AN INVESTIGATION OF ATARAXICS IN LABOUR: MEPROBAMATE (EQUANIL®)

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IN THE SEARCH for safer and more effective methods with which to provide analgesia during labour, the staff of Vancouver Grace Hospital has conducted a number of clinical trials. These studies concerned certain of the ataractic agents, generally in combination with meperidine.

Of the numerous problems surrounding obstetrical analgesia, two factors received particular attention: (1) the principle pioneered by Grantly Dick Read, which teaches that mental and physical relaxation during labour is valuable and desirable, has been accepted, (2) there is a hard core of perinatal deaths in which hypoxia of the foetus appears to be an important if not the principal cause. By depressing the vital centres, analgesic drugs may aggravate an existing foetal hypoxia or may be wholly responsible for the reduction of blood oxygen tension in the foetus. Any improvement in obstetrical analgesia, therefore, must include decrease or even elimination of foetal depression.

This investigation concerned a trial of meprobamate (1–3)[2], an aliphatic compound unlike the phenothiazine derivatives studied previously (4). A close relative of mephenesin, meprobamate is said to act as a muscle relaxant and anticonvulsant, and to have "tranquillizing" properties (5–10).

This study was designed: (i) to assess the emotional status of the patient on admission and to observe any change after administration of the compound; (ii) to record alterations in blood pressure, pulse, and temperature; (iii) to note any side effects produced in the mother, and (iv) to evaluate the condition of the infant on delivery.

METHOD

Meprobamate was administered to seventy-four patients (fifty primiparas, twenty-four multiparas) on admission to Grace Hospital for delivery All were admitted directly to the labour room.

The emotional status of the patient on admission was classified as:-(*a*) calm, (*b*) tense, (*c*) apprehensive, and (*d*) unco-operative. The blood pressure, pulse, and temperature readings were taken on admission and recorded.

Initially, 800 mg. (two 400 mg. tablets) meprobamate were administered by mouth. Each patient was observed in one hour. Her emotional state was evaluated and the blood pressure, pulse, and temperature readings were taken and recorded. The same observations were made again two hours and five hours after the initial dose. An analgesic (such as meperidine) was administered if necessitated by increasing pain. If in the first five hours no analgesic had been given, the dose of 800 mg. meprobamate was repeated at the end of this interval.

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[2]Meprobamate is available as Equanil®, John Wyeth & Brother Limited.

The vital signs were observed and recorded frequently throughout labour. The condition of the infant was evaluated with particular regard to the presence of respiratory depression.

Results

Emotional Status

Primiparas. Of the fifty patients in this group, twenty-seven (54 per cent) were considered calm on admission and remained so throughout the period of observation. Seventeen patients were tense at the time of admission. Of these, six became calm within one hour after administration of meprobamate and an additional three within two hours. Thus nine (about 53 per cent) of the tense primiparas were relaxed within two hours after receiving meprobamate. Six of the patients who appeared calm on admission became tense in the two hours after administration of meprobamate (Table I).

Multiparas. Of this group of twenty-four patients, six were classified as tense on admission. One hour after meprobamate had been given, five had become calm and the sixth was considered calm after two hours. The other eighteen were calm throughout the first stage. Two patients in the group who were calm on admission became tense in the two hours after administration of meprobamate (Table I).

TABLE I

Analysis of Emotional Status of 74 Patients

	Primiparas		Multiparas	
	No	%	No.	%
Total patients	50		24	
Tense or apprehensive when meprobamate given	17	34	6	25 (of 24)
Tense or apprehensive converted to calm 1 hour after meprobamate	6	35 (of 17)	5	83 (of 6)
Tense or apprehensive converted to calm 2 hours after meprobamate	3	18 (of 17)	1	17 (of 6)
Tense or apprehensive converted to calm 1 or 2 hours after meprobamate	9	53 (of 17)	6	100 (of 6)
Calm when meprobamate given*—tense or apprehensive in 1 hour	3	6 (of 50)	1	4 (of 24)
Calm when meprobamate given*—tense or apprehensive in 2 hours	3	6 (of 50)	1	4 (of 24)
Calm when meprobamate given*—tense or apprehensive in 1 or 2 hours	6	12 (of 50)	2	8 (of 24)
Calm throughout	27	54 (of 50)	16	67 (of 24)

*Most of these patients were probably apprehensive but were able to conceal their emotions. Our further observations of responses to this drug would indicate that small doses (i e , 800 mg) tend to reduce but not entirely to remove inhibitions In such patients, larger doses are needed to achieve true relaxation—complete freedom from fear

Analgesia and Hypnosis

The relaxant effects of an oral dose of meprobamate developed in about one hour and lasted about six hours To maintain a state of tranquillity the compound was administered every five hours until need of an analgesic became apparent. Meprobamate seems to have no cumulative action, provides little sedation, and

does not potentiate the analgesic effects of narcotics. Thus larger doses of meperidine, for example, would be required to produce a satisfactory analgesia in the presence of pain than are necessary when meperidine is used in combination with promethazine (and would be accompanied by increased risk of foetal depression). Consequently, as labour progressed to the second stage in this series, and the pain increased in severity, more effective analgesia was necessary. It was decided, therefore, to substitute promethazine for meprobamate in the sedative-analgesic combination.

The lack of superiority of meprobamate as an analgesic potentiator is indicated by the fact that the average dose of meperidine required in the early first stage was little less than that used in previous trials employing meperidine with other compounds (Table II).

