dysuria is commoner in women who have had children (Waters, 1969) whereas age-adjusted mean systolic and diastolic blood pressures decrease with the number of children (Miall and Oldham, 1958).

Fifty-three (1.8%) of the women seen during the initial screening survey dated their first attack of dysuria to childhood. A comparison of symptoms in these women with those who had dysuria only in adult life suggests that their symptoms are more severe and more frequent and that they are more likely to consult a doctor (Table IV). After standardizing for age there is no evidence that their plasma urea, plasma creatinine, or blood pressure is different when compared with women who have never had dysuria. There is, however, evidence of a significant impairment of renal concentrating power. Loss of renal concentrating power is one of the earliest signs of chronic pyelonephritis, and the present finding suggests that dysuria in childhood is associated with kidney damage. The fact that women who report dysuria in childhood are significantly younger than the rest of the population could be the result of a higher mortality, but more probably this trend is simply an effect of memory.

Thus dysuria in women is unlikely to lead to impairment of kidney function but may be associated with higher than average blood pressure levels. In view of the large number of women with dysuria the present findings are on the whole reassuring, but they do not exclude the possibility that a few

women with dysuria may develop kidney damage. There is no evidence of such a group in the numbers examined. Women with histories of dysuria in childhood, however, do show evidence of a decreased renal concentrating power, which suggests that in childhood this symptom is associated with kidney damage which persists into adult life.

We thank Professor A. L. Cochrane, Director of the M.R.C. Epidemiology Unit (South Wales), other members of the unit, and Dr. John Henry Jones, Miss Margaret Hopkins, and Mrs. Susan Chick, of the Cardiff Royal Infirmary, for their help in this survey.

REFERENCES

- Davies, D. F., and Shock, N. W. (1950). *Journal of Clinical Investigation*, **29**, 496.
 Gallagher, D. J. A., Montgomerie, J. Z., and North, J. D. K. (1965). *British Medical Journal*, **1**, 622.
 Miall, W. E., Kass, E. H., Ling, J., and Stuart, K. L. (1962). *British Medical Journal*, **2**, 497.
 Miall, W. E., and Oldham, P. D. (1958). *Clinical Science*, **17**, 409.
 Mond, N. C., Percival, A., Williams, J. D., and Brumfitt, W. (1965). *Lancet*, **1**, 514.
 Smellie, J. M., and Normand, I. C. S. (1968). In *Urinary Tract Infection*, Ed. F. O'Grady and W. Brumfitt, p. 123. London, Oxford University Press.
 Steensberg, J., Bartels, E. D., Bay-Nielsen, H., Fanøe, E., and Hede, T. (1969). *British Medical Journal*, **4**, 390.
 Sussman, M., *et al.* (1969). *British Medical Journal*, **1**, 799.
 Waters, W. E. (1969). *British Journal of Preventive and Social Medicine*, **23**, 263.

Comparison of Pentazocine and Pethidine in Labour

J. MOWAT,* F.R.C.S. (GLASG., ED.), M.R.C.O.G. ; M. M. GARREY,† D.P.H., F.R.C.O.G.

British Medical Journal, 1970, **2**, 757-759

Summary: A double-blind between-patient study was carried out comparing pentazocine with pethidine in 94 women in labour. Similar analgesic and sedative effects were obtained with the two drugs, and Apgar scores were similar for babies of both drug groups. Fewer emetic sequelae were reported after pentazocine injections, though there was no statistically significant difference between the two drug groups in incidence of other side-effects.

Introduction

Childbirth may be more exhausting than painful, but for most women the first stage of labour is accompanied by pain severe enough to warrant alleviation by some form of analgesia. Epidural anaesthesia has attractions, but, as well as needing medical and nursing staff, demands personal care by a specially skilled anaesthetist (Brandstater, 1966). The technique is not without risk and is unsuitable for domiciliary practice or a general-practitioner obstetric unit. Parenteral analgesics such as pethidine may be used, but these drugs all cross the placental barrier to varying degrees and may give rise to neonatal depression (Crawford, 1966). Thus new parenteral analgesics with advantages over the standard drugs should still be evaluated for use.

