BLOOD LOSS DURING HYSTERECTOMY ASSOCIATED WITH THE USE OF TUBOCURARINE OR GALLAMINE

BY

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SUMMARY

Patients undergoing hysterectomy were divided into two groups, one of which was given tubocurarine and the other gallamine triethiodide as the muscle relaxant. In all other respects the anaesthetics were similar. During the course of operation those patients who were given gallamine showed significantly greater blood losses. This difference did not appear to be related to the surgeon performing the operation or to the duration of operation. It was concluded that the most likely cause was the higher heart rates, probably associated with higher cardiac outputs, in the gallamine group.

There is a widespread clinical impression that gallamine triethiodide is a cause of increased bleeding during surgical procedures. During the course of a study comparing the effects of gallamine and tubocurarine on arterial pressure and heart rate, it was noted that the volume of blood lost during hysterectomy appeared to depend on which relaxant was being used. Measurements of the blood loss, by routine clinical methods, were therefore analyzed retrospectively. The results suggest that blood loss is greater when gallamine, rather than tubocurarine, is used.

METHOD

Forty-two patients, undergoing abdominal hysterectomy, were studied. They were divided into two groups of twenty-one patients. In one group gallamine was used as relaxant, while in the other tubocurarine was used. Patients were allocated to one group or the other, according to a table of random numbers. Some patients were later excluded from the trial because they never showed a steady circulatory state (see below). The trial was continued until there was the same number in each group. The mean age of the patients given tubocurarine was 43 years (SD 4.8), and their mean weight 67 kg (SD 9.0). Those who were given gallamine had a mean age of 44 years (SD 5.4) and a mean weight of 59 kg (SD 7.0).

Patients with clinical evidence of respiratory or cardiac disease were excluded from the study. Some difficulty was experienced in deciding whether certain patients were normotensive or hypertensive. For this reason patients were admitted to the study whatever their pre-operative level of arterial pressure.

Anaesthetic procedure.

All patients were anaesthetized by one anaesthetist who used the same technique apart from changing the muscle relaxant. Premedication, consisting of papaveretum 20 mg and hyoscine 0.4 mg, was given to all patients, regardless of weight, approximately 1 hour pre-operatively. Thiopentone 5 mg/kg was used for induction followed by 50 mg of suxamethonium chloride. The larynx was sprayed with 100 mg of lignocaine aerosol and orotracheal intubation was achieved using a cuffed tube. Spontaneous ventilation was allowed to return and the anaesthetic was maintained with oxygen (2 l./min) and nitrous oxide (4 l./min). The patient was taken into theatre and prepared for surgery. During this period of approximately 5 minutes, 1 per cent halothane was added from a Fluotec Mark II vaporizer. An infusion of dextrose 4.3 per cent with 0.18 per cent saline was set up in the left arm; 200–300 ml was given in the course of the procedure in the majority of the patients. Stored whole blood was given to three patients whose blood loss exceeded 500 ml. The muscle relaxant was given intravenously, doses of gallamine or tubocurarine being 120 mg and 30 mg respectively. The table

was then placed in a 5-degree head-down tilt, and the operation allowed to proceed.

Artificial respiration was maintained with an East-Radcliffe ventilator with a 1-lb. soda-lime canister in the circuit. The tidal volume given was calculated on the basis of $9 \times \text{body weight in kg}$ and the ventilator was set at 16 cycles/min. Assuming a $V_d/V_t$ ratio of 0.45 and using Nunn's Blood Gas Predictor (Nunn, 1962) this volume would be expected to give an arterial carbon dioxide tension of between 30 and 35 mm Hg. During closure of the parietal peritoneum atropine 1.2 mg was given, followed by neostigmine 2.5 mg at skin closure.

Systolic and diastolic arterial pressure were measured with an upper arm cuff and aneroid manometer using a stethoscope over the brachial artery. The accuracy of the aneroid manometer used was checked against a mercury column. The heart rate was measured by palpating a peripheral artery. They were recorded prior to induction and at 5-minute intervals during the procedure. A "steady state" was assumed to have occurred when the pressures remained within ± 5 mm Hg and the heart rate within ± 5 beats/min over a period of 15 minutes. The mean of three readings was taken in each case. This steady state was usually established during the latter part of the operation. Figure 1 gives an example of the steady state from the anaesthetic record of a patient who received gallamine. Patients who did not show a steady state were excluded from the series. Further patients were substituted at random until both groups contained the same numbers.

