

# Some Clinical Impressions of Droperidol Used as Premedication in Children\*

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## SUMMARY

A short description is given of the indications and use of premedication, especially in children. The properties and toxic effects of the butyrophenone drug droperidol are given and emphasis is laid on how these differ when the drug is used alone and when it is combined with other drugs.

Its main advantages are considered to be the superior tranquillization in the pre-operative period and reduction of nausea and pain in the postoperative period.

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The reasons for administering drugs pre-operatively are four-fold, viz. to provide: (i) relief of anxiety, (ii) sedation, (iii) analgesia, and (iv) to decrease secretions from salivary glands and the upper respiratory tract.

Although the introduction of intravenous agents has reduced the unpleasantness of induction, most people awaiting surgery are nervous, and many, especially children, are terrified. It is this latter group that are not amenable to pre-operative explanations by the anaesthetist. Most anaesthetic textbooks recommend that the anaesthetist spend sufficient time with the patient on the night before operation, not only to acquaint himself with the patient's physical condition, but also to gain his confidence.

It is often possible, even in a poorly or unpremedicated child, to induce him to 'blow up the balloon' while slowly and surreptitiously increasing the concentration of anaesthetic. However, in spite of this and many other substitutes, one is still left with a hard core of children who simply have to be held down while a vein is sought or a mask clamped over the face. It is for this group that one should seek a more effective premedication. Rectal or

intramuscular inductions are possible answers and basal narcosis (premedication pushed to the point of unconsciousness) is another.

## ADMINISTRATION

### Rectal Induction

Thiopentone administered via a rectal catheter or as a suppository is the most commonly used drug. Its greatest advantage is that it is painless and that the atropine can be given intravenously after sleep has been induced. Disadvantages include:

- (i) Time factor—it takes longer than the normal induction.
- (ii) It is sometimes returned very promptly in spite of holding the buttocks together.
- (iii) Older children are embarrassed.
- (iv) The procedure may be dangerous if carried out in a ward where means of applying artificial ventilation are not available.
- (v) The large dose prolongs recovery and can be dangerous with, for instance, tonsillectomy.

### Intramuscular Induction

Intramuscular ketamine hydrochloride (Ketalar) is beginning to find a definite place in certain cases, e.g. examination of eyes in babies and small children. Its great advantages are:

- (i) The injection is much quicker and easier to administer than an intravenous one.
- (ii) It acts very quickly.
- (iii) No other anaesthesia is required and therefore there is no apparatus (mask, tube, etc.) near the face to impede the surgeon.

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The principal disadvantages are the painful injection and prolonged recovery time.

### Oral Induction

The ideal premedication for children would seem to be one which could be given by mouth in a dose sufficiently small so as not to cause a vomiting hazard and which would produce profound sedation just short of basal narcosis. It should be in a liquid form and pleasantly flavoured.

## DRUGS OF CHOICE

### Droperidol

On the advice of Dr P. Foster, Chief Anaesthetist, Karl Bremer Hospital, I have used droperidol by mouth in combination with various other sedatives to obtain the required result.

Droperidol (Inapsin) belongs to a group of drugs known as butyrophenones, closely allied to the phenothiazines. It is used mainly with a potent analgesic to produce neuroleptanalgesia. In this combination droperidol provides the neuroleptosis, which is a state of mental detachment, motor sedation, antagonism to apomorphine and amphetamine, and diminished sensitivity to adrenaline and noradrenaline. All the major tranquillizers, i.e. the butyrophenones and phenothiazines, are in fact neuroleptics.

Weak neuroleptic drugs may produce side-effects, e.g. adrenergic activity, hypotension, hypothermia, antihistamine activity, sedation and dyskinetic states. Potent neuroleptics are active at very low dose levels which produce minimal side-effects.<sup>1</sup>

Although droperidol has been likened to chlorpromazine, its main result is mental detachment, whereas chlorpromazine is a potent hypotensive, hypothermic and sedative drug.

### Side-effects

Droperidol produces very few side-effects. There are only two that need serious consideration: (i) peripheral vasodilatation and (ii) extrapyramidal symptoms.

**Peripheral vasodilatation** is centrally mediated so that vasomotor response to blood loss is not impaired. A degree of pre-operative reduction in blood pressure down towards basal levels for the patient may be seen. Such falls respond to fluid administration.<sup>2</sup> Literature supplied with the drug warns of the possible danger of severe hypotension developing if it is given in the immediate postoperative period. It is suggested that if fluid therapy does not correct the hypotension, then the use of pressor amines should be considered.

