METHOXYFLURANE IN DENTAL ANAESTHESIA: A BLIND TRIAL

BY

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SUMMARY
Anaesthesia with nitrous oxide and oxygen, alone or supplemented with methoxyflurane or halothane, was administered for dental extractions in 256 patients (204 children and 52 antenatal women). Anaesthesia was regarded as "good" in 69 per cent of patients with methoxyflurane and 75 per cent with halothane, but only 50 per cent with unsupplemented nitrous oxide and oxygen. A further trial was carried out in 144 children and 8 antenatal women, nitrous oxide and oxygen being supplemented in all cases with methoxyflurane or halothane. There were 59 per cent "good" results with methoxyflurane and 76 per cent with halothane. Methoxyflurane was found to be considerably cheaper than halothane. The shortcomings of purely inhalational anaesthesia for dental extractions was shown by the finding that in no series was the percentage of "good" results as high as 80.

Methoxyflurane (Penthrane) is a non-explosive fluorinated ether the use of which in clinical anaesthesia was first reported in 1960 by Artusio and his colleagues. It is the least volatile of inhalation anaesthetics in general use and at room temperature inspired concentrations over 2.5 per cent are difficult to achieve. This allied to high blood solubility leads to comparatively slow induction and recovery.

In concentrations required for full surgical anaesthesia methoxyflurane depresses respiration and may produce hypotension which is believed to be due primarily to a decrease in cardiac output (Walker, Eggers and Allen, 1962). Although methoxyflurane is a halogenated compound which may sensitize the dog heart to adrenaline (Bamforth et al., 1961), arrhythmias are uncommon and studies by Black and Rea (1964) in children indicated that ventricular irregularities were not a feature of methoxyflurane anaesthesia at either normal or elevated arterial carbon dioxide levels. They also implied that there is a greater resistance to the development of ventricular ectopic beats in conditions of carbon dioxide retention with methoxyflurane than with halothane.

Anaesthesia in the dental chair demands rapid induction and recovery. It would be reasonable to assume that methoxyflurane would have no application in this field. We found with surprise, therefore, that the replacement of halothane by methoxyflurane in the Goldman vaporizer of a Walton Mark Five machine resulted in anaesthesia apparently comparable in quality to that we are accustomed to obtaining with halothane. An initial series of 60 patients was anaesthetized at the Dundee Dental Hospital and the results proved to be sufficiently encouraging to stimulate further investigation of the possible application of methoxyflurane to dental anaesthesia. It was decided to embark on a blind trial which was carried out by one of us in the Dundee corporation dental clinics. Such an investigation would have been impracticable at the dental hospital where priority must be given to teaching dental students.

METHOD
The dental clinics offer a service to pre-school and school children (aged 3-17) and to antenatal women. The trial was carried out in two stages. In the first comparisons were made between nitrous oxide, oxygen and methoxyflurane; nitrous oxide, oxygen and halothane; nitrous oxide and oxygen.

In this stage there were 204 children and 52 antenatal women: 64 children received the first combination, 60 the second and 80 the third; 29 women received the first and 23 the second. No adult had only nitrous oxide and oxygen as it was
soon clear that this was giving inferior anaesthesia and, furthermore, most of the women were for multiple extractions. The series was consecutive except for 7 backward, excessively unco-operative boys who had to be induced with the full-size facepiece of a Vinesthene inhaler.

They were modified by fitting two McKesson halothane vaporizers in series. Into one was put methoxyflurane and into the other halothane, both being hidden from the anaesthetist by a cloth cover. The anaesthetic was selected at random and the dentist set the vaporizer control before each case. When one of the adjuvants was to be used he turned the appropriate vaporizer "three-quarters on" and this was unaltered throughout the anaesthetic. The machine was set to give 90 per cent nitrous oxide and 10 per cent oxygen for induction at an indicated pressure of 8 mm Hg. Except in the shortest cases oxygen was increased to 15 per cent after induction. The same percentages were used where only nitrous oxide and oxygen was given. No rebreathing bag was employed. To ensure that he did not detect the smell of methoxyflurane or halothane the anaesthetist wore a nose-clip and a mask treated with perfume (fig. 1). This was completely effective. He wrote his report after each anaesthetic and remained in ignorance of what he had been giving until the end of the session.

