Effects of Propanidid and Thiopentone on the Acid-Base Status of Babies Delivered by Elective Caesarean Section

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SUMMARY

The effects of propanidid and thiopentone on the acid-base status of babies delivered by elective Caesarean section have been compared. The only significant difference between the 2 groups was the lower umbilical cord venous blood pCO_2 levels in the propanidid group. The acid-base status in both these groups of babies was not as good as in those delivered after induction-delivery times of less than 6 minutes when thiopentone had been used as the induction agent.

The clinical state of the babies in the propanidid group was superior to that in the thiopentone group, and at least equal to that of the group with the short induction-delivery interval.

S. Afr. Med. J., **48**, 1019 (1974).

In a previous publication[1] we showed that babies delivered by elective Caesarean section after prolonged anaesthesia were more acidaemic than those delivered after an induction-delivery interval of less than 6 minutes. Since then we have shown that the elevation of maternal pO_2 at the time of delivery has had a mild but not marked effect on the acid-base and clinical state of the baby. Although there was less neonatal acidaemia in these cases the acid-base status of the babies was not as good as in those babies delivered after a short period of anaesthesia.

This article is a further attempt to find a method of anaesthesia which, despite a prolonged induction-delivery interval, will give results that are as good as those we have found with a very short induction-delivery interval.

Baraka *et al.*[2] have shown the beneficial effects of propanidid on the clinical state of the neonate, and Bradford and Moir[3] have suggested that propanidid is no worse and may even be superior to thiopentone in regard to the condition of the neonate after Caesarean section. Söder[4] considers propanidid to be the drug of choice for obstetrical anaesthesia; but Kölliker[5] did not find any significant advantage over thiopentone, as far as the condition of the neonate was concerned. All these authors judged their results on the clinical state of the babies at delivery, and to our knowledge no-one has compared the effect on the acid-base status of babies delivered at elective Caesarean section in which the two drugs were used. Downing and Coleman[6] recently made a plea for more detailed studies of propanidid in elective Caesarean section, including an analysis of maternal and fetal blood gas and acid-base status.

METHODS

The series consisted of 27 patients undergoing elective Caesarean section. They were divided into 3 groups:

1. The 'fast' group (delivery within 6 minutes of induction of anaesthesia—9 babies).

2. The 'slow' group (delivery between 16 and 42 minutes from induction—9 babies).

3. A 'propanidid' group (delivery between 16 and 36 minutes from induction in 7 cases and in 2 only 10 and 11 minutes—9 babies).

The method of anaesthesia for the propanidid group was identical with that of the slow group in all respects except that propanidid was used to induce anaesthesia in preference to thiopentone—the technique of anaesthesia is fully described in an earlier paper.[1] The usual dose of thiopentone varied between 200 and 250 mg, but 300 mg was given in one case. The dose of propanidid varied between 300 and 500 mg.

The indications for Caesarean section and the ages and parity of the patients were fully comparable in the 3 groups. Of the 27 patients, 12 fell into the class defined by Crawford[7] as group A. Of these, 3 were in the fast, 4 in the slow and 5 in the propanidid groups. All but 4 of the babies weighed more than 3 kg. In the slow group 3 babies weighed between 2,85 and 2,95 kg and 1 in the propanidid group weighed 2,38 kg at 38 weeks' gestation, and were therefore light-for-dates (under the 10th percentile of birthweight for gestation as defined[8]). The surgical technique was virtually identical in all cases.

The blood samples were taken from the hyperaemic maternal finger-tip at the time of delivery and from a loop of cord clamped immediately after delivery. The

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Date received: 7 January 1974.

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samples were obtained and examined in the manner described previously.[1]

The resident paediatric medical officer examined each baby at delivery and made a completely independent assessment of the Apgar scores at 1 and 5 minutes after delivery. The 2 points usually allocated for the colour of the baby have been omitted and the scores stated are out of a total of 8 points (Apgar minus colour).