Pentazocine (Fortral) is of interest not only because the World Health Organization (1969) recommended that it should be free from narcotics control but also because Beckett and Taylor (1967) showed that pentazocine crosses the

placenta to a lesser degree than pethidine. In addition, recent studies have shown pentazocine to have analgesic properties as good as or better than pethidine (Duncan, Ginsberg, and Morris, 1969; Moore, Carson, and Ball, 1970). Filler and Filler (1966) regarded pentazocine as an effective analgesic which does not retard uterine contractility or the process of labour, and Gonzales Munoz (1966) suggested that babies born to mothers who have been given pentazocine before childbirth have higher Apgar scores than babies born to mothers who have been given pethidine.

In the present study pentazocine, in doses up to 60 mg., is compared with an equivalent dose of pethidine, up to 150 mg.; both drugs were given by intramuscular injection to patients requiring analgesia during the first stages of labour.

Methods

Ninety-four women aged 18 or over and more than 35 weeks pregnant were included in this double-blind between-patient comparison of intramuscular injections of pentazocine and pethidine. Forty-six women received pentazocine and 48 pethidine. There was no specific selection of women for inclusion in the trial, though patients were excluded if they were diabetic, had a history of hepatic or renal impairment, or were taking monoamine oxidase inhibitors. In addition the study was limited to patients who were para-three or less.

When labour was established and the mothers complained of pain considered to be severe enough to require an analgesic, pentazocine or pethidine was given according to a pre-determined random order. Results of the analgesic and sedative responses at one hour after each injection were analysed. Each patient received up to three injections of the test drugs, the

*Senior Registrar, Royal Maternity Hospital, Glasgow C.4.

†Consultant Obstetrician, Royal Maternity Hospital, Glasgow C.4.

interval between injections being not less than three hours. The infants' Apgar scores were recorded at one, five, and ten minutes after delivery.

Results

Homogeneity of Treatment Groups

The age distribution between the two groups was similar, the mean age for both groups being 24 years; the age range was 18 to 38. The groups were also similar with respect to the number of previous pregnancies; 28 patients in the pentazocine group and 29 in the pethidine group were primigravida. Deliveries for all patients were single, and all presentations cephalic; eight patients in each group had labour induced. Eighty-six per cent. of all patients had normal unassisted deliveries, and only one patient required a caesarian section; the groups were similar in the distribution of normal and forceps deliveries. There were no differences between the two treatment groups in the duration of the three stages of labour.

Analgesic Efficacy of Injections

The number of injections of the trial drugs given during the study is shown in Table I; the distribution between the two groups is almost identical: 68% of the patients received one injection, 21% two injections, and 11% three injections. At the first injection 29 patients in the pentazocine group and 27 in the pethidine group were given the full dose; at the second injection 10 in the pentazocine group and nine in the pethidine group received the full dose, and at the third injection three in the pentazocine group and four in the pethidine group received the full dose. There is no difference between these distributions and the distributions of the other doses given ($P=0.05$). For both drug groups the analgesic effects of the high doses were found to be similar to the analgesic effects of the low doses.

TABLE I.—Distribution and Number of Injections

Treatment	No. of Injections			Total
	1	2	3	
Pentazocine	32	10	4	46
Pethidine	32	10	6	48
Total	64	20	10	94

Seventy-three patients were included in the analgesic assessment of the first injection. There was very little difference between the groups: 40% of the patients obtained relief of their pain, 13 out of 34 in the pentazocine group and 16 out of 39 in the pethidine group. Of the 30 patients who received a second injection 23 were assessed for analgesia. Second injections were given to most patients three to four and a half hours after the first injection; 43% of the patients obtained some degree of analgesia—7 out of 13 in the pentazocine group and 3 out of 10 in the pethidine group—and though it would appear that pentazocine affords better relief than pethidine, the difference between the two groups is not significant at the 5% level.

Only 10 patients received a third injection, and for most patients this was given three to six hours after the second injection. The number of patients involved is too small for any meaningful conclusions to be drawn.

Sedative Effects

Seventy-seven per cent. of the patients who received pentazocine and 78% of those who received pethidine were sedated after the first injection. After the second injection 8 out of

12 patients in the pentazocine group and 4 out of 10 in the pethidine group were well sedated and co-operative, and after the third injection two of the four patients in the pentazocine group and all three in the pethidine group were sedated. There are no statistically significant differences in sedation between two groups after any of the three injections ($P=0.05$).