RESULTS

Anaesthesia in the dental chair remains a sphere where quality cannot be taken for granted and it was assessment of this which was the primary purpose of our investigation. We attempted to judge it as follows:

Good — the patient stayed still or moved insufficiently to need any restraint.

Fair — the patient moved enough to need restraint but his activity did not interfere with the operator.

Poor — anaesthesia was so disturbed that operating conditions were difficult. Necessity to spray ethyl chloride on the mouth-pack to regain control automatically put a case into this group.

The results of the first stage of the trial are shown in tables I and II. Among all patients (table I) or among the antenatal women only (table II) there was no definite difference in quality of anaesthesia between methoxyflurane and halothane, but anaesthesia where either adjuvant was used was superior to that obtained with only nitrous oxide and oxygen (table I). This came out especially in those who had multiple extractions; with both methoxyflurane and halothane...
### Table I
**Trial, first stage. Quality of anaesthesia in 256 patients (204 children and 52 antenatal women).**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Total No.</th>
<th>All cases</th>
<th></th>
<th></th>
<th></th>
<th>Three or more extractions</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>% good</td>
<td>% fair</td>
<td>% poor</td>
<td>% good</td>
<td>% fair</td>
<td>% poor</td>
<td>% good</td>
<td>% fair</td>
</tr>
<tr>
<td>Nitrous oxide, oxygen and methoxyflurane</td>
<td>93</td>
<td>68.8</td>
<td>11.8</td>
<td>19.3</td>
<td>74.1</td>
<td>12.0</td>
<td>13.8</td>
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<td></td>
</tr>
<tr>
<td>Nitrous oxide, oxygen and halothane</td>
<td>83</td>
<td>74.7</td>
<td>10.8</td>
<td>14.4</td>
<td>77.7</td>
<td>4.4</td>
<td>17.7</td>
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<tr>
<td>Nitrous oxide and oxygen</td>
<td>80</td>
<td>50.0</td>
<td>16.2</td>
<td>33.7</td>
<td>40.0</td>
<td>11.1</td>
<td>48.8</td>
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</table>

### Table II
**First stage of trial. Quality of anaesthesia in 52 antenatal women.**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Total No.</th>
<th>% good</th>
<th>% fair</th>
<th>% poor</th>
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<tbody>
<tr>
<td>Nitrous oxide, oxygen and methoxyflurane</td>
<td>29</td>
<td>75.8</td>
<td>7.0</td>
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<tr>
<td>Nitrous oxide, oxygen and halothane</td>
<td>23</td>
<td>78.2</td>
<td>4.3</td>
<td>17.3</td>
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</table>

### Table III
**Trial, second stage. Quality of anaesthesia in 152 patients (144 children and 8 antenatal women).**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Total No.</th>
<th>All cases</th>
<th></th>
<th></th>
<th></th>
<th>Three or more extractions</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>% good</td>
<td>% fair</td>
<td>% poor</td>
<td>% good</td>
<td>% fair</td>
<td>% poor</td>
<td>% good</td>
<td>% fair</td>
</tr>
<tr>
<td>Nitrous oxide, oxygen and methoxyflurane</td>
<td>80</td>
<td>58.7</td>
<td>21.2</td>
<td>20.0</td>
<td>52.3</td>
<td>12.0</td>
<td>35.7</td>
<td></td>
<td></td>
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<tr>
<td>Nitrous oxide, oxygen and halothane</td>
<td>72</td>
<td>76.4</td>
<td>12.5</td>
<td>11.1</td>
<td>67.6</td>
<td>11.7</td>
<td>20.6</td>
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### Table IV
**Comparison of combined figures (in percentages) of "good" and "fair" anaesthetics obtained from first and second stages of trial respectively.**

<table>
<thead>
<tr>
<th>Agent</th>
<th>All cases</th>
<th>Three or more extractions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st stage</td>
<td>2nd stage</td>
</tr>
<tr>
<td>Nitrous oxide, oxygen and methoxyflurane</td>
<td>80.6</td>
<td>79.9</td>
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<td>Nitrous oxide, oxygen and halothane</td>
<td>85.5</td>
<td>88.9</td>
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### Table V
**Average induction, total anaesthetic and recovery times in minutes in 100 patients.**

<table>
<thead>
<tr>
<th>Agents</th>
<th>Induction time</th>
<th>Total anaesthetic time</th>
<th>Recovery time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrous oxide, oxygen and methoxyflurane</td>
<td>1.7</td>
<td>3.6</td>
<td>1.9</td>
</tr>
<tr>
<td>Nitrous oxide, oxygen and halothane</td>
<td>1.5</td>
<td>3.6</td>
<td>1.9</td>
</tr>
<tr>
<td>Nitrous oxide and oxygen</td>
<td>1.7</td>
<td>3.0</td>
<td>1.7</td>
</tr>
</tbody>
</table>
over 70 per cent of the anaesthetics were "good", whereas with nitrous oxide and oxygen alone the figure was 40 per cent.