Alpha-adrenergic blocking properties have been claimed for the butyrophenones and hypotension was generally attributed to this factor; but recently it has been suggested by several authors that this effect has been over-estimated.

**Extrapyramidal symptoms:** Excitatory disturbances of the extrapyramidal system, from mild hypertonus to par-

kinsonian crises, have been described.<sup>3</sup> They are not common but appear to occur more readily if droperidol is used alone.

Morrison *et al.*<sup>4</sup> describe several episodes of extrapyramidal symptoms in volunteers given droperidol only. They include diplopia, spasm of sternomastoid muscles and facial twitching. They may be controlled by the reduction of dosage or by simultaneous administration of one of the anticholinergic or antihistaminic drugs normally used for the treatment of paralysis agitans. Johnstone<sup>5</sup> claims that the narcotic drugs as well as many mild hypnotics prevent these symptoms. In his own words 'this happy coincidence allows us to take advantage of the anxiolytic action of the butyrophenones for the alleviation of pre-operative anxiety'.

**Other side-effects:** Although the butyrophenones are major tranquillizers, reports of mental restlessness and agitation have been made.<sup>6</sup> These effects are more likely to occur with large doses (more than 5 mg of haloperidol or 10 mg of droperidol),<sup>1</sup> and when given alone. In my experience they are more common in big men than in women and children.

Droperidol apparently does have a protective influence against adrenaline-induced cardiac arrhythmias during anaesthesia. This was at first thought to be due to the alpha-adrenergic blockade, but Johnstone<sup>5</sup> suggests that the butyrophenones may be local analgesic substances, which in large doses would have a quinidine-like action.

Droperidol has no respiratory depressant effect though Morrison *et al.*<sup>4</sup> reported a significant incidence of coughing and hiccup during induction, but this finding has not been reported by other authors. It must be repeated that in Morrison *et al.*'s series droperidol was used alone.

From the foregoing it would seem that hypotension is the most likely complication resulting from the use of droperidol. Extrapyramidal symptoms only occur in certain susceptible individuals and they can be reduced by the concomitant use of an anticholinergic, antihistaminic or narcotic drug.

### Additional Drugs

**Anticholinergic drugs** in the form of atropine or scopolamine are given almost as a routine with most premedications.

**The antihistaminics** which I have used are trimeprazine tartrate (Vallergan) and promethazine (Phenergan). Vallergan is a phenothiazine derivative similar to, but less potent than, chlorpromazine (Largactil). It possesses chlorpromazine's sedative and anti-emetic actions but lacks its anti-adrenaline effect. It has very powerful antihistaminic properties and is commonly used as a sedative syrup for children (Vallergan and Vallergan Forte). Promethazine too is a phenothiazine derivative with powerful sedative, antihistaminic and anticholinergic effects. It is specifically recommended for parkinsonism.

**The narcotics** which have been used are Physeptone (methadone hydrochloride) and pethidine. Physeptone is a potent analgesic but a poor sedative. It is a potent respiratory depressant and the dose has therefore to be kept very small. It is well absorbed by mouth.

Pethidine is also a potent analgesic and has a mild sedative action. Its action is potentiated by many of the phenothiazines and is more reliable by injection than by mouth, but the dose remains the same. It is a powerful respiratory depressant.

### Dosage

Dosage depends on a variety of factors, e.g. physical state of patient, other drugs being used at the same time, route of administration, etc. I have used three different mixtures of these drugs. All mixtures are kept in brown bottles because droperidol darkens on exposure to light.

#### Mixture A:

Vallergan Forte syrup 19.5 mg in 3.25 ml  
Droperidol 1.25 mg in 0.5 ml  
Physeptone linctus 0.7 mg in 1.75 ml  
*aq. ad* 6 ml.

This is the mixture originally suggested to me by Dr Foster, though the amounts of each drug have been changed. The dose which I have found most satisfactory is 1 ml/2 kg body weight given by mouth, 1 - 1½ hours pre-operatively.

#### Mixture B:

Droperidol 0.8 mg in 0.3 ml  
Vallergan 17.5 mg in 0.7 ml

In this mixture the Vallergan is taken from the ampoule which contains 25 mg per ml whereas the syrup contains only 6 mg per ml. The idea was to reduce the volume and to exclude the habit-forming drug. The dose used is 1 ml/4.5 kg body weight orally 1½ hours pre-operatively.

