REPORT ON THE USE OF DIPIPANONE HYDROCHLORIDE AS A POSTOPERATIVE ANALGESIC[1]

S. M. CAMPBELL, M.B., F.R.C.P.(C), F.F.A.R.C.S.[2]

DIPIPANONE HYDROCHLORIDE, since its action on rats was first described by Offner *et al.* (1) in *Nature* in 1949, has been sporadically reported by various investigators as an analgesic in medical, obstetrical, and postoperative conditions, and also as an adjunct intravenously in light anaesthesia for obtunding pain reflexes and for controlled central respiratory depression (2,3,4).

This drug is the piperidine analogue of amidone since it is morphine-like in its analgesic action and, when given in sufficient dosage, produces respiratory depression which can be reversed with Nalline® or Lorfan®.

This report is based on its use in alleviating pain in four hundred postoperative patients in the recovery room. There are many variables in assessing the analgesic properties of a drug under these conditions such as preoperative sedation, site and duration of operation, anaesthetic agents used, sensitivity to drugs, physical condition and personality of the patient, and the knowledge and judgment of the investigator and his assistants.

Preoperatively the patients in the series were given equivalent doses of meperidine or morphia and hyoscine or atropine, depending on age and physical condition, and most of them were anaesthetized with thiopentone, nitrous oxide, and a relaxant. Some received intravenous meperidine and a few had cyclopropane. There were also some epidural and spinal blocks.

Table I shows the field of operation, nearly half the series (198) being abdominal cases; ages ranged from 11 to 81 years.

TABLE I

Site of operation	No.
Head and neck	23
Spine	19
Extremities	76
Chest	29
Abdomen	198
Perineum	55
TOTAL	400

The drug was given subcutaneously in the recovery room when the patient complained of pain or was very restless after recovering consciousness. If sufficient relief was not apparent in 30 min. a repeat dose was given. Table II shows that fifty-two of the four hundred received a repeat dose. Eight received no relief until some other drug was used, and twelve complained of pain no matter what was given. When relief was very good the drug was effective in 5 to 20 min. with the patient relaxing into a quiet sleep from which he or she was easily roused to answer questions sensibly.

[1]Presented at the Annual Meeting, Canadian Anaesthetists' Society, June 23–25, 1958.

[2]Department of Anaesthesia, University of Toronto, and Toronto General Hospital, Toronto, Ontario.

TABLE II

Pipadone amount of first dose	10 mg	20 mg	25 mg	30 mg	Total
No of patients	7	246	146	1	400
No given repeat doses	4	35	13	0	52
No given other drugs for relief	0	4	4	0	8
No receiving no relief with other drugs	0	6	6	0	12
Vomiting, 1½ to 11 hr after Pipadone	0	6	1	0	7
Respiratory depression	0	3	2	0	5

Blood pressures, pulse, and respiration were taken on arrival in the recovery room, at the peak of the drug effect, and at intervals of one-half to one hour subsequently. Blood pressure and pulse changes, if they occurred, were not significant. If the pulse rate was fast before injection of the drug, it might decrease; if it happened to be slow, it might increase. Changes ranged from ten to forty per minute, but followed no set pattern. Blood pressure changes also were not significant.

Vomiting occurred in seven patients but never within 90 min. of giving the drug and in five of them it was between 3½ and 11 hr. after. It was more often recorded that any immediate postoperative nausea was relieved.

Respiratory depression (Table III) occurred in five patients. A decrease in respiratory rate to twelve or under was considered to require treatment. Three of these patients had been given Phenergan as well as Pipadone® to control extreme restlessness. This is apparently a very potent combination. Nalline in one patient and Lorfan in another quickly restored respiration to a safe level. The slowly progressive depression in the 73-year-old patient to a rate of six should have been reversed earlier. A 17-year-old girl with a plastic revision of the nose, showed a slowly progressive depression over a 70-min. period to a respiratory rate of eight. Someone ordered Megamide® and Daptazol® to which she responded!

TABLE III

DEPRESSED RESPIRATION

Age	Dose of Pipadone (mg)	Other drugs	Respiration rate	Interval after "P" given (min)	Treatment
17	20	None	8	70	Megamide and Daptazol
73	20	Phenergan 25 mg.	6	130	Nalline 5 mg.
43	25	Phenergan 37 5 mg	8	25	Lorfan 1 mg
61	25	None	12	25	Oxygen
57	20 10	Phenergan 25 mg	10	30	Oxygen

Duration of sedative effect is difficult to estimate, but records were kept of the time and nature of subsequent sedation used. Many patients received no further sedation, but in 127 abdominal and abdomino-perineal cases the average time to subsequent sedation was 4½ hr.

A comparative series with other sedative and analgesic drugs has not been completed.

Summary

A record has been kept on the effect of dipipanone hydrochloride on four hundred postoperative patients, noting the dose, the time intervals between injection and satisfactory effect, and between the injection and subsequent use of sedation, and any side effects on blood pressure, pulse, respiration, and nausea or vomiting.

Conclusion

Dipipanone hydrochloride is a useful analgesic drug with hypnotic qualities and a minimum of side effects in the dosage used. Respiratory depression has not been noticeable but can occur and is increased where phenathiazine derivatives are used.

We wish to thank Burroughs Wellcome Company (Canada) for the opportunity of trying out Pipadone.

Résumé

Au cours des suites opératoires, chez 400 malades, nous avons étudié les effets du chlorhydrate de dipipanone et, plus particulièrement, la dose, l'intervalle entre les injections et l'apparition d'un effet appéciable entre l'injection et l'administration d'un autre sédatif ainsi que les effets secondaires sur la tension artérielle, le pouls, la respiration, les nausées et les vomissements.

Le chlorhydrate de dipipanone possède un pouvoir analgésique utile, des qualités hypnotiques et très peu d'effets secondaires aux doses employées. La dépression respiratoire n'a pas attiré notre attention, mais on peut l'observer et elle est aggravée lorsqu'on emploie en même temps des dérivés de la phenathiazine.

REFERENCES

1. Offner, P., Thorp, R. H, & Walton, E Nature *113* 479 (1949)
2. Gillhespy, R. O., Cope E., & Jones, P. O Brit. Med J *2*. 1094 (Nov. 10, 1956).
3. Coleman, D. J., Levin, J, & Jones, P. O. Brit Med J. *1*· 1092–95 (May 11, 1957).
4. Coleman, D. J., Hargrove, R. L., & Jones, P. O. Anaesthesia *13* 59–62 (January, 1958).
5. Masson, A. H. B. Anaesthesia *11* 59 (January, 1956).