ataxia, and began to vomit. She then became semiconscious and on admission to hospital had a grand mal convulsion. Her blood pressure was 300+/185 mm Hg, the pulse rate 110/min, and the fundi showed widespread flame-shaped haemorrhages and cotton-wool spots together with mild papilloedema. The plasma creatinine had increased to 230 μ mol/l (2.6 mg/100 ml). The blood pressure was controlled with intravenous diazoxide and her clinical condition improved dramatically when clonidine by mouth was reintroduced. A 2.5-hour urine collection begun on admission to hospital had a normal vanillylmandelic acid ratio and contained only 1 μ g of urinary catecholamines (normal up to 100 μ g/24 hours).

Discussion

Because a rebound rise in blood pressure may occur if clonidine is stopped suddenly or taken inconsistently the importance of taking the drug regularly must be emphasised to the patient. An alternative drug might be a better choice for patients thought to be unreliable with their medication and for elderly patients. We think that the blood pressure "overshoot" resulting from abrupt clonidine withdrawal in our patient was potentiated by coexisting beta-adrenoreceptor blockade. Clonidine should always be withdrawn slowly, and when the patient is also taking a beta-blocking drug clonidine should be withdrawn even more carefully.

¹ Hunyor, S N, *et al*, *British Medical Journal*, 1973, 2, 209.

² Bailey, R R, *New Zealand Medical Journal*, 1975, 81, 268.

Department of Renal Medicine, Christchurch Hospital, Christchurch, New Zealand

ROSS R BAILEY, MD, FRACP, nephrologist

T J NEALE, BMEDSC, MB, senior renal registrar

Adverse neonatal reaction to maternal administration of intravenous chlormethiazole and diazoxide

Chlormethiazole ethandisulphonate (Heminevrin) was first used to treat alcoholism and delirium tremens. It has sedative and hypnotic actions together with inhibitory effects on the respiratory, thermoregulatory, and vomiting centres. It has no neuromuscular blocking effect. The manufacturers claim that the doses used have no appreciable depressive effect on the fetal respiratory centre. The drug was first used as a 0.8% solution by continuous intravenous infusion to treat severe maternal pre-eclamptic toxæmia.^{1 2} The dose used was variable as the drip rate varied during labour to keep mothers heavily sedated but capable of responding to speech. Only nine out of 50 infants had Apgar scores of less than five at one minute and none less than five at five minutes. There were no untoward side effects. The hypotensive agent used by MacGillivray³ and Varma⁴ was Protervatrine A and B, and, again, there were no untoward effects.

Patients and results

From 5 May 1974 to 5 September 1975 21 live-born infants of 21 mothers with toxæmia of pregnancy were admitted to the neonatal intensive care unit. Nineteen of the mothers had moderate to severe pre-eclamptic toxæmia and two had eclampsia. All had received, during labour, a 0.8% intravenous infusion of chlormethiazole in doses ranging from 500 to 3000 ml (4-24 g). The state of their infants bore no relation to the dose used. Fourteen mothers received, in addition, intravenous boluses of 75 to 150 mg of diazoxide, which were repeated as necessary to control hypertension. All infants whose mothers had been treated with chlormethiazole in this hospital over the 16-month period are included in this report. Other drugs used both before and during labour bore no relation to the state of the infant in the immediate neonatal period. These included methyldopa, barbiturates, reserpine, clonidine, general anaesthesia, and pethidine in varying combinations.

In the immediate neonatal period 13 of the 21 infants suffered hypotonia, hypoventilation, or apnoea. The duration of the hypotonia was fairly constant

(24 to 36 hours) except in cases 3 and 6 (see table). Apnoea requiring intermittent positive pressure ventilation (IPPV) occurred from birth in cases 9, 10, and 11 but not until 2 to 3 hours of age in cases 1 and 4. In retrospect, case 13 should also have been managed on IPPV. Seven infants were atonic from birth. Five of these required IPPV. The remaining two had considerable hypoventilation but their short periods of apnoea were managed by using an Ambu bag. There were three deaths. One was a 900-g infant of 28 weeks gestation who had marked hypotonia. He was well oxygenated but died of the respiratory distress syndrome.

