Anesthesiology
71:827–834, 1989

Intravenous Propofol during Cesarean Section: Placental Transfer, Concentrations in Breast Milk, and Neonatal Effects. A Preliminary Study

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Placental transfer and neonatal effects of propofol were investigated in 21 women undergoing elective cesarean section under general anesthesia. This study was conducted in two separate phases according to the use of propofol. In both phases, anesthesia was induced with an iv bolus of 2.5 mg/kg of propofol. In phase 1 (n = 10), anesthesia was maintained with 50% nitrous oxide in oxygen and halothane. In phase 2 (n = 11), a continuous infusion of propofol at a rate of 5 $mg \cdot kg^{-1} \cdot h^{-1}$ was started after the induction dose. Maternal venous and umbilical cord arterial and venous samples were obtained at delivery. The propofol concentration in whole blood was measured with a high performance liquid chromatography method. Where possible, breast milk/colostrum was expressed for both phases postoperatively and a sample of blood was collected during phase 2 from neonates *via* a heel prick 2 h after birth. Propofol crossed the placenta, as demonstrated by concentrations found in umbilical venous blood in phase 1 (0.13–0.75 μg/ml) and in phase 2 (0.78–1.37 μg/ml). At delivery, the ratio of the drug concentration in umbilical venous blood to that in maternal blood was 0.70 ± 0.06 for phase 1 and 0.76 ± 0.10 for phase 2. The ratio of propofol concentration in the umbilical artery to that in the umbilical vein was 1.09 ± 0.04 for phase 1 and 0.70 ± 0.05 for phase 2. The mean propofol concentration in samples taken *via* a heel prick 2 h after birth in 8 neonates during phase 2 was low (0.078 ± 0.011 μg/ml) and represented about 10% of the corresponding umbilical cord artery concentration at time of delivery. The very limited milk/colostrum data indicated that propofol concentrations were low (phase 1: 0.089–0.24 μg/ml; phase 2: 0.04–0.74 μg/ml). Furthermore, propofol is cleared rapidly from the neonatal circulation and exposure of the neonate through breast milk/colostrum would be negligible compared to the placental transfer of the drug. In both phases, propofol seemed to have minimal effects on the healthy newborns. These results justify the performance of additional studies of propofol administration during general anesthesia for cesarean section, especially to compare propofol with thiopental and to evaluate the effect of this drug on the high risk fetus. (Key words: Anesthesia: obstetrics. Anesthetics, intravenous: propofol. Anesthetic technique: continuous infusion. Colostrum. Placenta: placental transfer.)

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Received from the Département d'Anesthésie et de Réanimation Chirurgicale, Groupe Hospitalier Cochin-Maternités, Université Paris V, Paris, France; ICI Pharmaceuticals, Cheshire, United Kingdom; ICI Pharma, "Le Galien", Cergy, France. Accepted for publication July 7, 1989. Presented in part at the annual meeting of the American Society of Anesthesiologists, Atlanta, Georgia, October 1987.

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PROPOFOL, 2,6 diisopropylphenol, (Diprivan®) formulated as an emulsion in soy bean oil, was first used in 1983 and shown to be safe and effective for induction of anesthesia when injected intravenously.[1,2] In 95% of the patients given 2.5 mg/kg propofol, induction is rapid and smooth and is followed by a rapid recovery with a low incidence of postoperative side effects.[3–7] Its duration of action is short, related to its rapid metabolism to inactive conjugates.[8] Its pharmacokinetic profile has been well described and makes propofol also suitable for maintenance of anesthesia by continuous iv administration.[9–13] All these characteristics suggest that propofol may prove to be a useful agent in obstetric anesthetic practice. Although light general anesthesia in obstetric procedures is desirable for the fetus, it may be associated with maternal awareness during surgery. If iv anesthetics are used only as induction agents, awareness can be avoided by the use of volatile anesthetic agents.[14] Total iv techniques using propanidid, ketamine, and althesin have also been reported.[15–17]

Obstetric surgery is a specialized field in which both the acute effects of the anesthetic agent on the fetus and the efficiency of fetal metabolism must be considered. The major route of elimination of propofol in the adult is by glucuronidation,[8] but glucuronyl transferase processes in the neonate may not be fully developed at delivery. Early breast feeding is gaining popularity and it is therefore important to ascertain whether propofol passes into human milk and whether propofol concentrations may be regarded as safe for the nursing infant. This open, noncomparative study was therefore designed to investigate the placental transfer of propofol, the transfer of propofol into breast milk/colostrum, and the neonatal assessments when propofol was used either for induction of anesthesia or for induction and maintenance of anesthesia during elective cesarean section.