Blood loss was measured using a beam balance which was checked against known weights and found to be accurate to within ± 5 per cent. Commercially available gauze swabs and abdominal packs were found to weigh 5 g and 20 g respec-

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**Fig. 1**
Anaesthetic record showing "steady state".
tively when dry. Wrung-out wet packs weighing 40 g were occasionally used. Blood loss was calculated by subtracting these standard weights from single weighings of the swabs or packs as they were being discarded. The surgical drapes were not weighed. The figures for blood loss were not recorded in one patient in the gallamine group, and two patients in the tubocurarine group. Results were analyzed by Student's t test using a computer program kindly made available to us by Dr. J. L. Haybittle.

Not all the operations were performed by the same surgeon, although they all used a similar operative technique. One consultant gynaecologist did fourteen of the twenty-one operations in each group, and these provided a further sub-grouping (see table II). The remaining seven patients in each group were operated on by either another consultant, a senior registrar, or one of two registrars.

The operating time was taken from the skin incision to the start of closure of the parietal peritoneum. The mean duration of operation was 51 minutes in the tubocurarine group and 58 minutes in the gallamine group.

RESULTS

The mean pre-operative arterial pressure in the tubocurarine group was 130/73 mm Hg whereas in the gallamine group it was a 115/66 mm Hg. The heart rates were 80 and 76 beats/min respectively.

During the steady state the mean systolic and diastolic pressures were 127/88 mm Hg in the tubocurarine group and 132/94 mm Hg in the gallamine group. The heart rates were 63 and 95 beats/min respectively, a difference of 32 beats/min (SE 3.6; P<0.001). These results are summarized in table I.

The mean blood loss in the nineteen patients given tubocurarine was 132 ml, while the twenty who had gallamine showed a mean loss of 292 ml. The variance ratio between the two groups was 11.6 but, although taking this into consideration,

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<tr>
<th>Table I</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recordings of arterial pressure and heart rate in the pre-operative and steady states.</strong></td>
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<td><strong>Pre-operative</strong></td>
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<td>Arterial pressure</td>
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<th>Table II</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood loss analysis.</strong></td>
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<td><strong>All surgeons</strong></td>
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<td><strong>Mean (ml)</strong></td>
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<td>Degrees of freedom</td>
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the difference between the means of 159 ml was still highly significant (P<0.01).

The mean blood losses were then compared in the sub-groups who were operated on by the same surgeon. When these operations were compared the blood loss was 123 ml with tubocurarine and 248 ml with gallamine. The difference in mean blood loss was 125 ml (P=0.07) (table II).

DISCUSSION

The patients in the two groups were of similar ages but, although selected at random, the weights of the patients who had gallamine were significantly lower than those who had tubocurarine. This difference was statistically significant (SE 2.6; P<0.01). The premedication, papa-veretum 20 mg and hyoscine 0.4 mg, was given irrespective of weight, so that the patients who received gallamine had larger doses per unit of body weight. The use of hyoscine has been shown to be associated with bradycardia, low arterial pressure and low cardiac output (List and Gravenstein, 1965). This factor would account for the lower mean heart rate and arterial pressures in the gallamine group. This unfortunately makes it difficult to interpret differences between the pre-anaesthetic and steady state figures in the two groups.

The measurement of systolic and diastolic pressure by auscultation is reasonably accurate but subject to observer variations; however, in this series, the same person took all the measurements.

The method used for measuring blood loss can be faulted for various reasons. The surgical drapes were not weighed although they were seldom obviously soiled. The actual weighings were performed by a variety of nurses whose techniques were not likely to have been identical. Three to five wet abdominal packs were used at operation. The weights of these varied according to how long and how hard they were wrung out by the scrub nurse. Although the standard weight was taken as 40 g, trial weighings showed a variation of up to 10 g above this figure, leading to over-estimation of blood loss. The degree of accuracy achieved is accepted in clinical practice and is used as one of the guides to blood replacement during operations. The wide scatter of the readings of both groups is probably due as much to inaccuracies in

the method of measurement as to other factors. However, it is likely that inaccuracies would be evenly distributed between the two groups.