The first stage of the trial having demonstrated little difference between methoxyflurane and halothane it was decided to proceed with a direct comparison of the two adjuvants. The second stage of the investigation was conducted in the same way as the first except that no patient was given nitrous oxide and oxygen alone. These results (table III) differed in that the number of "good" anaesthetics obtained with halothane (76.4 per cent) was appreciably higher than with methoxyflurane (58.7 per cent). The combined figures for "good" and "fair" anaesthetics, however, corresponded closely in both parts of the trial, with the exception of those for methoxyflurane in the longer cases, which emerged inferior in the latter stage of the study (table IV).

Other factors noted included induction, total anaesthetic and recovery times which were recorded by stopwatch in 100 consecutive patients (table V). Recovery was defined as the time taken to come round sufficiently to walk unsupported (but attended) to the adjoining room. Nobody took over 5 minutes to recover except one woman whose anaesthetic had to be supplemented with ethyl chloride.

The incidence of sickness was studied in the first part of the trial; 3 patients vomited out of the total 256. All had been given ethyl chloride in the course of stormy anaesthetics.

No patient was allowed to become cyanosed and none gave cause for anxiety.

**DISCUSSION**

In view of the physical properties of methoxyflurane the first question was whether it was producing any anaesthetic effect at all. This was the main reason for the inclusion in the first stage of the trial of a group who were given only nitrous oxide and oxygen. That methoxyflurane was not inert was shown by the improvement in quality of anaesthesia which accompanied its use compared with nitrous oxide and oxygen alone.

The first part of the investigation did not demonstrate a definite difference in quality of anaesthesia between methoxyflurane and halothane. The trial was therefore carried to a second stage in which only the combinations including one or other adjuvant were compared. Taking the "good" anaesthetics alone, methoxyflurane was now found to be inferior. The combined figures for the "good" and "fair" anaesthetics, however, corresponded closely in both parts of the study, excepting those for methoxyflurane in the longer case which were inferior. This similarity suggests that the discrepancy between the findings of the two stages of the trial was due in part to difficulty in assessing consistently quality of anaesthesia. The absence of a nitrous oxide and oxygen group in the second stage might also have thrown into relief differences between methoxyflurane and halothane. Despite these inconsistencies we believe that the trial has shown that methoxyflurane is a useful adjuvant to nitrous oxide and oxygen for anaesthesia in the dental chair but that it is not so efficient as halothane.

The pattern of anaesthesia was similar with either adjuvant. Induction, dependent predominantly on nitrous oxide, varied little. It is facilitated by delaying insertion of the mouth-prop until the patient is anaesthetized. Positioning it beforehand upsets him, discourages nasal breathing and predisposes to crying, salivating, coughing and retching. Opening the mouth under anaesthesia is simple, if necessary with gentle use of a gag, if cyanosis and associated masseteric spasm is avoided. Deeper anaesthesia, indicated by disappearance of the eyelid reflex, occurred more readily with halothane because it is possible to vaporize effective anaesthetic concentrations of halothane from a McKesson vaporizer. Recovery times were similar, but more prolonged cases tended to be slower in regaining full consciousness after halothane. This was a peculiarity of the trial where of necessity both agents were vaporized throughout the entire anaesthetic; with halothane this sometimes meant continuing deeper anaesthesia longer than required instead of discontinuing it before the end. Using methoxyflurane, however, it is our usual practice to employ it throughout the whole anaesthetic and always to introduce it at the beginning of induction.

Sickness was not a feature of these short administrations. The only patients who vomited had been given ethyl chloride in the course of a stormy anaesthetic. There were no other complications and all were "well" afterwards.
the avoidance of cyanosis as of paramount importance in this respect.

In concentrations to produce full surgical anaesthesia methoxyflurane frequently causes respiratory and cardiovascular depression. This is not relevant to dental chair anaesthesia where so little of the drug is vaporized and the operations are so brief.