RESULTS

The measurements (means and standard deviations) obtained from the maternal capillary blood and the cord arterial and venous blood in the fast and slow and propanidid groups are shown in Table I. The statistical significance of the differences between the means of the results in the different groups using an analysis of variance technique is shown in Tables II, III and IV. Table V shows the coefficients of linear correlation between the individual results and the induction-delivery times for all cases in the series.

pH Value

The mean maternal capillary blood pH at the time of delivery in the propanidid group was 7,47 and this does not differ significantly from that of either the fast or slow groups. The mean cord arterial pH in the propanidid group

TABLE I. MEAN VALUES OF MATERNAL CAPILLARY BLOOD AT DELIVERY, CORD ARTERIAL AND CORD VENOUS BLOOD IN THE FAST, SLOW AND PROPANIDID GROUPS
(THE STANDARD DEVIATIONS ARE SHOWN IN BRACKETS UNDERNEATH)

		pH (units)	pCO_2 (mmHg)	Base excess (mEq/L)	Standard bicarbonate (mEq/L)	pO_2 (mmHg)	Oxygen saturation (%)
Fast group	Maternal capillary blood	7,46	21,9	−6,4	19,6	100,6	95,9
		(0,07)	(5,6)	(2,9)	(2,1)	(41,7)	(3,8)
	Umbilical cord arterial blood	7,33	38,0	−5,6	20,1	21,9	49,9
		(0,03)	(7,0)	(2,1)	(1,7)	(8,6)	(22,2)
	Umbilical cord venous blood	7,33	38,4	−5,7	20,0	29,7	62,4
		(0,06)	(5,8)	(1,7)	(1,3)	(9,5)	(15,6)
Slow group	Maternal capillary blood	7,41	27,6	−6,2	19,7	67,2	87,1
		(0,09)	(6,6)	(2,0)	(1,5)	(20,6)	(19,9)
	Umbilical cord arterial blood	7,22	52,2	−7,5	18,8	16,2	31,8
		(0,07)	(10,9)	(4,7)	(3,3)	(13,1)	(20,8)
	Umbilical cord venous blood	7,25	50,3	−6,7	19,4	22,1	43,4
		(0,06)	(10,0)	(3,3)	(2,4)	(9,3)	(18,8)
Propanidid group	Maternal capillary blood	7,47	20,7	−7,3	19,1	72,9	91,1
		(0,10)	(8,6)	(3,6)	(2,6)	(25,1)	(11,0)
	Umbilical cord arterial blood	7,26	48,7	−5,9	20,1	13,2	27,1
		(0,09)	(7,0)	(4,9)	(3,5)	(5,0)	(12,0)
	Umbilical cord venous blood	7,30	42,4	−5,8	20,1	19,9	41,6
		(0,24)	(7,2)	(4,2)	(3,0)	(4,7)	(16,9)

TABLE II. STATISTICAL SIGNIFICANCE OF THE DIFFERENCES BETWEEN THE MEANS OF THE RESULTS IN THE SLOW AND PROPANIDID GROUPS

	pH	pCO_2	Base excess	Standard bicarbonate	pO_2	Oxygen saturation
Maternal capillary blood at delivery	NS	NS	NS	NS	NS	NS
Umbilical cord arterial blood	NS	NS	NS	NS	NS	NS
Umbilical cord venous blood	NS	<0,05	NS	NS	NS	NS

TABLE III. STATISTICAL SIGNIFICANCE OF THE DIFFERENCES BETWEEN THE MEANS OF THE RESULTS IN THE FAST AND PROPANIDID GROUPS

	pH	pCO_2	Base excess	Standard bicarbonate	pO_2	Oxygen saturation
Maternal capillary blood at delivery	NS	NS	NS	NS	NS	NS
Umbilical cord arterial blood	<0,01	<0,01	NS	NS	NS	<0,01
Umbilical cord venous blood	NS	NS	NS	NS	<0,01	<0,01

