OPERATIVE BLOOD LOSS AND THE FREQUENCY OF HAEMORRHAGE ASSOCIATED WITH ADENOTONSILLECTOMY IN CHILDREN: A DOUBLE-BLIND TRIAL OF ETHAMSYLYATE

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SUMMARY

One hundred children were allocated randomly to receive either ethamsylate (Dicynene) or a placebo before undergoing adenotonsillectomy. Blood loss at operation was estimated from the haemoglobin content of swabs and aspirated fluid. Mean blood loss in the ethamsylate-treated group was not significantly less than in the controls. The frequency of secondary haemorrhage was significantly less in children treated with ethamsylate ($P<0.01$). No side-effects were reported in either group.

Although removal of tonsils and adenoids is by far the commonest operation performed in children, little has been written about the amount of blood lost during this operation. Shalom (1964) in a review of the literature about blood loss in the 5-year period from 1958 to 1962 found more than 900 articles which referred to tonsillectomy, but of these only five mentioned measurement of blood loss during the removal of tonsils and adenoids.

Ethamsylate (Dicynene, Delandale Laboratories Limited) is a capillary haemostat which has been shown to decrease blood loss in various surgical procedures (Deacock and Birley, 1969; Arnot et al., 1975; Symes et al., 1975; MacKenney, 1979) and in patients with menorrhagia (Jaffe and Wickham, 1973; Harrison and Campbell, 1976). The use of ethamsylate in tonsillectomy was studied by de Reynier (1965) and Papatheodosslou (1973) who conducted double-blind trials in adults and children. Both found a significantly smaller operative blood loss in the patients given ethamsylate than in those receiving a placebo. Another double-blind trial of ethamsylate in adults and children undergoing tonsillectomy showed no significant difference between the operative blood losses in the two groups although fewer ligatures were used on average in the ethamsylate-treated group (Gray and Noble, 1966). More recently, Verstraete and colleagues (1977) reported no significant difference between the blood loss following ethamsylate or a placebo at tonsillectomy, adenoidectomy and adenotonsillectomy in children in a double-blind trial.

The purpose of this trial was to eliminate, as far as possible, factors known to increase bleeding and then to assess the effect of ethamsylate on operative blood loss and the frequency of primary and secondary haemorrhage in a carefully controlled series of adenotonsillectomy in children.

METHOD

Patients

One hundred children admitted to hospital for adenotonsillectomy were studied. All were admitted one day before operation. They were in good general health and none had an acute respiratory tract infection. There were 52 males and 48 females, aged between 3 and 12 yr and weighing 13.2-43.5 kg on admission. The minimum acceptable haemoglobin concentration was 11 g dl$^{-1}$.

The children were allocated randomly, using statistical tables, to receive either ethamsylate or a placebo before operation. Ethamsylate was supplied as 250-mg tablets and ampoules containing a solution of 250 mg in 2 ml. Identical placebo tablets of lactose and placebo ampoules containing 2 ml of physiological saline were prepared. The administration was double-blind.

Each child received either the following doses of ethamsylate or the identical placebo preparation:

- two 250-mg tablets on the night before operation,
- two 250-mg tablets 4 h before operation,
- one 250-mg ampoule i.v. immediately after induction of anaesthesia.

Premedication and anaesthesia

Children weighing less than 30 kg received triclofos

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syrup 80 mg kg\(^{-1}\) or diazepam 0.2 mg kg\(^{-1}\) with atropine sulphate 0.03 mg kg\(^{-1}\). Nine children who weighed more than 30 kg received papaveretum 10 mg and hyoscine 0.2 mg i.m.

Anaesthesia was conducted or supervised by the same anaesthetist for all the operations in this study. Those children who were asleep or drowsy on arrival in the anaesthetic room received an inhalation induction with oxygen and cyclopropane, while in those who were still awake anaesthesia was induced with an i.v. injection of methohexitone or thiopentone. Following the administration of suxamethonium 1.5–2.0 mg kg\(^{-1}\) i.v., the trachea was intubated with a latex armoured endotracheal tube attached to an Ozorio connector with a modified Ayres T-piece, or a Magill circuit. Anaesthesia was maintained with halothane 1.5–2.0% in nitrous oxide in oxygen.

**Operative technique**

All the operations were performed by the same surgeon. The adenoids were removed by curettage and a gauze swab was left in the post-nasal space until the end of the operation to act as a haemostatic. The tonsils were dissected, bleeding points secured and ligated with linen thread. Care was taken not to stain the drapes with blood, all used instruments being laid on a towel which was subsequently subjected to analysis for haemoglobin content, together with all swabs used and all fluid aspirated from the operation site. The average time for the operation was 18–20 min.