#### Mixture C:

Vallergan 27.5 mg in 11 ml  
Droperidol 17.5 mg in 7 ml  
Physeptone 10.0 mg in 1 ml  
*aq. ad* 34 ml.

The dose here is 1 ml/4.5 kg body weight given by mouth 1½ hours pre-operatively. Physeptone and Vallergan were again taken from the ampoules.

TABLE I. TYPE OF OPERATION AND MIXTURE USED

| Operation          | Number of cases |           |           |
|--------------------|-----------------|-----------|-----------|
|                    | Mixture A       | Mixture B | Mixture C |
| Eye ... ..         | 12              | 4         | —         |
| Orthopaedic ... .. | —               | 14        | —         |
| Abdominal ... ..   | 12              | 4         | 6         |
| ENT ... ..         | 42              | 18        | 12        |
| Other ... ..       | 4               | —         | —         |
| <b>Total</b>       | <b>70</b>       | <b>40</b> | <b>18</b> |

To mixtures B and C, saccharin is added to improve the taste. Sugar was considered inadvisable owing to the danger

of fermentation. To all of these mixtures atropine sulphate or hyoscine hydrobromide is added at the time of administration to the patient. They are used not only to decrease salivary and bronchial secretions and to lessen the risk of vagal inhibition, but also to protect against possible extrapyramidal symptoms.

Table I shows the different mixtures used in various operations and Table II shows the age range of the children.

TABLE II. AGE RANGE

| Years       | No. of cases |
|-------------|--------------|
| Less than 1 | 6            |
| 1           | 6            |
| 2           | 12           |
| 3           | 16           |
| 4           | 24           |
| 5           | 16           |
| 6           | 12           |
| 7           | 8            |
| 8           | 10           |
| 9           | 10           |
| 10          | 8            |

### RESULTS

For the most part the results with all 3 mixtures have been very gratifying (Table III).

Mixture A was the first one available and has been used more than either of the others. In big children the volume required is on the large side with the obvious danger of vomiting. Presumably because droperidol and trimeprazine are potent anti-emetics there has to date been no report of this happening. Mixture C is identical to Mixture A in composition and they differ only in concentration.

We have found Mixture A easier to use with babies and small children so that small fractions of a ml do not have to be given. Mixture C is better for bigger children obviating the necessity for large volumes.

The actual quantities of each drug per 0.45 kg/body weight are as follows:

#### Mixtures A and C:

Trimeprazine 0.8 mg  
Droperidol 0.05 mg  
Physeptone 0.03 mg

#### Mixture B:

Trimeprazine 1.7 mg  
Droperidol 0.08 mg

Usually the child settles down after about half an hour and is 'asleep' after 45 minutes. A common reaction on being moved on to the theatre trolley is to sit up with a dazed expression on the face, but on being told to lie down, he does so, and more often than not he falls asleep again on his way to the theatre.

I prefer to induce children on the trolley and to put them on the operating table when they are anaesthetized. In most cases a mask can be applied to the face immediately provided that it is done gently. In those who are still too 'light' for this, the same result can be obtained by holding

TABLE III. RESULTS

|  | Mixture A | Mixture B | Mixture C |
|--|-----------|-----------|-----------|
| <b>Sedative effect</b>                         |           |           |           |
| Good ... ..                                    | 63        | 35        | 16        |
| Fair ... ..                                    | 6         | 5         | 2         |
| Poor ... ..                                    | 1         | —         | —         |
| <b>Antisialagogue effect</b> ... ..            | Good      | Good      | Good      |
| Pre-operative vomiting ... ..                  | Nil       | Nil       | Nil       |
| Postoperative vomiting ... ..                  | 2         | Nil       | Nil       |
| Postoperative sedation given ... ..            | 20        | 4         | 4         |
| Postoperative sedation not given ... ..        | 50        | 36        | 14        |
| <b>Time before waking after return to ward</b> |           |           |           |
| 0 - 15 min ... ..                              | 60        | 35        | 16        |
| 15 - 60 min ... ..                             | 10        | 5         | 2         |
| <b>Reaction on awakening</b>                   |           |           |           |
| Restless ... ..                                | 20        | 15        | 6         |
| Quiet ... ..                                   | 50        | 25        | 12        |

the mask just above the face for 1-2 minutes. It is rare indeed to have to induce by force.

