

CHLORPROMAZINE AND PROMETHAZINE IN OBSTETRICS*

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THE alleviation of pain during labour and childbirth can be attained with ease, but what is the price often paid for this relief, and for the very inadequate comfort most maternity patients receive? This price is far greater than many of us realize. It is the cause of a great number of foetal and neonatal deaths, and probably of a much larger number of babies who survive mentally and physically maimed.

Hansen (1) states. "Every cog in the wheel is important in making the newborn a bouncing pink bawling infant, rather than a cyanotic limp infant who some day may be spastic, convulsant or idiotic." The obstetricians have improved their care of the mother to such an extent that she need have little fear for her own safety. Anaesthesiologists offer her many choices of pain relief during delivery. But what has been done to reduce morbidity and mortality during the foetal and neonatal period? Statistics on morbidity are, from their nature, unobtainable, but the children's sections of our mental hospitals offer mute but ample evidence of the trauma occurring during these periods. The literature abounds in figures on neonatal and infant death rates. Bundesen, Potter, Fishbein, Bauer, and Plotzke (2) in their excellent monograph point out that in Chicago, although the mortality rate in infants of one month to one year of age had been reduced from 36.8 in 1925 to 6.3 in 1950, the neonatal rate during the same period had been reduced from 36.1 to only 19.4. These figures are representative of most North American centres where well-qualified obstetrical anaesthesiologists do not share the responsibility of the obstetrical team. Our own experience during the past four and a half years would indicate that where the neonatal death rate rises higher than 12, there is a weak or missing link in the chain of the obstetrical team. I venture to predict that the results will be more gratifying, and the returns more profitable, when we are prepared to spend on this stage of life even a small proportion of the effort and money we now devote to prolong the lives of our aged.

The medical staff of the Vancouver Grace Hospital is well aware of this fact. Based on a careful analysis of the causes of our foetal and neonatal losses, a concentrated effort is in constant progress to reduce them further. We realize that among other factors the routine orthodox sedatives and hypnotics used during labour give inadequate relief to the mother and frequently are hazardous to the baby. It is our conviction that a serious attempt to replace them by more effective and less dangerous preparations is long overdue. A review of the drugs now available led us to conclude that two of the newer Phenothiazine derivatives, namely Chlorpromazine (Largactil) and Promethazine (Phenergan) merited clinical consideration.

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The combination of these drugs has been widely studied in hypothermia, but for our purpose it was considered advisable to assess them separately. Both have a sedative action. They potentiate the hypnosis and analgesia of other drugs, apparently without depressing respiratory activity, and they reduce the necessary amounts of anaesthetic agents. They are among the most effective of the anti-emetics. Laborit (3), Martin (4), Davies (5), and others have reported favourably on the use of intravenous chlorpromazine during labour. They conclude that the drug has no ill effect on the baby. We feel that their methods are not practical in most institutions, and wonder if they are not without danger unless the mother is under constant medical observation. We have found no reports on the use of Promethazine alone.

In our series there was no selection of patients; all were of doctors who supported our efforts to find safer and more effective sedation during labour. Our approach to this study has been a purely clinical one. Our results are based exclusively on the observations and impressions of our obstetricians, our anaesthesiologists, our case room nursing staff, and our patients.

At the time of admission, and throughout their labour, patients were carefully observed and pertinent data were recorded. An attempt was made to evaluate their emotional status. Their blood pressure, pulse rate, progress, and response to sedation, as well as foetal heart rate, were recorded. To avoid a possible state of hypotension the patients were not allowed out of bed within six hours of their last sedation. Early in the study it was found that the response from oral administration of the drugs was too slow to make them of value to the patient in labour. Therefore we report only on their intramuscular use.

CHLORPROMAZINE

When labour was well established a dose of 25 mgm. Chlorpromazine was given by deep intramuscular injection; Demerol 25-50 mgm was given, when need for analgesia became apparent. Chlorpromazine and Demerol were given thereafter, in the same amounts, at the case-room nurses' discretion. In order to evaluate better the action of this combination, the use of barbiturates and other opiates was discouraged. They were used in only 9 per cent of this series.