Apgar Scores

Apgar scores were analysed only for those babies who had a normal unassisted delivery. One minute after delivery 15 babies whose mothers had received pentazocine and 11 babies whose mothers had received pethidine had an Apgar score of 7 or less. Five minutes after delivery seven of these 26 babies, two from the pentazocine group and five from the pethidine group, still had Apgar scores of 7 or less. At the 10-minute Apgar assessment two babies whose mothers received pethidine scored between 5 and 7. The percentage of babies in each treatment group who reached a minimum score of 8 at the end of each time interval is given in Table II.

TABLE II.—Comparison of Apgar Scores

Treatment Received by Mother	Percentage of Babies Scoring 8 or More After:		
	1 Minute	5 Minutes	10 Minutes
Pentazocine	60.5	94.7	100.0
Pethidine	72.5	90.0	94.9

None of the mothers required an antidote to the analgesic drugs, though two babies received an antidote—one mother had been given a single injection of pentazocine just over two hours before a normal unassisted delivery and the other mother received two trial injections of pethidine, the second within one and a quarter hours of a normal unassisted delivery.

Side-effects

The side-effects of the first and second injections are shown in Table III. After the third injection one of the 10 patients complained of retching following a pethidine injection. There were fewer emetic sequelae with pentazocine than with pethidine after the first injection, and no reports of any

TABLE III.—Side-effects of First and Second Injections

Treatment	No. Complaining of Side-effects				Total No. of Complaints	Total No. of Patients
	A	B	C	D		
First Injection:						
Pentazocine	3	4	1	4	12	10
Pethidine	7	5	1	2	15	14
Second Injection:						
Pentazocine	—	—	—	—	—	—
Pethidine	1	2	2	—	5	4

A = Nausea. B = Vomiting. C = Retching. D = Other.

side-effects at all with pentazocine after the second injection. After the second injection of pethidine side-effects were reported by four patients, and included nausea, vomiting, and retching. Side-effects other than emetic sequelae occurred only after the first injection, and included dizziness and lightheadedness.

Pre-eclamptic Toxaemia

Pre-eclamptic toxaemia was present in 13 (14%) of the patients in this trial—six received pentazocine and seven pethidine. One patient receiving pethidine required instru-

mental delivery because of fetal distress, but none of the mothers in this group showed any consistent or significant changes in blood pressure following injection of pethidine. In the pentazocine group five patients had instrumental deliveries—two because of a delay in the second stage, one because of an increase in systolic blood pressure, one because of fetal distress, and one because of deep transverse arrest. Two patients who received pentazocine had a sustained increase in blood pressure. One of these showed a rise of more than 10 mm. Hg after the first or second injections but a sustained increase of 20–25 mm. Hg after the third injection. This patient was one of the older primigravida who had hypertension during the later stages of pregnancy.

Discussion

The results of this study indicate that the two drugs have similar analgesic and sedative properties. Complaints of side-effects occurred more frequently after pethidine, though the difference between the drugs in this respect was not statistically significant ($P=0.05$). It is, however, interesting to note that no patient given pentazocine complained of any side-effects after the second or third injection, and emetic sequelae were less frequent with pentazocine than with pethidine after the first injection. These results agree with those of other workers. With doses comparable to those used in this trial, a study performed in Reading reported an incidence of nausea and vomiting after pethidine which was three times greater than that following pentazocine (County Borough of Reading Midwifery Service, 1969). In addition to finding no difference in analgesic efficacy between the two trial drugs, we were unable to establish a difference in the duration of action as shown by the demand for further analgesia.

Only two infants required resuscitation, and both had factors which complicated the delivery. The Apgar scores

show slightly better results for the pentazocine group than for the pethidine group after the final assessment, but up to this time there is little difference between the two drugs reflected in the scoring. The scores with both drugs were not low, and these results agree with those of Massinger and Lazaridis (1968) and of the County Borough of Reading Midwifery Service (1969). Though babies born to mothers given pentazocine had slightly higher Apgar scores after 10 minutes than babies born to mothers given pethidine, the number of infants involved is insufficient to confirm the finding of Gonzales Munoz (1966) described above.