Materials and Methods

The design of the protocol was approved by the hospital ethics committee and informed consent was obtained from each participant. Twenty-one ASA physical status 1 women about to undergo elective cesarean section under general anesthesia at between 37–40 weeks gestation were studied. They were taking no medications other than iron and folate supplements. Indications for cesarean section were previous cesarean section, breech, or transverse

presentation and predicted cephalopelvic disproportion. Patients demonstrating evidence of fetal distress were excluded from study.

Anesthetic Procedures

This protocol was conducted in two separate noncomparative open phases according to the use of propofol. Phase 1 was designed to investigate propofol as an induction agent after a single bolus iv dose. Phase 2 was designed to assess propofol for induction and maintenance of anesthesia.

In both phases of the study, patients received 30 ml of 0.3 M sodium citrate given orally 20–30 min prior to induction of anesthesia and an iv injection of 0.5 mg atropine, 10 min before induction. An iv infusion of lactated Ringer's solution was started *via* a 16-G cannula in the antecubital fossa. All patients were placed supine, a left side lateral tilt was ensured to avoid aortocaval compression by the gravid uterus. Oxygen at a flow rate of 8 l/min was breathed until induction of anesthesia. Vecuronium bromide (0.015 mg/kg; based on nonpregnant body weight [NPBW]) was given immediately prior to induction. General anesthesia was induced with 2.5 mg/kg (NPBW) propofol injected intravenously over a period of approximately 20 s. Cricoid pressure was applied as consciousness was lost and vecuronium bromide (0.08 mg/kg NPBW) was given. When paralysis was adequate, laryngoscopy and tracheal intubation were performed. After confirmation of the correct placement of the tracheal tube, the cuff was inflated and cricoid pressure released.

Phase 1. Anesthesia was maintained with 50% nitrous oxide in oxygen and 0.25–0.5% halothane.

Phase 2. Anesthesia was maintained with 50% nitrous oxide in oxygen together with a continuous infusion of propofol at a rate of 5.0 $mg \cdot kg^{-1} \cdot h^{-1}$ NPBW started after the induction dose. The rate of infusion was adjusted thereafter according to clinical signs of the depth of anesthesia.

In both phases, the administration of all anesthetic agents was stopped between uterine incision and delivery of the baby, and the lungs were ventilated with 100% oxygen. After clamping the umbilical cord, fentanyl (0.10–0.15 mg) and oxytocin were given and anesthesia continued according to phase 1 or 2.

The intervals from induction of anesthesia to delivery (I–D), and uterine incision to delivery (U–D) were recorded.

Blood and Breast Milk/Colostrum Analysis

In all patients, a venous blood sample was obtained *via* a 16-G cannula that had been inserted into a large vein in the contralateral antecubital fossa. The catheter was kept free flowing and flushed with heparinized saline, as required. Approximately 5 ml of blood was collected from the mother at the time of umbilical cord clamping for analysis of propofol levels. Umbilical cord artery and vein samples (1.25–3 ml) were taken simultaneously from a doubly clamped segment of umbilical cord to assess the degree of placental transfer. Blood samples were collected in tubes containing potassium oxalate and, after thorough mixing, were stored at 4° C prior to analysis by the method described by Plummer.[18] The limit of sensitivity of the assay was approximately 2 ng/ml and the coefficient of variation over the concentration range measured was approximately 8%. A sample of blood was also collected in phase 2 from each neonate *via* a heelprick immediately after the 120-min neurobehavioral assessment.

Breast milk/colostrum was expressed 4 h and 8 h postoperatively. At each time, as much milk/colostrum as was available was collected and shaken. Aliquots of up to 5 ml were taken from each sample for analysis of propofol levels. The milk was stored at −20° C until analysis. The propofol content of milk samples was measured by the procedure described for propofol in blood but with a modified solvent for reconstituting the cyclohexane extract residues prior to analysis by HPLC (HPLC eluent: methanol 3:2 v/v).

Neonatal Assessment

At time of delivery, blood samples were taken from maternal artery, umbilical vein, and artery for acid base and blood gas status. The condition of the infant was evaluated using Apgar score at 1, 5, and 10 min; time to sustained spontaneous respiration (TSR) was recorded, and the Neurologic and Adaptative Capacity Score (NACS)[19] was assessed at 30 min, 2 h, and 24 h after birth. The Apgar score gives a maximum total score of 10; an infant scoring 7 or greater was considered vigorous. The NACS gives a maximum score of 40. Choosing 35–40 as the score denoting a vigorous baby, the percentage of infants scoring 35 or higher was determined. Apgar scores and NACS were obtained by an investigator who did not know which anesthetic drug had been administered.

