A CLINICAL STUDY OF THE VALUE OF A MIXTURE OF NITROUS OXIDE AND OXYGEN AS AN ANALGESIC IN RELIEF OF PAIN FOLLOWING THORACIC SURGERY AND ITS USAGE PHYSIOTHERAPEUTICALLY

by

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When patients have been subjected to thoracic and abdominal surgery, the ability to cough and ventilate the lungs adequately is inhibited post-operatively by pain and apprehension. The use of anaesthetic agents to relieve pain on stretching the incision has been investigated previously, particularly with patients following abdominal surgery.

The purpose of this present investigation was to evaluate the use of a premixed gas (consisting of 50% nitrous oxide (N₂O) and 50% oxygen (O₂)) in relieving pain sufficiently to facilitate effective coughing and thus assist removal of secretions, in patients subjected to thoracic incisions. Also, as nitrous oxide is a weak anaesthetic agent, to see if its effect was increased when combined with an adequate narcotic.

HISTORY OF NITROUS OXIDE

In 1772 Joseph Priestley synthesised and recognised nitrous oxide as a separate entity. Since then its use has become widespread. Today it is the basis of present-day inhalation anaesthesia and shows promise in fields of medicine unrelated to anaesthesia, as well as in non-medical use, in aerosol packaging and freezing mediums, and as a "tracer gas" in leak detection. Mixtures of N₂O and O₂ have also been advantageously used for many years in midwifery.

The term "laughing gas" is said to have originated during experiments in 1800 when Humphrey Davy, firmly convinced of its practicability, published a paper following administration of nitrous oxide to the poets of the day, Samuel Taylor Coleridge and Robert Southey, to the potter Josiah Wedgewood and to the author Peter Roget.

In 1872 Dr. E. W. Andrews recognised that oxygen in the molecule of nitrous oxide was not available for the metabolic functions of the body tissues.

However, it was not until 1949 that Falconer, Pender and Bickford proved nitrous oxide a true anaesthetic agent, that its effects were not just the result of hypoxia, and that narcosis was produced by virtue of other than asphyxiating properties.

In 1964 Parbrook and Kennedy investigated the value of premixed nitrous oxide and oxygen mixtures in the relief of post-operative pain in a trial with patients following upper abdominal operations, because of the tendency in these patients to develop chest complications. Pain relief was assessed by improvement of vital capacity following administration of the gas mixture. They concluded that inhalation of a mixture of 25% nitrous oxide and 75% oxygen for brief periods can be of value in the early post-operative period and that use of this analgesic commends itself by the absence of respiratory depression and speed of action. The use of premixed gases avoided cumbersome apparatus and the danger of variation in concentration of the gases.

Parbrook, Rees and Robertson (1964) then investigated the combined use of morphine and nitrous oxide, finding the combina-

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tion more potent than either analgesic alone. Side effects noticed were a tendency to feel and appear sleepy. In another article, they published their conclusions, namely, that short-term combined therapy of N₂O and O₂ mixtures and a narcotic may, by producing better relief from pain, facilitate coughing and vigorous physiotherapy and thus relieve the mild anoxia from which many patients suffer within the first twenty-four hours following surgery.

They further stated that the main indication for an analgesic after operation is during the initial twenty-four to forty-eight hours and this period appeared to be within the safety margin for reversible bone marrow depression which occurs on more prolonged therapy and with higher concentrations of nitrous oxide.

A third article by Parbrook (1966) stated that:

"Post-operative atelectasis, hypoxia or cough after upper abdominal operations are in part due to abdominal pain, which causes shallow respirations and reluctance to take deep breaths. Routine therapy by intermittent short-term 25% N₂O inhalation can be combined usefully with conventional relief of pain with methadene as a preparation for physiotherapy. It helps to prevent atelectasis by allowing the patient to take deeper breaths and alternately can be used to permit patients who have developed a cough to clear their secretions. In the latter case the N₂O analgesic is found to persist for several minutes after each administration of the gas and this allows time for coughing. During coughing, of course, the abdomen should be supported."

SIDE EFFECTS

The pharmacological actions of N₂O have been found to be mainly on the central nervous system and are mild. (The mechanism by which anaesthesia is produced is unknown).

With moderate concentrations of the gas, cerebellar functions are affected causing ataxia, disco-ordinated movements and nystagmus.

Although many individuals experience euphoria, a minority find low percentages of N₂O unpleasant. As the concentration of N₂O is raised from 30-40% there is progressive impairment of memory, time sense and rise of sensory thresholds. Subjective sensory changes include tingling, numbness, dizziness, spinning and auditory disturbances.

Two more serious side effects may occur:

(1) Unconsciousness — occasionally subjects lose contact with their environment when N₂O concentrations of 30-40% have been inhaled for over ten minutes.

(2) Unpleasant psychological and neurological disturbances may occur (e.g., nausea, delusions, aggressive tendencies, disorientation and visual phenomena).

There is also the possibility of addiction in patients who experience euphoria, and a tolerance to the drug may develop as has been shown by its decreased effectiveness with patients needing repeated inhalations for burns dressings.

Toxicity has been reviewed comprehensively by Cloed D. Green (1964). Conclusions were that N₂O is less toxic than other inhalation anaesthetic drugs. Following continuous and prolonged administration, haematological complications can develop (e.g., bone marrow depression, granulocytopenia and leukocytopenia). However, there is no evidence that any toxic property of N₂O becomes manifest during its use as an aesthetic agent in less than forty-eight hours.

PRECAUTIONS FOR USAGE

To prevent hypoxia at least 20% O₂ in the inspired gas mixture should be used.