Dihydrocodeine tartrate 1–1.25 mg kg\(^{-1}\) i.m. was given after operation for pain relief.

The children left hospital on the 4th day after operation normally, but any who had evidence of bleeding remained for longer (10 children).

**Laboratory estimations**

Venous blood was sampled for haemoglobin concentration on the morning of operation and between 36 and 48 h after operation. The haemoglobin content of all swabs, towels and fluid collected at each operation was estimated using the E.E.L. Colorimeter (Rains, 1955; Roe, Gardiner and Dudley, 1962; Rustad, 1963; Thornton et al., 1963). All estimations were carried out by the same senior technician.

The statistical analysis of the results was carried out using Student's \(t\) test for the significance of the difference between means. To assess the significance of the distributions of postoperative haemorrhage and operative blood loss the Fisher exact test and the chi-square test were used respectively.

**RESULTS**

No significant difference was shown in mean age and weight of the two groups, or in the sex distribution (table I). The haemoglobin values before and after

| Table I. Clinical data and results for operative blood loss at adenotonsillectomy (mean values, n.s. = not significant) |
|---|---|---|---|---|
| Placebo (50 patients) | Ethamsylate (50 patients) | Difference between means | Statistical significance |
| Age (yr) | 5.9 ± 0.2 | 6.0 ± 0.2 | 0.1 | n.s. |
| Sex | M 22 | M 30 | n.s. | |
| F 28 | F 20 | |
| Weight (kg) | 21.6 ± 0.7 | 22.3 ± 0.8 | 0.7 | n.s. |
| Haemoglobin concn before op. (g dl\(^{-1}\)) | 12.2 ± 0.1 | 12.3 ± 0.1 | 0.1 | n.s. |
| Haemoglobin concn after op. (g dl\(^{-1}\)) | 11.5 ± 0.1 | 11.7 ± 0.1 | 0.2 | n.s. |
| Estimated blood loss (ml) | 48.0 ± 3.4 | 42.5 ± 2.7 | 5.4 | n.s. |
| (ml kg\(^{-1}\)) | 2.2 ± 0.15 | 2.0 ± 0.1 | 0.2 | n.s. |

| Table II. Haemorrhage after adenotonsillectomy (n.s. = not significant; \(P\) = level of significance) |
|---|---|---|
| Placebo (50 patients) | Ethamsylate (50 patients) | Statistical significance of distribution between groups |
| Primary haemorrhage | 1 | 0 | n.s. |
| Secondary haemorrhage | 10 | 1 | \(P \leq 0.01\) |
surgery did not differ significantly between the two groups.

The mean blood loss for the placebo group was 48.0 ml (2.2 ml kg\(^{-1}\)) compared with 42.6 ml (2.0 ml kg\(^{-1}\)) in the ethamsylate-treated group. The difference between the mean values for blood loss in the two groups was not statistically significant. Figure 1 shows the distribution of the blood loss in each group; fewer ethamsylate-treated patients lost more than 3 ml kg\(^{-1}\) blood, but the difference was not statistically significant.

No correlation was demonstrated between the dose of ethamsylate (range 5.7–17.3 mg kg\(^{-1}\) (mean 11.8 mg kg\(^{-1}\)) and operative blood loss.

Only one patient in the placebo group suffered primary haemorrhage (first 24 h) and none in the ethamsylate-treated group (table II). The frequency of secondary haemorrhage (after 24 h) was significantly greater in the placebo group (10 children) compared with one in the ethamsylate group \((P \leq 0.01)\). No patients required re-admission on account of further bleeding.

No side-effects occurred in either group.

**DISCUSSION**

Previous trials have indicated that the decrease in blood loss produced by ethamsylate is proportional to the blood loss with placebo (Deacock and Birley, 1969; Harrison and Campbell, 1976). Thus, ethamsylate is most effective where the untreated blood loss is great. In this series of adenotonsillectomy, operative blood losses were small in the placebo group compared with those reported by other authors carrying out dissection tonsillectomy and curettage of the adenoids under general anaesthesia in children (table III). This may account for the fact that in this trial the mean blood loss was not substantially reduced with ethamsylate.