Two hundred patients received Chlorpromazine during labour. Of these, 127 (63.5 per cent) were primiparae and 73 (36.5 per cent) were multiparae. Two were mildly and one severely toxic. An average of thirty-one mgm. of Chlorpromazine and 75 of Demerol was given to patients in this series. The largest amount used for one individual was 175 mgm. of Chlorpromazine and 350 of Demerol. This was given to a thirty-six year old primipara during a thirty-hour labour. Sixty-eight per cent were considered calm and relaxed on admission but as labour progressed 12 per cent of these became tense, poorly controlled, and inadequately sedated. In contrast 29 per cent were classified as tense on admission, and of these, 60 per cent soon relaxed and became well controlled on the Chlorpromazine-Demerol therapy. Only one was considered hysterical when first seen. She did not improve during her four and one-quarter hours of labour. She obviously received inadequate sedation, having been given only 50 mgm. of Demerol and 25 of Chlorpromazine.

The analgesia and hypnosis from this combination we found most unpredictable. A few patients, on small doses, slept soundly throughout their labour and could not be aroused. These caused us some concern and prevented us from giving doses of Chlorpromazine larger than 25 mgm. at any one time. Some appeared to have obtained no sedation and no analgesia, but the majority were noted to be sleeping well between contractions, awakening and appreciating their pains as they occurred. Many patients recalled their labour as one long continuous pain and had no memory of sleeping between contractions.

The duration of labour appeared to be prolonged. In primiparae the first stage averaged sixteen hours and the second stage one hour. In multiparae these stages averaged ten hours, and fourteen minutes respectively. Most of those patients who were adequately sedated showed evidence of decreased muscle tone. This limpness caused our case-room nurses some concern, and might partly account for the prolongation of labour.

The patient's pulse and the foetal heart rates were not altered. Blood pressure in the normo-tensive patients was not appreciably affected. Thirty-four per cent showed an average systolic fall of 10 and a diastolic fall of 14 mm. of mercury, whereas 23 per cent averaged a rise of 11 mm. in systolic pressure. The only noteworthy change occurred in a toxic twenty-one old primipara whose pressure had risen from 130/90 to 180/120 in less than twelve hours. Subsequent to receiving 25 mgm. of Chlorpromazine and 50 mgm. of Demerol, she became very drowsy, and her pressure reverted to 120/90 where it remained until she was delivered one hour and three minutes later.

Anaesthesia required for delivery was noticeably reduced. Many, even of those who were considered poorly sedated during labour, were adequately anaesthetized for forceps delivery by Nitrous Oxide and Oxygen in the ratio of three to one. Emesis was infrequent. Even after Ergometrine had been given, very few showed any evidence of nausea, or any inclination to vomit.

Although we were dissatisfied with the quality of relief obtained by the mothers during their labour, we were well pleased with the results in the babies. In this small series of two hundred cases there were no foetal or neonatal deaths. Ninety-two per cent of the babies cried spontaneously within thirty seconds of delivery. They were remarkably pink and their muscle tone was excellent. Seven per cent were mildly depressed, but breathed spontaneously within one minute of birth. Of this 7 per cent, one half were of mothers who had been given additional barbiturates or heroin. The other half had been delivered with difficulty, and the mothers had been given more than the usual amounts of cyclopropane. Only one baby caused us concern. It required ten minutes of maintained respiration, was intubated and a considerable quantity of mucus was aspirated from the pulmonary tree. This baby made an apparently uneventful recovery. The mother had received only 25 mgm. each of Chlorpromazine and Demerol and delivery was spontaneous and easy. No evidence of foetal distress had been detected during her labour, and we were unable to account for the depressed state of this baby.

PROMETHAZINE

In this second series, combinations of Promethazine and Demerol were given to 300 patients in labour. When the need for sedation became apparent, these

patients were given, by intramuscular injection, 25 mgm. of Promethazine and 50 of Demerol. If, within one hour, relief was inadequate, nurses were instructed to repeat the sedation, and to increase the Demerol to 100 mgm. if greater analgesia was needed. Further sedation of whichever dose had been effective was permitted at the case-room nurses' discretion. As in the Chlorpromazine series, the use of other sedative drugs was discouraged.