Correlations between variables were investigated by linear or log-linar regression analysis. $P < 0.05$ was considered statistically significant.

Results

Data on maternal weight, height, parity, and infant gestational age and weight are summarized in table 1. The intraoperative anesthetic requirements and time characteristics are presented in table 2. The incidence of maternal awareness was 40% in phase 1 and 9% in phase 2.

TABLE 1. Patient Data

	Phase 1 (n = 10)	Phase 2 (n = 11)
Age (yr)	31.6 (4.3)	32.1 (4.7)
Weight* (kg)	61.3 (9.7)	59.6 (11.1)
Height (cm)	161.9 (6.9)	161.1 (6.75)
Parity		
Nulliparous	2	3
Multiparous	8	8
Gestational age (weeks)	39.0 (0.3)	38.7 (0.92)
Infant weight (g)	3342 (97)	3298 (147.9)

Values are mean SD.
* Nonpregnant body weight.

PLACENTAL TRANSFER OF PROPOFOL

Individual propofol concentration data for both maternal and umbilical samples are shown in table 3 (phase 1) and table 4 (phase 2). With the exception of the umbilical samples from neonates 1 and 6 (phase 1) and neonates 8 and 9 (phase 2), propofol concentrations in umbilical blood samples were lower than those in the corresponding maternal samples. In phase 1, there was an apparent decreasing trend in propofol blood concentration with increased postinduction time for both maternal and umbilical samples (fig. 1). There were also significant correlations between umbilical venous (UV) and maternal venous (MV) propofol levels at delivery for both phases (fig. 2); between umbilical artery (UA) and MV at delivery ($r = 0.72$, $P < 0.01$) and between UV and UA at delivery ($r = 0.97$, $P < 0.001$) only for phase 1. The umbilical-vein-to-maternal-vein ratio (UV/MV) at the time of delivery was 70% and 76% for phase 1 and phase 2, respectively. The ratio of drug concentration in umbilical arterial blood to that in umbilical venous blood (UA/UV) was 109% and 70% for phase 1 and phase 2, respectively.

TABLE 2. Operative Characteristics

	Phase 1 (n = 10)	Phase 2 (n = 11)
Induction dose (mg/kg)	2.55 (.04)	2.51 (.02)
Total induction dose (mg)	155.5 (6.82)	149.5 (8.15)
Infusion dose ($mg \cdot kg^{-1} \cdot h^{-1}$)	NA	5.08 (.07)
Total propofol to delivery (mg)	155.5 (6.82)	247.4 (20.1)
I–D (min)	25.9 (3.42)	20.2 (1.86)
range	13–45	7–31
U–D (s)	136.8 (24.8)	114.5 (15.8)
range	60–240	60–180

Values are mean SEM.
I–D = Induction to Delivery interval. U–D = Uterine incision to Delivery interval.

TABLE 3. Propofol Concentrations at Delivery: Phase 1, μg/ml

Patient	MV	UV	UA	UV/MV	UA/UV
1	0.38	0.40	0.35	1.05	0.88
2	0.58	0.43	0.43	0.74	1.00
3	1.09	0.48	0.50	0.44	1.04
4	0.61	0.44	0.48	0.72	1.09
5	0.49	0.32	0.32	0.65	1.00
6	0.86	0.75	0.91	0.87	1.21
7	0.25	0.13	0.16	0.52	1.23
8	0.53	0.36	0.44	0.68	1.22
9	0.42	0.33	0.39	0.79	1.18
10	0.41	0.23	0.25	0.56	1.09
Mean	0.56 (.08)	0.39 (.05)	0.42 (.06)	0.70 (.06)	1.09 (.04)

Values are mean SEM.
MV = Maternal Vein. UV = Umbilical Vein. UA = Umbilical Artery.

Both ratios did not vary with time within the duration of the study.

In phase 2, the propofol concentration in the samples, taken *via* a heel prick in eight of the neonates 2 h after delivery, was low (table 4). This represented about 10% of the corresponding UA concentration at time of delivery.