In the present study there was a statistically significant difference between blood loss in the tubocurarine group and the gallamine group. Blood losses during similar operations on patients of similar ages and weights depend on several factors. The length of operation appears to have surprisingly little influence on blood loss (Safar, 1955; Donald, 1969). The mean operating times for the two groups were very similar, so differences are unlikely to have been due to this cause. Different surgeons will affect the blood loss depending on their attitude to haemostasis, experience and dexterity. It was for this reason that the fourteen patients in each group who were operated on by the same surgeon were compared separately. These figures seem to show that there is little individual variation in mean blood loss related to the surgeon performing the operation, and we would agree with Donald (1969) and other writers that blood loss is not greatly influenced by the experience of the surgeon and that there is a large range of mean blood loss with the same surgeon.

The effect of blood pressure on blood loss has been extensively studied and hypotensive techniques, with the aid of posture, have been advocated to minimize blood loss at operation. The procedures have recently been discussed by Donald (1969). In our study the mean differences between steady states in the two groups were 5 mm Hg for the systolic pressures and 6.5 mm Hg for the diastolic pressures. The differences were not significant and would not adequately explain the significant extra blood loss in the gallamine group.

An increased heart rate has been associated with increased bleeding and attempts to decrease the heart rate, as well as blood pressure, have been used in attempts to reduce operative loss (Hellewell and Potts, 1966). In the present study the mean heart rate during the steady state in the gallamine group was significantly greater than in the tubocurarine group. Gallamine has a positive chronotropic effect on the heart. This has been ascribed to an atropine-like effect, blocking the post-ganglionic muscarinic receptors of the cardiac vagus (Riker and Wescoe, 1951; Paton,
BLOOD LOSS ASSOCIATED WITH TUBOCURARINE OR GALLAMINE

1959), but a direct stimulating effect on the intra-cardiac beta-receptors has recently been demonstrated (Brown and Crout, 1968). Kennedy and Farman (1968) showed that moderate doses of gallamine given to anaesthetized patients who had been previously given tubocurarine and ventilated artificially, caused a 35 per cent increase in cardiac output, accompanied by a fall in peripheral resistance of between 15 and 20 per cent. Riker and Wescoe (1951) were unable to find evidence that gallamine has any action on blood vessels, suggesting that the effect of gallamine on the peripheral circulation is secondary. Leigh and Tyrrel (1968) have shown that hypotensive anaesthesia is only achieved when there is a fall in cardiac output, suggesting that cardiac output is a major determinant of blood loss. We would therefore suggest that patients who have gallamine during their anaesthetics probably have higher cardiac outputs than those who receive tubocurarine. This would explain the increased bleeding when gallamine is used.

REFERENCES


LA PERTE DE SANG DURANT L’HYSTERECTOMIE, ASSOCIEE AVEC L’EMPLOI DE TUBOCURARINE OU GALLAMINE

SOMMAIRE

Des patientes qui devaient subir une hystérectomie, ont été partagées en deux groupes, dont l’un a reçu tubocurarine et l’autre gallamine triéthiodide comme relaxant musculaire. On a observé au cours de l’opération chez les patientes, qui avaient reçu gallamine, des pertes de sang significativement plus grandes. Cette différence ne semble pas due au chirurgien, faisant l’opération, ni à la durée de l’intervention. On en conclut que la cause la plus probable est la fréquence cardiaque élevée, probablement associée à un débit cardiaque plus grand, dans le groupe gallamine.

WAHREN Hysterektomien im Zusammenhang mit der Anwendung von Tubokurarin oder Gallamin. Auftretender Blutverlust

ZUSAMMENFASSUNG

Patientinnen, die sich einer Hysterektomie zu unterziehen hatten, wurden in zwei Gruppen eingeteilt; als Muskeltaxans wurde der einen Gruppe Tubokurarin, der anderen Gallamintriäthiodid verabreicht. Im übrigen wurden in beiden Gruppen die gleichen Anaesthesietika verwandt. Im Verlauf der Operation wurde bei den mit Gallamin behandelten Patientinnen ein wesentlich größerer Blutverlust beobachtet. Dieser Unterschied schien weder mit dem die Operation durchführenden Chirurgen noch mit der Operationsdauer in Verbindung zu stehen. Es wurde der Schluss gezogen, daß die höhere Herzfrequenz und das vermutlich damit verbundene größere Herzschlagvolumen in der Gallamin-Gruppe als wahrscheinliche Ursache anzusehen ist.