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CLINICAL IMPRESSIONS OF PROMETHAZINE IN ANAESTHESIA

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The ideal premedicant drug has yet to be discovered. At present no single agent achieves the two general purposes of pre-anaesthetic medication as suggested by Beecher:[1] (1) To present an acquiescent, well-rested, serene patient to the surgeon and (2) to minimize as far as possible the hazards of anaesthesia and surgery.

Much interest has recently been shown in promethazine and other derivatives of phenothiazine. Promethazine possesses a central depressant effect with predominant action at a subcortical level, as compared with a drug like morphine, where the depressant effect is marked at the cortical level.

Reticular Formation

The subcortical level referred to is the reticular formation—small islands of grey matter interspersed with fine bundles of nerve fibres.[2] It lies dorsal to the pyramidal tracts in the medulla, pons and midbrain. The reticular system comprises descending medial and lateral reticular tracts arising from the midbrain and pons and passing down in the reticular spinal tracts to the anterior-horn cells of the spinal cord.[3,4] These tracts are both inhibitory and facilitatory in nature, and effect a degree of control over reflex muscle tone, the respiratory centres, and the vasomotor centre. They also serve to transmit impulses received from the cortex, the basal ganglia and the hypothalamus.

Ascending reticular fibres are also recognized in the spinal cord. These receive connections *via* collaterals from the sensory spinal tracts and from the nuclei of the 9th, 10th and 11th cranial nerves. Passing through the pons, they receive further collaterals from the auditory and vestibular nuclei. After passing through the midbrain these fibres synapse with neurones from the cortical area.

There exists, therefore, a widespread interconnection between the classical sensory system, the reticular system, the hypothalamus and the cortex.

Arousal Reaction

Direct electrical stimulation of the reticular formation, especially in the region of the hypothalamus, causes a transition from a sleeping to a wakeful state.[2,4-6] The original experiments were performed by Moruzzi and Magoun[6] in 1949 on anaesthetized cats, and they demonstrated a sudden change in the EEG from a tracing indicating sleep to one indicative of wakefulness. This arousal reaction can also be produced by peripheral stimulation of a visceral or somatic nerve, or by direct stimulation of certain cortical areas.[2] Destructive lesions of the reticular formation render the animal permanently comatose. It does not exhibit the arousal reaction, although conduction is unimpaired in the classical sensory tracts.

French and King[2] have shown that electrical stimulation of the sciatic nerve of an anaesthetized cat produces no potential in the reticular system, whereas a potential can be recorded in the classical sensory tracts. When anaesthesia wears off, potentials can be recorded in the reticular system at about the time the animal regains consciousness.

It would appear, therefore, that an intact reticular system is required to initiate and maintain the state of wakefulness.[4]

PROMETHAZINE

Promethazine appears to be an approach to the ideal premedicant drug. It depresses the wakeful state without direct cortical depression, prolongs the action of barbiturates, and prevents vomiting of central origin.[4] The drug depresses the autonomic nervous system and has a tonic action on the pre-capillary sphincters. In addition it has an antihistaminic and a slight hypotensive and hypothermic action. Promethazine may, therefore, assist in reducing operative and anaesthetic shock and blood loss.

The drug was first used in anaesthesia by Laborit and Huguenard[7] in combination with pethidine and chlorpromazine in their 'lytic cocktail'.

Method

An attempt has been made to assess the patient's mental state and degree of nervousness before operation, and to premedicate accordingly with a combination of promethazine, pethidine and atropine. Adult patients were given a tablet consisting of 15 mg. of promethazine hydrochloride and 75 mg. of butobarbitone the evening before operation. In addition, during anaesthesia, blood pressure, pulse, colour and blood loss were observed and charted at regular intervals. A state of 'balanced anaesthesia' was maintained as far as possible by means of additional doses of either thiopentone, pethidine or promethazine.

Patients were assessed immediately after operation, and seen again some 6 hours later after return of consciousness. The time taken to recover from anaesthesia was noted, as was blood pressure, colour, and the amount of pain and of post-operative sedation required. Attention was also paid to restlessness, respiratory depression and vomiting.