TABLE IV. STATISTICAL SIGNIFICANCE OF THE DIFFERENCES BETWEEN THE MEANS OF THE RESULTS IN THE SLOW AND FAST GROUPS

	pH	pCO_2	Base excess	Standard bicarbonate	pO_2	Oxygen saturation
Maternal capillary blood at delivery	**NS**	**NS**	**NS**	**NS**	**NS**	**NS**
Umbilical cord arterial blood	**<0,01**	**<0,01**	**NS**	**NS**	**NS**	**<0,05**
Umbilical cord venous blood	**NS**	**<0,01**	**NS**	**NS**	**NS**	**<0,05**

of 7,26 (if the light-for-dates baby is omitted the mean becomes 7,28) is higher than the mean of the slow group (7,22), but this difference is not statistically significant. The mean of the fast group is significantly higher than that of the slow and the propanidid groups (both $P<0,01$). The mean cord venous pH is highest in the fast group (7,33) and lowest in the slow group (7,25), but the difference between the means of the different groups is not significant.

Partial Pressure of Carbon Dioxide

The mean maternal capillary blood pCO_2 was lower in the fast and propanidid groups but these means were not significantly different from the mean of the slow group. The mean cord arterial pCO_2 of the fast group was significantly less ($P<0,01$) than the slow and propanidid groups, but the differences between the means of the slow and propanidid groups were not significant. The mean cord venous pCO_2 was lower in the fast group than in the other 2 groups and the difference between the means of the slow and fast groups and the slow and propanidid groups is significant ($P<0,01$ and $P<0,05$, respectively). The difference between the means of the fast and propanidid groups is not significant.

Base Excess and Standard Bicarbonate

The differences between the mean maternal and cord base excess and standard bicarbonate values in the 3 groups are not statistically significant.

Partial Pressure of Oxygen

The mean maternal and cord pO_2 levels were higher in the fast group than in the other 2 groups, but the only statistically significant difference between the means of the different groups was that where the cord venous pO_2 of the propanidid group was significantly less than that of the fast group ($P<0,01$).

Oxygen Saturation

There is no statistically significant difference between the mean maternal capillary blood oxygen saturation levels of the 3 groups. The mean cord arterial oxygen saturation was higher in the fast group than in the other 2 groups and it was lowest in the propanidid group. The difference between the mean of the fast group and those of the slow and propanidid groups is significant ($P<0,05$ and $P<0,01$, respectively), but again there is no significant difference between the mean of the slow group and that of the propanidid group. Similarly, the mean cord venous oxygen saturation was highest in the fast group and lowest in the propanidid group. The difference between the mean cord venous oxygen saturation levels of the slow and propanidid groups is again not significant but the mean of the fast group is significantly higher than that of the slow group ($P<0,05$) and that of the propanidid group ($P<0,01$).

Table V shows that the induction-delivery times for all cases correlate with the cord arterial and venous pH ($r = -0,85$ and $-0,65$), pCO_2 ($r = +0,65$ and $+0,50$) and to a lesser extent with the base excess ($r = +0,41$ and $-0,40$) and standard bicarbonate ($r = -0,40$ and $-0,31$). The maternal pCO_2 correlated with the induction-delivery time ($r = +0,43$) but the pO_2 and the oxygen saturation did not.

The Apgar minus colour scores were equally favourable in the fast and propanidid groups and in both of these groups they were superior to those of the slow group. At 5 minutes all 9 babies in the propanidid group had scores of 8. All babies in the series were alive and well at late review.

Bleeding

Only 1 case in the series required a blood transfusion and this patient was given 2 units of blood.

TABLE V. COEFFICIENTS OF LINEAR CORRELATION BETWEEN THE INDIVIDUAL RESULTS AND THE INDUCTION-DELIVERY TIMES FOR ALL CASES

	pH	pCO_2	Base excess	Standard bicarbonate	pO_2	Oxygen saturation
Maternal capillary blood	**−0,32**	**+0,43**	**−0,06**	**+0,04**	**−0,36**	**−0,17**
Umbilical cord arterial blood	**−0,85**	**+0,65**	**+0,41**	**−0,40**	**−0,11**	**−0,29**
Umbilical cord venous blood	**−0,65**	**+0,50**	**+0,35**	**−0,31**	**−0,14**	**−0,24**

DISCUSSION

Others[2,3] have shown that propanidid used to induce anaesthesia at elective Caesarean section results in the delivery of babies in better clinical condition than in those cases where anaesthesia was induced with sodium thiopentone. The present series was designed to compare the effect of these drugs on the acid-base status of babies delivered by elective Caesarean section.

