Effect of Diazepam Administered to Mothers During Labour on Temperature Regulation of Neonate

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Owen, J. R., Irani, S. F., and Blair, A. W. (1972). *Archives of Disease in Childhood*, 47, 107. **Effect of diazepam administered to mothers during labour on temperature regulation of neonate.** Falls in temperature in the first nine hours after delivery were studied in a group of 12 babies whose mothers had received diazepam in labour, and in 13 comparable babies not exposed to diazepam. A significantly lower mean temperature was found in the test group within the first three hours. Cord blood levels of diazepam did not correlate with either maternal levels at delivery, the extent of the temperature drop, or the condition of the baby at birth, though there was an increased incidence of assisted delivery and resuscitation of the infants in the test group.

Diazepam is proving to be a useful drug in the management of labour, not least because it has a pethidine-sparing effect (Niswander, 1969). It seems likely that it will be used increasingly and that it may be of considerable value to obstetricians dealing with pre-eclampsia or hypertension, because of its tranquillizing effects (Bepko, Lowe, and Waxman, 1965).

It has been shown that diazepam crosses the placenta achieving concentrations in the fetus comparable to, or in excess of, the maternal levels (De Silva, D'Arconte, and Kaplan, 1964; Cavanagh and Condo, 1964). Bepko *et al.* (1965) and Niswander (1969) were unable to show any depressant effect on the Apgar score of babies which could be definitely attributed to diazepam administered to the mother.

The impression was gained at Southmead Hospital that babies born to mothers treated with the drug were liable to sustain a larger temperature drop than babies not so treated, and it was in order to clarify this impression that the following study was undertaken.

Material and Methods

Twelve babies were studied whose mothers had been treated with diazepam because of a rise in blood pressure before or during labour. 13 similar babies whose mothers had not received diazepam were used as controls. Preterm infants were not accepted for the

trial, and 2 infants, both of whom showed a steep initial temperature drop but whose initial rectal temperatures were in excess of 38.5 °C, were excluded. Hypertension was classified as mild, moderate, or severe according to the criteria of Butler and Bonham (1963) for hypertension in pre-eclampsia.

Diazepam was usually administered by continuous intravenous infusion, but was occasionally given by intravenous or intramuscular injection. A variety of other drugs was administered in labour as follows.

Ten mothers in the control group and 3 in the test group received pethidine; 3 mothers in the control group received glutethimide and codeine; and in the same group there was one woman who received sodium amylal, one who received promethazine, and one who received nitrous oxide. Promazine was administered to 3 mothers in the control group and one in the treated group. Apresoline was included in the intravenous regimen of 6 mothers in the test group.

Levels of diazepam were estimated in cord blood and in maternal blood collected within 10 minutes of delivery from 10 of the 12 baby and mother pairs in the treated group. Diazepam was estimated using an adaptation of the method of De Silva, Koechlin, and Bader (1966).

Temperatures were measured with an electric thermometer. Central temperature was measured with a rectal probe at 5, 10, 15, 30, and 45 minutes, and thereafter hourly up to 9 hours. Skin temperatures were measured with surface probes placed in the interscapular area and on the skin of the abdomen. Surface temperatures were only recorded from one hour to eliminate errors arising from surface cooling during physical measurements and other routine procedures shortly after delivery. The babies in both groups were

TABLE I
Comparison of Diazepam-treated and Control Infants

	Maternal Hypertension				Birthweight (g)		Gestation (wk)	Delivery				Resuscitation		Apgar Score <7	
	Nil	Mild	Mod.	Severe	Mean	Range		Normal	Forceps	Other	Caesarean	Routine	Intubated	At 1 min	At 5 min
Treated	—	3	3	6	3080	2440–3520	37–40	1	7	1	3	9	3	4	0
Control	1	6	5	1	3200	2450–3880	37–40	8	4	0	1	13	0	0	0

handled in a routine fashion as regards nursing procedures and transfer out of the labour suite.

Table I compares the two groups in terms of maternal blood pressure, birthweight, gestation, type of delivery, type of resuscitation required, and Apgar scores at 1 and 5 minutes. The degree of hypertension recorded is more severe in the diazepam treated group, in which there is also an excess of assisted deliveries, only one mother delivering normally. 3 babies in the treated group required intubation; one after delivery by caesarean section. No babies in the control group required intubation. Apgar scores reflect the resuscitation requirements and, with one exception, all were more than 8 by 5 minutes.

Results

Mean rectal temperatures and surface temperatures (abdominal and interscapular) in the two groups are shown in the Figure. The temperatures at all sites were found to be lower throughout the 9-hour period in the babies whose mothers had been given diazepam during labour. The differences in rectal temperatures are significant at 1 hour ($P < 0.025$) and at 2 hours ($P < 0.01$). The difference at 3 hours is less significant ($P < 0.05$), and at 4 hours it is not significant.

Abdominal skin temperatures were also significantly lower at 1 hour ($P < 0.001$) and 2 hours ($P < 0.005$), and the same applied to the interscapular temperature at 1 hour ($P < 0.01$) and 2 hours ($P < 0.005$).

The mean difference between abdominal and interscapular skin temperatures in the control group was 0.3°C and in the test group 1.0°C , and the difference between the two groups in this respect is not statistically significant.