In order to evaluate clinical impressions, it was felt desirable to divide the patients into several arbitrary groups. A grouping based solely on the type of operation and anaesthetic technique employed would introduce many variables and tend to make clinical judgment difficult. Each case

therefore was individually assessed in the light of past experience and the impressions gained were correlated. In this way it was hoped to determine the position of promethazine as a premedicant drug, and to evaluate its efficiency as an anaesthetic agent resulting, by means of selective depression of the reticular system, in smoother, quieter and safer anaesthesia and surgery.

This report covers 201 patients between the ages of 7 and 82 years operated upon for a variety of conditions (Table I). In order to facilitate observations a simple chart and graph were used to record the patient's condition before, during and after operation.

TABLE I. CASES BY GROUPS

Group A. Children 7-14 *years*		
Tonsillectomy Appendicectomy Inguinal Herniorraphy		30
Group B. Intra-thoracic Procedures		
Lobectomy		7
Mitral Valvotomy		2
Bronchoscopy+Bronchogram		20
Group C. Major Abdominal Procedures		
Gastrectomy		7
Cholecystectomy		20
Hemi-colectomy		3
Group D. Minor Abdominal Procedures		
Appendicectomy		35
Inguinal Herniorraphy		20
Group E. Elderly Age Group		
Smith-Petersen pin		8
Appendicectomy		3
Intestinal obstruction		2
Group F. Potentially Haemorrhagic Procedures		
Thyroidectomy		6
Radical Mastoidectomy		6
Vaginal Hysterectomy and repair		20
Orthopaedic procedures		12
Total		201 cases

RESULTS

Group A

Age-group 7-10 *years.* These patients were given 12·5 — 25 mg. of promethazine 1 hour before operation. Upon arrival in the theatre, 9 out of the total of 20 patients appeared to be adequately sedated, and although not asleep showed no signs of apprehension. Induction in most cases was smooth with thiopentone or nitrous oxide, oxygen and ether sequence. Salivation was only marked when ether was used, otherwise the antisialogogue action of the drug appeared to be sufficient. Of the 9 well-sedated children, 6 had spent 3 days or longer in hospital, and when seen on the day before operation had settled down well in their new surroundings. The remaining 11 children showed various degrees of sedation; 5 of them were restless and 2 cried while being induced with thiopentone.

Age-group 10-14 *years.* The 10 patients in this group were given 25 mg. of promethazine and 1/150 gr. of atropine. 2 received 25 mg. of pethidine as well. This group was lightly sedated upon arrival in the theatre, and in most cases induction with thiopentone was smooth and the course of anaesthesia uneventful.

In group A, 20 patients vomited at the end of the operation, but showed few signs of nausea when seen later in the wards. They had all received ether during anaesthesia.

With 6 exceptions all slept for 2-4 hours after surgery, and there were no complications which could be attributed to anaesthesia.

In this group promethazine alone appeared to be a satisfactory premedicant drug, producing in most cases a light degree of sedation. Recovery from anaesthesia was fairly rapid and post-operative nausea was not troublesome.

Groups B and C

Patients in groups B and C were given 50 mg. of promethazine, 50-100 mg. of pethidine, and 1/100 gr. of atropine 1 hour before operation. With 10 exceptions, all 59 were well sedated upon arrival in the theatre. Few patients in this group showed subjective or objective signs of apprehension, although a routine check on blood pressure before induction showed a rise above resting level in the ward in 8 cases. It is interesting to note that where blood pressure was elevated just before operation, the course of anaesthesia was often not smooth.

Relaxants and controlled respiration were used in every case, and supplementary doses of thiopentone, promethazine or pethidine were given during the course of anaesthesia. Small doses of thiopentone appeared to be most effective in producing smooth anaesthesia. Results with fractional doses of promethazine were not impressive, and even after repeated doses of 10-15 mg. several patients continued to move and showed signs of returning consciousness. In most cases blood pressure showed an initial rise and then remained fairly constant throughout the operation. When anaesthesia was not smooth the rise was greater, and fractional doses of promethazine were not effective in reducing it to the normal pre-operative level.