Experimental inhalation of oxygen passing over methoxyflurane in a McKesson halothane vaporizer “three-quarters on” at an indicated pressure of 8 mm Hg from a Walton machine (as in the trial) produces a mild and pleasant sensation of central nervous depression after 60–90 seconds. It would be convenient to attribute the effect of methoxyflurane, as an adjuvant to nitrous oxide and oxygen in the dental chair, to an analgesic action for which, despite conflicting reports, it has some reputation. Dundee and Love (1963) reported no significant change in the pain threshold following inhalation of 0.25 per cent for 5 minutes; with 0.5 per cent there was no increase in pain threshold except where drowsiness supervened and on occasions drowsiness was even accompanied by an increased sensitivity to pain. On the other hand, Torda (1963), using 0.2 per cent for 12 minutes, concluded that, unlike halothane, methoxyflurane appeared to exert an analgesic action but that in some subjects there may be an initial anti-analgesic effect. None of his 9 volunteers lost consciousness. The fact that operating conditions were frequently better than the light level of anaesthesia suggested lends support to the theory of an analgesic effect.

Methoxyflurane is marketed at approximately the same price as halothane but we found it appreciably cheaper to use, as it vaporized at about one-quarter the rate of halothane. In normal practice this difference would be less marked, as halothane usually does not have to be administered right through the anaesthetic.

One finding of the trial which cannot be overlooked is that no matter which adjuvant was used anaesthesia was classified “good” in under 80 per cent of 408 patients. Our experience elsewhere indicates that the inclusion of men in the series would have made this figure worse. In this connection the observations of Bourne (1960) of dental anaesthesia (nitrous oxide and oxygen supplemented in about one-third with trichloroethylene or ethyl chloride) in London dental teaching hospitals and L.C.C. clinics are of interest. Of 591 administrations he judged 61 per cent “good”, i.e., little or no restraining force required; consultant anaesthetists gave 152 with 68 per cent “good”. These findings confirm—if confirmation were needed—the deficiencies of simple inhalation anaesthesia in the dental chair. Choice of agent is relatively unimportant measured against the often impossible task of achieving and maintaining effective tensions of anaesthetic in the patient. Nervousness, nasal obstruction, shortness of time, feeble inspired mixtures and air dilution through an open mouth are factors which mitigate to varying degree against satisfactory anaesthesia. Intravenous induction with methohexitone where possible has gone far to solve these problems. In the writers’ view, however, except in the shortest cases, anaesthesia should be continued with inhalation methods as this gives operating conditions that are both smoother and more controllable than are obtainable with methohexitone alone.

ACKNOWLEDGMENTS

We should like to thank Mr. David A. Finlayson, Chief Dental Officer, Dundee Corporation, and the staff of the Dundee Corporation Dental Clinics for their cooperation in the trial. We are grateful also to Messrs. Abbott Laboratories Ltd. for interest and general assistance, including supplies of Penthrane.

REFERENCES


LE METHOXYFLURANE EN ANESTHESIE DENTAIRE: UN ESSAI A L'AVEUGLE

SOMMAIRE
Une anesthésie par le protoxyde d'azote et l'oxygène seule ou complétée par le méthoxyflurane ou l'halothane a été utilisée pour des extractions dentaires chez 256 malades (204 enfants et 52 femmes enceintes). L'anesthésie a été considérée comme "bonne" chez 69 pour cents des malades avec méthoxyflurane et chez 75 pour cents des malades avec halothane, mais seulement chez 50 pour cents des cas avec protoxyde d'azote et oxygène seuls. Un autre essai a été exécuté chez 144 enfants et chez 8 femmes enceintes, le protoxyde d'azote et l'oxygène étant complétés dans tous les cas par le méthoxyflurane ou l'halothane. Il y eut 59 pour cents de "bons" résultats avec le méthoxyflurane et 76 pour cents avec l'halothane. Le méthoxyflurane était considérablement moins cher que l'halothane. Les insuffisances de l'anesthésie pure par inhalation pour des extractions dentaires ont été mises en évidence par le fait que dans aucune des deux séries le pourcentage des "bons" résultats n'atteignait 80 pour cents.

METHOXYFLURAN IN DER ZAHNÄRZTLICHES NARKOSE EIN BLINDVERSUCH

ZUSAMMENFASSUNG