In this series of 300 patients, 135 (45 per cent) were primiparae and 165 (55 per cent) were multiparae. An average of 38½ mgm. of Promethazine and 98 of Demerol was given. Seventy-five per cent were considered calm and were relaxed on admission, but as labour progressed 19 per cent of these became tense and poorly controlled. Of the 25 per cent considered tense on admission, 44 per cent improved and became well relaxed and easily controlled.

The addition of Promethazine to Demerol increased its analgesic action, but most apparent was the marked increase in the relief of emotional stress and apprehension. Most patients became pleasantly sleepy but remained mentally alert. No undue depression or unfavourable side actions were noted. Most multiparae, when questioned, replied that although they were aware of their contractions they were having very little discomfort, and that their labours were less unpleasant than on previous occasions. The response to this combination was no more unpredictable than when Demerol alone was used.

Duration of labour in primiparae was appreciably shortened. The first stage averaged eleven hours and forty-three minutes, the second stage one hour and two minutes. In multiparae the first stage averaged eight hours and fifty-one minutes, and the second stage nineteen minutes.

There was no evidence of reduced muscle tone. The patients' blood pressures, pulses, and the foetal heart rates were not appreciably altered. As in those who had been given Chlorpromazine, less anaesthesia appeared necessary for delivery, and the incidence of vomiting was reduced.

In this series there was one neonatal death. This was in a baby who had been severely asphyxiated by a tight nuchal cord during the second stage. Ninety-five per cent of the babies cried spontaneously within thirty seconds of delivery; 4% per cent were mildly depressed but cried spontaneously within one minute of birth. Only three babies, exclusive of the one who died, required active resuscitation. The first had a marked bilateral atelectasis, the second had been severely asphyxiated during the second stage by two tight loops of nuchal cord. No explanation could be found for the depressed state of the third. All made apparently uneventful recoveries.

We are convinced that Promethazine, as used in this series, shortens labour, affords the mother greater relief than any other drugs we have used, and has no ill effects on the baby.

CONCLUSIONS

At the termination of these two series a critical review of our results led us to the following conclusions:

Chlorpromazine and Promethazine, given as described above, to the patient in labour appear to have no ill effect on the baby. Both potentiate the analgesic action of Demerol (Table I), reduce the quantity of anaesthetic agents required for delivery, and lower the incidence of vomiting. The response of the mother

to Chlorpromazine is too unpredictable to make the drug of value for routine sedation during labour. This unpredictable factor might be overcome by giving the drug intravenously in the quantity required to attain the desired sedation.

The response of the mother to Promethazine and Demerol is as predictable as to Demerol alone. This drug shows great promise of reducing the discomforts and the duration of labour without harm to the baby.

TABLE I
POTENTIATION OF THE ANALGESIC ACTION OF DEMEROL BY CHLORPROMAZINE
AND PROMETHAZINE

	Number patients	Total Demerol	Demerol/patient
Routine sedation (controls)	435	68,200 mgrn	156.8 mgm
Chlorpromazine series	200	15,000 mgrn	75 mgm
Promethazine series	300	29,400 mgrn	98 mgm

The duration of labour appears to be increased by Chlorpromazine but is shortened appreciably in primiparae by Promethazine (Table II). It is our impression that this reduction in the duration of labour can be attributed to a decrease in endogenous adrenalin resulting from lowering of emotional stress. Adrenalin has been shown to increase the cervical tone in the pregnant patient (6, 7).

TABLE II
AVERAGE DURATION OF LABOUR IN CONTROL, CHLORPROMAZINE-DEMEROL,
AND PROMETHAZINE-DEMEROL SERIES

	Number	PRIMIPARAE		MULTIPARAE		
		Stage 1	Stage 2	Stage 1	Stage 2	
<i>Controls</i>						
Eastman(8)		16 hr	1 hr 45 min	11 hr	1 hr	
DeLee and Greenhill(9)		16 hr	1 hr 45 min	12 hr	15-30 min	
Grace Hospital	130	12 hr 53 min	1 hr 12 min	150 7 hr 26 min	16 min	
Chlorpromazine-Demerol	127	16 hr	1 hr	72 10 hr	14 min	
Promethazine-Demerol	135	11 hr 43 min	1 hr 7 min	165 8 hr 55 min	19 min	

Sufficient data have been made available to confirm the compatibility of Chlorpromazine and Promethazine in other aspects of anaesthesia, and as both studies outlined here offer worthwhile consideration for further investigation, it would appear logical to assume that a possible solution to sedation during labour could be found in the judicious use of these drugs, employing a combination of the methods now undergoing investigation.