The only statistically significant difference in the cord blood values between the slow and propanidid groups was that the cord venous pCO_2 was lower in the latter group. Although the mean cord arterial pCO_2 in the propanidid group was less than that of the slow group, the difference was not statistically significant. The lowered cord venous pCO_2 may be explained by the fact that propanidid causes the mother to hyperventilate initially and so reduce her pCO_2 level. This did in fact happen in this series, the mean maternal pCO_2 in the propanidid group being lower even than that of the fast group. Although the difference between the mean maternal pCO_2 of the slow and propanidid groups is not significant, it is this difference which probably resulted in the significantly lower mean pCO_2 values in the cord venous blood of the propanidid group compared with that of the slow group. There are no other statistically significant differences between the different acid-base values of the slow and propanidid groups, although it will be noted that, while not statistically significant, the mean cord arterial and venous pO_2 and oxygen saturation levels are even lower in the propanidid group than in the slow group.

The babies in the propanidid group did not achieve the good acid-base status of those in the fast group. The cord arterial pH was significantly higher ($P<0,01$), the pCO_2 was significantly lower ($P<0,01$) and the cord arterial oxygen saturation was significantly higher ($P<0,01$) in the fast group than in the propanidid group. The cord venous pO_2 and oxygen saturation were also significantly higher ($P<0,01$ and $P<0,01$) in the fast group than in the propanidid group.

Although the babies in the propanidid group did not have as good acid-base status or oxygen levels as those in the fast group, their clinical state, as judged by Apgar minus colour scores, was equal if not superior to that of the fast group. Baraka[2] explains the better clinical state of the baby when propanidid has been used by the fact that the drug itself is rapidly hydrolysed by esterases in the body to form pharmacologically inert products. Both maternal and fetal blood levels of propanidid are negligible within 3 - 4 minutes of intravenous injection to the mother.[9] Cholinesterase is also present in large quantities in placental tissues and could play a part in the breakdown of propanidid, thus minimising the concentration of propanidid reaching the fetus.[10]

Unlike propanidid, thiopentone undergoes metabolic degradation in the liver very slowly. It is known to cross the placental barrier within 45 seconds of intravenous administration to the mother and to attain a maximum concentration in the fetus after 2 - 3 minutes. Baraka considers that when thiopentone is used as an induction agent for nitrous oxide anaesthesia, the latent depressant effect becomes manifest particularly if the induction-delivery time is prolonged. Marx *et al.*[11] have shown that the umbilical artery-vein nitrous oxide concentration ratio which parallels the fetal uptake of nitrous oxide increases progressively with increasing duration of anaesthesia. As the induction-delivery time is prolonged, the brain concentration of nitrous oxide is built up and might summate with the residual effect of thiopentone, resulting in a high incidence of neonatal depression.

This series also confirms our earlier work[1] and shows that the acid-base and clinical state of the neonate delivered by elective Caesarean section deteriorate with the prolongation of the induction-delivery time.

CONCLUSION

Propanidid, used as an induction agent for anaesthesia for Caesarean section, is probably preferable to thiopentone. Although it produces very little improvement in the acid-base status of the babies delivered, the clinical state was markedly better than that in the thiopentone group when the induction-delivery time was prolonged.

The beneficial effect of propanidid may be due to rapid hydrolysis; initial maternal hyperventilation; or the lesser toxic effects than thiopentone has on the central nervous system of the neonate.

We wish to thank Messrs W. S. Crawford and C. W. Mortimer for allowing us to include their patients, Dr W. Castle and Miss I. A. Edmonstone for statistical help, and the Birmingham Regional Hospital Board for financial assistance.

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