In conclusion, this trial has shown that pentazocine is a suitable parenteral analgesic in labour and can safely be used in circumstances where pethidine would otherwise be the drug of choice.

We wish to thank the labour ward staff at Ross Hospital and the Royal Maternity Hospital; the Sterling Winthrop Research Division for the matching supplies of drugs; and Mr. T. S. Muir, of that company, for his help and encouragement. The statistical analysis was performed by Mr. N. Jackman.

REFERENCES

- Beckett, A. H., and Taylor, J. F. (1967). *Journal of Pharmacy and Pharmacology*, **19**, Suppl. p. 50S.
- Brandstater, B. (1966). *Acta Anaesthesiologica Scandinavica*, Suppl. No. 25, p. 345.
- County Borough of Reading Midwifery Service (1969). *Midwives Chronicle and Nursing Notes*, **82**, 400.
- Crawford, J. S. (1966). *American Journal of Obstetrics and Gynecology*, **96**, 382.
- Duncan, S. L. B., Ginsberg, J., and Morris, N. F. (1969). *American Journal of Obstetrics and Gynecology*, **105**, 197.
- Filler, W. W., jun., and Filler, N. W. (1966). *Obstetrics and Gynecology*, **28**, 224.
- Gonzales Munoz, E. (1966). *Bibliografia Médica Internacional*, **26**, (October 1966).
- Massinger, H., and Lazaridis, S. T. (1968). *Gynaecologia*, **163**, 40.
- Moore, J., Carson, M., and Ball, H. (1970). *Midwives Chronicle and Nursing Notes*, **83**, 12.
- World Health Organization (1969). *Technical Report Series*, No. 407, p. 23.

Mental Deterioration in Epilepsy due to Folate Deficiency

C. NEUBAUER,* M.D.

British Medical Journal, 1970, 2, 759–761

Summary: Folate deficiency in 50 epileptic children aged 5 to 18 years was treated with a combination of folic acid and vitamin B₁₂. Improvement in mental condition occurred from five to eight weeks after beginning treatment in some of the younger children; no change was noticed, however, in 31. Similarly, in 19 children fits became less frequent and less severe. It is recommended that both folic acid and vitamin B₁₂ should be given as soon as a patient is started on anticonvulsant drugs to prevent mental deterioration.

Introduction

Mental deterioration is the most serious aspect of epilepsy. The deterioration is caused by a hereditary mental defect in some cases and by brain damage in others. Anticonvulsant drugs, however, can produce adverse effects on cerebration in any epileptic patient. It is common experience to see patients under treatment becoming slower, their span of attention becoming shorter, and their manual dexterity deteriorating. Even medically untrained people—for example, teachers—notice a change in performance of epileptic children at school.

They find the pupil has poor co-ordination, appears unable to perform many of the tasks which previously he could do well, and is no longer able to take part in school activities.

The side-effects of treatment with anticonvulsant drugs which first attracted the attention of clinicians were anaemia and vitamin B₁₂ deficiency. These complications were investigated in the early 1950s, and reports of folate deficiency in non-anaemic epileptics treated with drugs followed (Hawkins and Meynell, 1958; Malpas, Spray, and Witts, 1966; Reynolds, 1967a). Malpas and his co-workers studied 48 patients receiving anticonvulsant drugs at Chalfont Colony. Of these, 11 had serum folate levels of 2.1 ng./ml. or less, and two low vitamin B₁₂ levels. The vitamin B₁₂ content of the patients' diet was normal. Moreover, it was confirmed that the patients suffering from folate deficiency had no inherent defect of folate metabolism. In five cases epilepsy developed after head injury, while four patients developed macrocytosis and a low folate level during treatment. To prove that the drugs were the cause of the haematological changes they were stopped, and the blood picture then returned to normal. When the drugs were restarted the changes recurred.

In an investigation of the effect of folic acid on the mental state and frequency of fits of epileptics treated with anticonvulsants, improvement in speech, action, alertness, and concentration were found (Reynolds, 1967b). The patients became more sociable and the quality of their work improved. Three

* Consultant, Prudhoe and Monkton Hospital, Northumberland.