## DISCUSSION

It is my impression that the amount of anaesthetic agent required is slightly reduced, and it is usually possible to maintain an adequate depth of anaesthesia using 0.5% halothane. When using ketamine hydrochloride, the dose can certainly be reduced to two-thirds or sometimes even to half the usual dose.

The mixtures have not been used on shocked or severely ill children where absorption from the stomach is doubtful. In normal children for cold surgery there has been no report of hypotension, respiratory depression or other serious complication when using the lower concentration of halothane.

Rather naturally, these children do not wake as soon after surgery as they do with less potent premedication, but this fact has lessened rather than increased the strain on the over-worked nursing staff.

The child usually returns to the ward or recovery room with an airway in the mouth but rejects this within 5-15 minutes. At this stage he usually sits up, looks around and then lies down and goes back to sleep for several hours. During this time he can be roused and has all his reflexes, but unless disturbed, makes no complaint. Some children become very restless on awakening and in the early part of this trial, postoperative sedation was given at this stage. As the trial progressed, it was found that this restlessness seldom lasted more than 15 minutes and less and less postoperative sedation is now being given.

Postoperative pain seems to be very much reduced and a high proportion of the cases have required no postoperative analgesics.

When analgesics are given the effect seems to last much longer than usual. The mixtures containing Physeptone can be used for postoperative pain, generally half the pre-operative dose being adequate. One of the most pleasing features has been the great reduction in postoperative vomiting.

These results conflict very markedly with those of Brown.<sup>7</sup> He was completely unable to sedate children with even very large doses of droperidol given by mouth, but found it satisfactory in children up to the age of 7 years when given intramuscularly in large doses.

On reviewing the literature, droperidol seems to be both inefficient and toxic when used alone, but in combination with other sedative and narcotic drugs, its efficacy is enhanced and its toxicity decreased.

I consider that one of the principal advantages of this type of premedication is the avoidance of an injection, as many small children become most upset after getting one.

## Droperidol in Adults

In adults I have merely added droperidol to whatever other premedication I had been going to use. The dose has been kept small and has varied from 1.25 to 5 mg, depending on the robustness of the patient. In very frail patients I have halved my usual premedication and replaced it with 1.25 mg of droperidol.

Under the prevailing conditions it is hard to give figures but I can usually reduce the thiopentone dose by approximately a quarter, or replace it with methohexital (Brietal), and get a 'thiopentone-like' effect. The concentration of halothane, methoxyflurane, etc., is also usually lower than with conventional premedication. There has been no trouble with respiratory depression, coughing or hiccupping and in normotensive patients there have been no cardiovascular side-effects.

I avoid using it in hypertensive patients, especially in those on hypotensive drugs, and on a patient where the surgeon is likely to demand hypotensive anaesthesia.

This premedication has been associated with a very low incidence of postoperative nausea and vomiting and with some anterograde amnesia. Many patients have remarked that they remember speaking to the anaesthetist in the theatre but have no memory of the injection. This amnesia is not uncommon when scopolamine is used but I have not noticed it before with atropine. Provided a low con-

centration of anaesthetics is given, postoperative awakening is not delayed, but often the need for analgesia is.

### CONCLUSIONS

When I first began using these premedications, I was well satisfied with them, but it was not until the nursing staff began exhorting the other anaesthetists to use them that I considered writing this article. Nurses may not be the best pharmacologists, but they do know when their patients are unhappy—particularly when they are children.

Most articles on droperidol are about its use in neuroleptanalgesia where it is naturally compared with chlorpromazine and the 'lytic cocktail'. By comparison it naturally shows up very well and its stabilizing action on the cardiovascular system is emphasized. While agreeing that it is perfectly safe with normotensive patients, I think that it should be used with care in hypo- or hypertensive individuals and in geriatrics. Parkinsonism is not a contra-indication. The only absolute contra-indication is hypersensitivity to the drug, and as its safety in pregnancy has not been established, it should be used with caution.

It appears to potentiate other central nervous system depressant drugs, therefore the dose of such drugs should be carefully considered. It would seem to prolong the action of analgesics well into the postoperative period.

While the various combinations of drugs described above have proved efficacious, I have no doubt that other combinations might be even better.

I should like to thank Dr P. Foster, Chief Anaesthetist at Karl Bremer Hospital, for help and advice; Mr R. Bradley and the dispensary staff of Frere Hospital, East London, for their advice and patience in preparing the mixtures; and the nursing staff of Frere Hospital for their interest and extra work in keeping records.

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