Blood loss appeared normal in all cases and there was no great reduction in bleeding in groups B and C. Several patients in these two groups exhibited marked vasoconstriction of the face during operation. This condition did not respond to promethazine, but did improve after additional doses of relaxant and/or thiopentone.

Twelve patients were very restless after operation and required immediate sedation with pethidine in the ward. Most of these patients had received fractional doses of promethazine only during anaesthesia.

Post-operative nausea was uncommon and recovery from anaesthesia was only delayed when promethazine and pethidine had both been used during the course of the operation. No patients in groups B and C showed any signs of respiratory depression which could be attributed to drugs used during anaesthesia, and in all cases protective reflexes were present before they were returned to the ward.

Group D

The 55 patients in group D received the same premedication as groups B and C. None were completely paralysed during the operation and respiration was assisted whenever necessary. Surgery was usually of short duration. All were well sedated upon arrival in the theatre and 12 were asleep but could be roused and answered questions satisfactorily. Left to themselves they would fall asleep readily.

Induction and maintenance of anaesthesia was smooth with thiopentone and minimal ether. Most patients in group D slept for 1-4 hours after operation, although protective reflexes had returned before they left the theatre. This group did not receive supplementary doses of promethazine during anaesthesia.

Post-operative respiratory depression was not observed, and nausea and vomiting was troublesome in 7 cases. Restlessness was not evident and only light post-operative sedation was necessary in most cases.

Group E

The 13 patients in group E were all above 70 years of age and were premedicated with 25-50 mg. of promethazine and 1/100 gr. of atropine. Four patients in this group suffered from chronic bronchitis and one was an asthmatic. Sedation appeared to be adequate and all showed rapid recovery from anaesthesia. The course of anaesthesia was smooth and no complications occurred.

Group F

The 44 patients in group F received 50-100 mg. of pethidine, 50 mg. of promethazine, and 1/100 gr. of atropine 1 hour before operation. Sedation was again adequate in most cases, only 4 patients in this group appearing apprehensive. All patients were positioned after induction in order to minimize bleeding.

Haemorrhage seemed to be less than usual in this group, although only 5 patients showed a marked drop in systolic blood pressure after half an hour of surgery. Quiet induction and maintenance contributed in no small measure to freedom from undue haemorrhage and on 2 occasions the surgeon remarked upon the relatively dry operating field when promethazine had been used. Post-operative restlessness was never very evident and there were no anaesthetic complications in this group.

SUMMARY AND CONCLUSIONS

The results in this investigation brought out the importance of well chosen, adequate and properly timed premedication. Promethazine alone gave very good results when used for children and elderly patients. Sedation was usually light but satisfactory, and the antisialogogue action was adequate when a thiopentone, nitrous oxide and oxygen sequence was employed.

In combination with pethidine it gave very good results in major surgery when used as a premedicant drug. Fractional doses during anaesthesia did not appear to be as efficient as fractional thiopentone in producing quiet anaesthesia. Patients were frequently restless, and vasoconstriction of the face and a rising pulse and blood pressure were often seen.

Post-operative restlessness was often marked when promethazine only had been given during a major operation. Delay in recovery from anaesthesia usually occurred when pethidine and promethazine had both been used in fractional doses during surgery.

It would seem that in order to obtain smooth and safe anaesthesia, depression of the cortex and classical sensory routes is as important as depression of the reticular system.

Promethazine is an aid to quiet induction and smooth anaesthesia. Bleeding is reduced, especially if the patient is properly positioned, and alarming drops in blood pressure do not occur.

The incidence of vomiting was reduced and it was only troublesome when ether had been used.

Post-operative anaesthetic complications were minimal. Excluding group B, where pulmonary complications were very likely to occur, only 18 patients in this series developed a post-operative cough. One patient developed a patchy atelectasis of the left lung after gastrectomy. It is impossible to state that the use of promethazine reduced the incidence of post-operative pulmonary complications; nevertheless, it is a useful premedication for patients suffering from chronic bronchitis and asthma.

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