusion from a small number of cases about the importance of measurement of blood volume and establishing the deficit from the predicted blood volume. Brunjes (1960) reported deficits of 17% and 7% respectively in two cases, subsequently they reported blood volume of a patient and it was normal. Sjoerdsm (1966) concluded from studies on 15 patients that a significant fall in blood volume occurs only rarely. Predicted blood volumes are not sufficiently accurate and even serial measurements made pre-operatively will not on their own permit correct conclusions to be drawn concerning the deviation from normal.

The treatment with alpha-blocker phenoxycbenzamine, which is a long acting drug, is said to result in spontaneous restoration of the blood volume to normal. It seems that the blood volume expansion during operation if hypotension is accompanied by a fall in central venous pressure is the most logical therapy in such situation.

As stated by Sjoerdsm (1966) and Ross (1967), it is possible with modern drugs to minimize the cardiovascular crisis that complicate the operation by preoperative alpha and beta adrenergic blockade. This approach needs further clinical trial.

REFERENCES