It is not possible to compare the results of this trial directly with previous reports of the use of ethamsylate in tonsillectomy, as all differ in some respects. De Reynier (1965) studied adults, while Papatheodosslou (1973) and Gray and Noble (1966) studied adults and children, and in these trials tonsillectomy alone was performed. The work of Verstraete and co-workers (1977) is probably that most comparable to this trial, the blood loss being estimated from the haemoglobin

<table>
<thead>
<tr>
<th>Source</th>
<th>No. of patients</th>
<th>Age range (yr)</th>
<th>Method of estimation</th>
<th>Blood loss</th>
<th>ml</th>
<th>Range (ml)</th>
<th>ml kg(^{-1})</th>
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<tbody>
<tr>
<td>King and Story (1959)</td>
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<td>4–13</td>
<td>Colourimetric</td>
<td>82.5</td>
<td>22–232</td>
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<td>17</td>
<td>3–15</td>
<td>Radioactive (^{131})I-labelling</td>
<td>121</td>
<td>54–305</td>
<td>4.5</td>
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<td>Shalom (1964)</td>
<td>50</td>
<td>22(\frac{1}{2})–9(\frac{1}{2})</td>
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<td>100</td>
<td>30–400</td>
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<td>36–389</td>
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<tr>
<td>Haq and Dundee (1968)</td>
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<td>4–10</td>
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<td>48–213</td>
<td>5.0</td>
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<td>4–11</td>
<td>Volumetric and gravimetric</td>
<td>76</td>
<td>34–140</td>
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<tr>
<td>Arora and Manford (this study)</td>
<td>100</td>
<td>3–12</td>
<td>Colourimetric</td>
<td>48</td>
<td>11.5–120</td>
<td>2.2</td>
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</table>
content of swabs used during adenotonsilllectomy in children, although Sluder tongs were used for the tonsillectomy. For this procedure they reported a mean blood loss with placebo of 4.55 ml kg⁻¹ which was considerably greater than in our trial. Blood loss was not significantly less with ethamsylate, but as six different surgeons carried out the operations there is likely to have been considerable variation in blood loss within the groups.

The effectiveness of ethamsylate in reducing the blood loss at operation in adenotonsilllectomy in children remains uncertain. The most striking feature of this series was the highly significant reduction in the frequency of secondary haemorrhage with ethamsylate. The use of ethamsylate to prevent haemorrhage following adenotonsilllectomy appears to be worthwhile and may help to reduce the small but tragic number of deaths resulting annually from operations on the tonsils.

ACKNOWLEDGEMENTS
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REFERENCES


PERTE DE SANG A LA SUITE D'UNE OPERATION ET FREQUENCE DE L'HEMORRAGIE ASSOCIEE A L'ADENO-AMYGDALECTOMIE CHEZ LES ENFANTS: ESSAI A DOUBLE INCONNU DE L'ETHAMSYLATE

RESUME
Une centaine d'enfants ont été pris au hasard et il leur a été administré soit de l'ethamsylate (Dicynone), soit un placebo avant de subir une adéno-amygdalectomie. La perte de sang, lors de l'opération, a été estimée à partir de la teneur en hémoglobine des tampons et du fluide aspiré. La perte de sang moyenne dans le groupe traité à l'éthamsylate n'a pas été sensiblement inférieure à celle du groupe témoin. La fréquence d'hémorragie secondeaire a été nettement moindre chez les enfants traités à l'éthamsylate (P ≤ 0,01). Il n'a été signalé aucun effet secondaire dans l'un ou l'autre groupe.

OPERATIVER BLUTVERLUST UND DIE BLUTUNGSHÄUFIGKEIT IN VERBINDUNG MIT ADENOTONSILLEKTOMIE BEI KINDERN: EIN DOPPELBLIND-VERSUCH MIT ETHAMSYLAT(DICYYNE)

ZUSAMMENFASSUNG
Hundert Kinder wurden wahllos vor einer Adenotonsillektomie entweder mit Ethamsylat (Dicycen) oder mit einem Placebo anästhesiert. Der Blutverlust bei der Operation wurde nach dem Haemoglobingehalt der Tupfer und der Aspirationsflüssigkeit geschätzt. Der mittlere Blutverlust bei der Ethamsylat-Gruppe ist wesentlich geringer als bei der Kontrollgruppe: die Häufigkeit sekundärer Blutungen war bei den Kindern der Ethamsylat-Gruppe wesentlich geringer (P ≤ 0,01). In keiner Gruppe traten Nebenwirkungen auf.
PERDIDA DE SANGRE EN CIRUGÍA Y FRECUENCIA DE LAS HEMORRAGIAS ASOCIADAS CON LA ADENTONSILECTOMIA EN LOS NIÑOS: UNA PRUEBA CIEGA DOBLE CON ETAMSILATO

SUMARIO
Se seleccionó al azar a 100 niños para administrarles ya sea etamsilato (Dicineno), ya sea un placebo antes de hacerles una adenotonsilectomía. Se determinó la pérdida de sangre en la operación a partir del contenido de hemoglobina de los escobillones y de los fluidos aspirados. La pérdida media de sangre en el grupo tratado por etamsilato no era significativamente inferior a la de los controles. La frecuencia de la segunda hemorragia era mucho menor en los niños tratados por etamsilato ($P \leq 0.01$). No hubo efectos colaterales en ninguno de los dos grupos.