TABLE II

SEDATION AND ANALGESIA REQUIRED

	No of patients	Total		Total	
		Meperidine (mg)	Promethazine (mg)	Meperidine per patient (mg)	Promethazine per patient (mg)
Meprobamate series	75	6,950	3,520	92 6	46 9
Routine sedation (4) (meperidine-promethazine)	300	29,400		98	38.5

Hypnosis is not a prominent feature of meprobamate medication Patients who received 50 mg promethazine by intramuscular injection later in labour showed a much more pronounced tendency to drowsiness Meprobamate is of advantage for the patient for whom sedation is undesirable.

Duration of Labour

Meprobamate appeared to have no adverse effect on the establishment or progress of the first stage. The average total length of labour in this series was somewhat prolonged in comparison with the same observations recorded in previous studies (4) (Table III).

TABLE III

AVERAGE DURATION OF LABOUR

	Primiparas					Multiparas				
	No.	Stage 1 (hrs)	(min)	Stage 2 (hrs)	(min)	No	Stage 1 (hrs)	(min.)	Stage 2 (hrs)	(min.)
Meprobamate	50	13	50	0	54	24	9	20	0	18
Routine sedation (4) (meperidine-promethazine	135	11	43	1	7	165	8	55	0	19

Delivery

Forty-nine single infants and one pair of twins were delivered to the primiparous mothers, and twenty-four single infants to the multiparous

Among the infants of the primiparas, seven were delivered spontaneously, including one of twins; thirty-nine were delivered by low forceps, including the second twin, and two by mid-forceps; two were breech deliveries.

One primipara was eventually delivered by Caesarean section after forty-eight hours of trial labour in the first stage. A well-developed constriction ring was present. Therefore, the predelivery medication could not be held responsible for the ineffectiveness of labour in this patient.

Of the multiparas, eighteen delivered spontaneously, five were delivered by low forceps and one by mid-forceps. No abnormalities of the labour mechanism developed in this group.

Condition of Infants

There were no stillbirths and no neonatal deaths (that is, in the first seven days).

Among the fifty infants delivered vaginally of primiparous mothers, respiration occurred spontaneously (that is, within thirty seconds of delivery) in forty-five. Respiration was delayed for sixty seconds in five infants. Two of these were breech deliveries. In two infants manual rotation from the posterior position and mid-pelvic forceps delivery were performed. There was no apparent cause for the slightly delayed initiation of respiration in the remaining infant. All infants in whom breathing was delayed responded immediately to administration of oxygen by mask, and progressed normally thereafter. Intubation was not required in any case, nor was there any indication for use of nallorphine.

All infants born to multiparas breathed spontaneously within thirty seconds In one instance meconium staining appeared at the time of delivery. The infant, however, breathed immediately and cried well The cord was wound once around its neck.

The *blood pressure, pulse rate,* and *temperature* showed no significant variations in either the primiparas or the multiparas during the period of observation In all patients the rise or fall in blood pressure was no greater than 10 mm Hg The pulse rate was increased or reduced by no more than ten beats per minute Surprisingly, none of the patients who were tense on admission and who became calm after meprobamate medication showed a consistent response These patients might have been expected to experience a slight fall in blood pressure and pulse rate in keeping with their improved state of relaxation.

Side Reactions

In general, meprobamate appeared non-toxic and free from side actions. No disturbance of gastro-intestinal function, urinary output, or lactation could be attributed to the compound.

One case of allergic dermatitis occurred. The sensitivity reaction exhibited by this patient resembled others previously reported (2, 5, 6, 8–11). Although

troublesome, the rash did not interfere with the processes of parturition. The infant was unaffected.

Other Possible Uses of Meprobamate

A patient suffering from severe toxaemia of pregnancy, who also showed a pronounced "functional overlay" of apprehension, received the conventional treatment with opiate and barbiturate drugs. When meprobamate (400 mg. three times a day) was added to the regimen, there was a definite improvement in her emotional state and her mental outlook was considerably brightened. Meprobamate apparently did not potentiate the hypotensive action of the drugs used for treatment of the toxaemia.

Summary and Conclusions

Meprobamate was used orally, early in labour, for relaxation of seventy-four patients (fifty primiparas, twenty-four multiparas). Emotional tension was relieved in a significant proportion of patients.

The findings in this study would seem to indicate that the compound should be used for the express purpose of allaying the anxiety and apprehension attendant upon the early phases of the first stage, prior to the need of analgesia. Meprobamate is neither an analgesic nor a potentiator of analgesics.

Meprobamate appears to have no deleterious effect on the mechanism of parturition or on the foetus. One patient exhibited cutaneous evidences of sensitivity. Labour proceeded normally, however, and the infant was delivered safely.

Résumé

Chez soixante-quatorze malades (cinquante primipares et vingt-quatre multipares) dans le but d'obtenir du relâchement, nous avons employé, au début du travail, du meprobamate per os. Dans une proportion importante des malades, la tension émotionnelle a été vaincue.

Les résultats de cette étude nous amènent à croire que ce médicament ne devrait être employé que dans un but précis: diminuer l'anxiété et l'appréhension des premiers moments du travail avant que l'analgésie ne soit requise. Le meprobamate n'est ni un analgésique ni un potentialisateur des analgésiques.

Le meprobamate, toutefois, ne semble pas avoir d'effets nuisibles sur le fœtus ni sur les mécanismes du travail. Une malade sensible au médicament a présenté des manifestations cutanées. Toutefois, le travail s'est poursuivi normalement et l'enfant est né sans signe de séquelles.

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