The temperature losses in the 6 babies in the test group whose mothers were given apresoline before delivery were similar to the 6 whose mothers received diazepam only. The mean falls in rectal temperature at 1 hour were 2.1 and 2.7°C respectively.

FIG.—Charts of the temperature means in the first 9 hours of life in babies whose mothers had been given diazepam during labour, compared with those babies in the control group. The differences between the two groups at 1 and 2 hours are significant.

Maternal blood levels of diazepam at the time of delivery and in cord blood are shown in Table II, with the resuscitation details and the temperature falls at 1 hour in these cases. Neither level correlates with either fall in temperature or with the resuscitation requirements of the infants.

TABLE II

Levels of Diazepam in Maternal and Cord Blood Shown with Related Fall in Temperature at 1 hour, Apgar Score, and Resuscitation Requirements

Case No.	Diazepam Level ($\mu\text{g/g}$ plasma)		Fall in Temp. at 1 hr ($^{\circ}\text{C}$)	1 Min Apgar Score	Resuscitation
	Mother	Baby			
1	0.62	1.15	2.5	6	Intubated at 4 min
2	0.42	0.17	0.5	3	0
3	0.35	1.23	2.8	4	Intubated immediately
4*	1.22	1.30	3.0	9	0
5*	1.22	0.55	2.5	9	0
6†	0.28	0.29	2.5	9	0
7†	0.28	0.32	3.5	9	0
8	0.48	1.93	0.4	9	0
9	0.91	1.20	1.8	8	0
10	0.32	0.68	2.1	8	0

*Twin pairs.

†Twin pairs.

Discussion

From our results it appears that diazepam given to the mother during labour is associated with an exaggerated fall in temperature in her infant after delivery, but it is not evident what the mechanism of this might be.

Dawkins and Hull (1964) showed that hypoxia interfered with thermogenesis in brown adipose tissue. In the present small series, no significant differences in temperature in the interscapular area between the test and control groups were noted, but recent thermographic studies have shown that the behaviour of surface temperatures over the nape and interscapular areas are in any case only erratically related to cooling (Rylander, Pribylova, and Lind, 1971).

Burnard and Cross (1958) demonstrated lower temperatures in infants who suffered asphyxial incidents at birth. It can be seen from Table I that there is a higher incidence of severe hypertension among the mothers in the treated group and a higher incidence of instrumental delivery. 4 infants in the test group had 1-minute Apgar scores of less than 7, and 3 of these required major resuscitation. However, the lower temperatures were not confined to these infants; and with one exception the 5-minute Apgar scores in both groups were all 8 or more. Nevertheless, the hypothermic effect

noted by Burnard and Cross (1958) was associated with clinically trivial asphyxia, and we cannot rule this out as the mechanism by which diazepam produces a hypothermic effect.

Burnard and Cross (1958) showed that pethidine given to parturient mothers could cause lower temperatures in the infants even when no asphyxia had occurred. The fact that more mothers in the control group received pethidine (77% compared with 25% of mothers in the test group) indicates that the hypothermic effect associated with diazepam was not mediated by pethidine; and incidentally supports the contention of Niswander (1969) that diazepam can have a pethidine-sparing effect in labour.

It is also possible that the temperature lowering effect is a direct effect of diazepam on the central regulation of temperature; or it might be mediated by a depression of muscle activity. Polygraphic observation of a 5-month infant given 3 mg diazepam intravenously for refractory salaam spasms showed not only control of the spasms but also a dramatic depression in the incidence and amount of normal skeletal muscle activity lasting several hours (A. W. Blair and K. Theorell, unpublished data).

Although not the primary object of the study, it is interesting that the cord blood levels of diazepam are generally higher than the maternal levels. This is in agreement with the findings of previous workers (Cavanagh and Condo, 1964; De Silva *et al.*, 1964) and suggests that the drug is eliminated more slowly by the fetus. This could be of clinical importance when the drug is used during labour, especially when the infant is likely to be immature. No relation appears to exist between cord blood diazepam levels and neonatal temperature loss, but it would have been more meaningful to measure the rate of disappearance of the drug by means of serial measurements. This was not done, as a micromethod for the estimation of diazepam was not available, though this now exists (S. Agurell and A. Berlin, unpublished data).

It has previously been stated that diazepam administered during labour has no deleterious effects on the baby (Cavanagh and Condo, 1964; Bepko *et al.*, 1965; Niswander, 1969), but our findings are not entirely in agreement with this. Nonetheless, it seems that the drug is a useful one to the obstetrician. In our small series the magnitude of the temperature difference between the two groups was such that in term infants it would not pose an insuperable problem to the clinician. But diazepam is often used in pre-eclampsia (Lean, Ratnam, and Sivasambo, 1968; Gorbach, 1968) when the baby is more likely to be

light-for-dates and/or preterm. Provided the clinician is aware of the possibility of such a hypothermic effect, however mediated, it should be possible to mitigate the temperature fall: for instance by reducing to a minimum exposure for physical measurements and cord dressing, and by taking steps to keep the baby warm in the labour suite, where temperatures are often more suited to the adult inmates than the newborn ones.

We are grateful to Dr. Beryl D. Corner and Dr. P. M. Dunn for allowing us access to babies under their care, to Dr. D. M. Hailey of the Roche Research Unit, University of Liverpool, for performing the diazepam estimations, and to the sisters and nursing staff of the obstetric and paediatric department of Southmead Hospital.

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