Because of the risk of unconsciousness and psychological effects, Parbrook and associates restricted their clinical investigations to the use of 25% N₂O. In considering toxicity they suggested that twenty-four hours was the safe margin for continuous inhalation.

Contraindications

(1) Pre-existing nausea — N₂O therapy may cause an exacerbation.

(2) Gaseous abdominal distention with continuous pain. Relief by N₂O, even with 25% concentration may cause slight
increase of distention. However, short term administration of the gas is not necessarily contraindicated here.

(3) Continuous treatment with the gas for more than twenty-four hours.

The Present Investigation

The present investigation was a subjective study without quantitative measurements.

Criterion for Patient Selection — no effective cough within twenty-four hours following surgery.

The Experimental Group totalled thirty-four patients. The ratio of males to females was 25:9. Ages ranged from 18-68 years.

The Type of Surgical Operation the patients had been subjected to included two open heart procedures (one having a thoracotomy and the other a sternotomy approach). The remainder were thoracotomy incisions with surgery ranging from biopsy, lobectomy, resection and pneumonectomy, to decortication and pleuridesis.

The Apparatus consisted of:

(i) a portable cylinder of premixed N₂O 50% and O₂ 50%,
(ii) a partial rebreathing circuit consisting of a reservoir bag and exhale valve to which was attached a mask as used with I.P.P. ventilators.

Method

An explanation was given to the patient prior to inhalation, about the analgesic effects of this odourless gas and the reason for its use to assist in producing an adequate cough. The patient was positioned upright, either in bed or a chair, to assist in breathing deeply and thus facilitating an effective cough.

Having established that the cough was ineffective prior to inhalation of the gas mixture, the cylinder valve was opened to allow a flow rate of eight litres per minute. It was considered that this flow rate would avoid significant rebreathing in the short inhalation period. The patient was given the breathing apparatus to hold and asked to breathe normally for a few seconds, then test the soreness of the wound by stretching with a deep inspiration. When the pain was less, but before he became too drowsy, he was asked to inspire deeply, remove the mask and cough maximally once. (As is usual practice, the chest wall was supported.)

As the analgesic lasted approximately from 2.5 minutes, repeated efforts at effective coughing were made, if necessary, to remove bronchial secretions. Encouragement was sometimes given to use the analgesic for maximal localized movement of the chest wall and to obtain full arm abduction/elevation with a patient particularly reticent in doing these exercises.

The effect of N₂O as an analgesic was estimated subjectively by the strength of the cough, classified as weak, moderate or strong.

The narcotics given were considered in relation to the inhalation of N₂O.

Noted were:

(1) The particular narcotic, its dosage and time of administration.
(2) The duration and time of inhalation of N₂O.

Results

Table I

<table>
<thead>
<tr>
<th>Total number of patients</th>
<th>Patients with a Mean Strong Cough</th>
<th>Patients with a Mean Moderate Cough</th>
<th>Patients with a Mean Weak Cough</th>
</tr>
</thead>
<tbody>
<tr>
<td>34</td>
<td>15</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Approximate Percentage</td>
<td>44%</td>
<td>35%</td>
<td>20%</td>
</tr>
</tbody>
</table>

The results were as tabulated in Table I. Thus N₂O had no effect on the strength of cough of 20% of patients, a moderate effect on 35% and a strong effect on 44%. For a patient to average a moderately forceful cough and not a weak one, he had to cough strongly at least once and this was invaluable. Therefore, the overall worthwhile effect was on 79% of patients.

Discussion

The usefulness of N₂O as an analgesic for relief of pain following thoracic incisions was made apparent early in its usage. In the presence of immediate post-operative pain (i.e. within forty-eight hours following sur-
gery), while N₂O alone was not as effective as when used in conjunction with an adequate narcotic. However the administration of N₂O alone was better than nothing at all in the absence of an adequate narcotic.

The actual narcotic did not appear to matter providing it was the effective one for that particular individual. The drug dosage of the three narcotics used ranged, with morphia, from 10-15 mg., with pethedine, 25-100 mg., and with omnopon, 10-20 mg. All narcotics were given intramuscularly, except on one occasion when it was administered intravenously.

The time of inhalation of N₂O ranged from 15-95 secs, varying with:

(1) The time of the last narcotic administration (optimum time usually ½-1 hour following intramuscular injection and 10-15 minutes following intravenous injection).

(2) Psychological factors such as during the first trial when the patient, because of apprehension, usually inhaled for a shorter period than with subsequent trials, or with over-anxious subjects who required greater dosages.

On analysis, the 20% failure included three extremely over-anxious patients with whom no benefit was observed, two with bronchospasm (one of whom later coughed strongly following inhalation of an aerosol bronchodilator-alupent); one pneumonectomy patient who probably did not have the ventilatory capacity for effective coughing; one whose narcotic had completely worn off.

One patient who complained of pre-existing nausea had a marked increase of this symptom following inhalation.

CONCLUSIONS

A correct balance for the majority of patients can be achieved between adequate narcotic and analgesic agent with avoidance of cardiac, circulatory and respiratory depression.

SUMMARY

This article reviews literature on N₂O, considering its history, pharmacological actions, side effects and toxicity, and the precautions and contraindications for its use.

A subjective study is described of thirty-four patients following thoracic incisions, in respect to the use of a gas mixture of N₂O and O₂ as an analgesic in relieving immediate post-operative pain (i.e. within forty-eight hours post-operatively) thus facilitating effective coughing and the removal of bronchial secretions.

Whether this gas mixture is more effective when used in conjunction with an adequate narcotic is also considered.

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APPENDIX

This trial was conducted at Chermside Hospital, Brisbane, in 1968. Since then N₂O has continued to be used as an analgesic postsurgically.

BIBLIOGRAPHY