Adverse neonatal reaction to maternal administration of intravenous chlormethiazole and diazoxide

Case No	Sex	Gestation (weeks)	Birth weight (g)	Grade and duration of hypotonia (h)	Apnoea (A) Hypoventilation (H)	Duration of IPPV (h)	Outcome
1	F	38	2380	++ + 30	A	24	Alive
2	F	37	3210	++ + 48	A and H		Alive
3	F	32-34	1170	+ 12	No side effects		Alive
4	M	40	2700	++ + 24	A and H	2½	Alive
5	M	38	3320	+ + 36	A (episodic)		Alive
6	F	33-34	1410	+ 12	No side effects		Alive
7	M	39	3650	+ + 38	A (episodic)		Alive
8	M	38	4270	+ 24	No side effects		Alive
9	M	36	1850	++ + 36	A	36	Alive
10	F	31	1350	++ + 36	A	36	Died
11	M	34-35	1850	++ + 36	A	44	Died
12	M	28-29	900	+ + 11	A		Died
13	M	36	2720	++ + 39	A and H		Alive

+ = Slight to moderate hypotonia. ++ = Severe hypotonia. +++ = Atonic. IPPV = Intermittent positive pressure ventilation.

Two of the five infants treated with IPPV from birth died of severe respiratory distress syndrome. Their hypotonia recovered at 36 hours of age as expected, together with the appearance of spontaneous respirations. Nevertheless, oxygenation could not be maintained by using continuous positive airways pressure and the infants subsequently died while on IPPV. A third infant (case 9) with severe respiratory distress syndrome was successfully managed on IPPV from birth and weaned on to continuous positive airways pressure. The three surviving infants treated with prolonged IPPV appear normal so far (at 16, 9, and 2 months of age). All affected infants apart from one (case 2) came from the group of mothers treated with both chlormethiazole and diazoxide (12 out of 14 mothers so treated). The mother of one (case 2) was treated with 1500 ml (12.0 g) of chlormethiazole, together with massive doses of anticonvulsants because of grand mal secondary to a cerebrovascular anomaly, and was thus possibly not suffering from eclampsia. Adverse reactions were not related to the doses used. For example—one mother (case 6) received 3000 ml (24 g) of chlormethiazole while two others (cases 5 and 7) received only 450-500 ml (3.5-4 g) during labour.

Discussion

Depression in infants of mothers with pre-eclamptic toxæmia who have been treated with intravenous chlormethiazole has not been reported. The hypotensive drugs used in combination, however, are different from those in other series. Milner and Chouksey⁵ have reported that diazoxide alone had no untoward effect on four infants studied. Possibly, therefore, chlormethiazole and diazoxide may act synergistically to produce such severely depressed infants, as both the dose of the drugs and the severity of the maternal pre-eclamptic toxæmia seem unrelated to the severity of this depression. Our experience suggests that when such depression occurs it may be managed successfully with intermittent positive pressure ventilation provided that the respiratory distress syndrome is not also present.

I thank the registrars and sisters of the neonatal intensive care unit who ensured the survival of these babies and Miss K Read for her secretarial help.

¹ Duffus, G M, Tunstall, M, and MacGillivray, I, *Lancet*, 1968, 1, 335.

² Duffus, G M, and MacGillivray, I, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1969, 76, 645.

³ MacGillivray, I, *Lancet*, 1972, 1, 198.

⁴ Varma, T, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1972, 79, 513.

⁵ Milner, R D G, and Chouksey, S K, *Archives of Disease in Childhood*, 1972, 47, 537.

Department of Paediatrics, Christchurch Hospital, Christchurch, New Zealand

ROSEMARY A JOHNSON, MB, FRACP, neonatal paediatrician