SUMMARY

Two hundred patients were given Chlorpromazine and Demerol intramuscularly during labour. Hypnosis and analgesia were found to be unpredictable. No appreciable alterations were noted in patient's pulse, blood pressure, or foetal heart rate in the normo-tensive patients. The amount of opiates during labour and of anaesthesia during delivery was lessened. Nausea and vomiting were practically absent, and no ill effects on the babies were noted.

Promethazine was given in the same way to 300 patients in labour. A satisfactory sedative dose was reasonably predictable. Hypnosis and analgesia from Demerol were appreciably potentiated by the drug. The labour rooms were noticeably quieter and the patients less concerned about their labour. As with Chlorpromazine, anaesthesia for delivery was decreased and the incidence of nausea and vomiting became remarkably low. The drug appeared to have no depressing or other undesired effect on the baby. It was our impression that Promethazine and Demerol given during labour offer the mother more effective sedation and her baby less harm, than any combination of drugs with which we are acquainted.

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RÉSUMÉ

Deux cents patients reçurent durant leur travail, du Chlorpromazine et du Démérol en intra-musculaire. Il fut possible de prévoir l'hypnose et l'analgésie. Chez celles à tension artérielle normale on ne nota pas de changement appréciable du pouls et de la tension de même que des pulsations cardiaques foetales. On a pu restreindre l'emploi des opiacés au cours du travail et de l'anesthésie au moment de la délivrance. Il n'y eut pratiquement pas de nausées et vomissements et aucun effet nocif put être noté chez les nouveaux-nés. Dans les mêmes circonstances, chez trois cents patients en travail, on donna du Promethazine. Il fut possible de prédire de façon raisonnable une dose sédatrice satisfaisante.

Les effets hypnotiques et analgésiques du Démérol furent augmentés de façon appréciable. Les salles d'accouchement devinrent plus tranquilles et les patients moins effrayées du travail. Comme avec le Chlorpromazine, l'anesthésie pour la délivrance put être réduite et l'incidence des nausées et vomissements devint très basse.

Le médicament ne semble pas avoir d'effets dépressifs ou indésirés sur le bébé. L'impression des auteurs fut que le Promethazine et le Démérol donnés durant le travail offrent à la mère une sédation plus effective et à son bébé, moins de danger que n'importe laquelle combinaison de médicaments que nous connaissons.

REFERENCES

1. HANSEN, A. E. Complications in the Post Anaesthetic Period of Parturition from the Pediatrician's Viewpoint *Texas Rep Biol & Med.* 12. 67-71 (1954).
2. BUNDESEN, POTTER, FISHBEIN, BAUER & PLOTZKE Progress in the Prevention of Needless Neo Natal Deaths, Annual Report of the Chicago Health Department (1951)
3. LABORIT, H. L'anesthésiologie obstétricale *Maroc méd* 330 (November, 1952).
4. MARTIN, E. M A Preliminary Clinical Report on Largactil (Chlorpromazine). Presented at the Academy of Medicine, Anaesthesia Section, Toronto, Ont, February 15, 1954.
5. DAVIES, JOHN I. The Use of Largactil in Obstetrics *Canad. Anaesth Soc. J.* 2 327 (1955).
6. KAISER, K H & HARRIS, J S *J Obst & Gynec* 59. 775 (1950)
7. SCHOFIELD, B M *J. Physiol.* 117: 317 (1952).
8. EASTMAN, N J *Williams Obstetrics* 10th ed, New York Appleton-Century-Crofts (1950).
9. DELEE, J. B. & GREENHILL, J. P *Principles and Practice of Obstetrics.* 9th ed, Philadelphia W B Saunders (1947).