BREAST MILK/COLOSTRUM PROPOFOL CONCENTRATION

It was not possible to collect milk/colostrum samples from all patients. Individual milk/colostrum sample data are presented in table 5. The volume of milk/colostrum produced at each sampling time were very small (range: phase 1 = 0.21–8 ml; phase 2 = 0.2–3.8 ml) and propofol concentrations in these samples were low (phase 1: 0.089–

TABLE 4. Maternal and Neonatal Blood Propofol Concentrations: Phase 2, μg/ml

Patient	MV	UV	UA	UV/MV	UA/UV	NHP
1	2.10	1.28	0.96	0.61	0.75	0.075
2	2.26	1.28	0.85	0.57	0.66	NS
3	2.22	1.37	0.91	0.62	0.66	NS
4	1.82	1.08	0.87	0.59	0.80	0.073
5	1.97	1.25	0.60	0.63	0.48	0.059
6	2.11	1.19	0.50	0.56	0.42	0.029
7	1.12	0.78	0.72	0.70	0.92	0.086
8	0.81	1.07	0.61	1.32	0.57	NS
9	0.85	1.26	0.96	1.48	0.76	0.14
10	1.35	0.99	0.87	0.73	0.88	0.075
11	1.64	0.98	0.78	0.60	0.80	0.088
Mean	1.66 (.16)	1.14 (.05)	0.78 (.05)	0.76 (.10)	0.70 (.05)	0.078 (0.011)

Values are mean SEM.
MV = Maternal Vein. UV = Umbilical Vein. UA = Umbilical Artery at delivery. NHP = Neonatal Heel Prick blood propofol concentration at 2 h after birth. NS = No Sample taken.

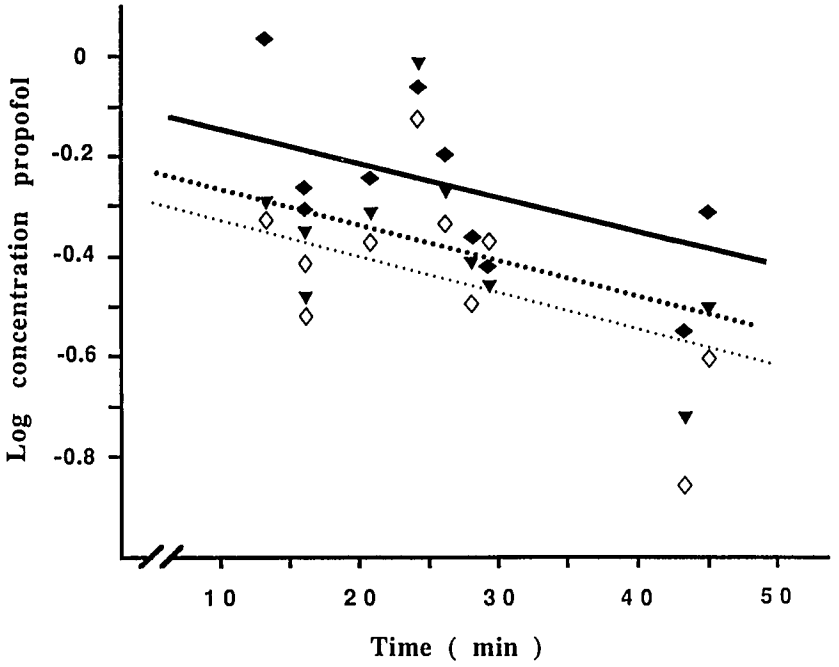

FIG. 1. Log propofol concentrations at delivery (μg/ml) *versus* I–D time during general anesthesia for cesarean section after a single iv induction dose of 2.5 mg/kg (phase 1). —— MV: r = −0.70, $P < 0.025$; ••• UV: r = −0.67, $P < 0.05$; · · · · · UA: r = −0.64, $P < 0.05$.

0.24 μg/ml; phase 2: 0.04–0.74 μg/ml). The second milk/colostrum sample taken at 24 h postdelivery from patient 1 in phase 2, contained only about 6% of the concentration in the 4-h sample.

NEONATAL ASSESSMENTS

Data on immediate cry, time to sustained spontaneous respiration, and Apgar scores in both phases are presented in table 6. In phase 1, an initial Apgar score of 7 was attained by eight neonates. This score had improved at 5 min in all but one case, which was attributed to delays in clearing fluids from the respiratory tract. In phase 2, one neonate had an initial score of 5 and was reported to be sleepy immediately after delivery, but achieved a score of 10 at 5 min. In both phases, all neonates achieved a maximum score when assessed 10 min after delivery. There was no correlation between the 1-min and 5-min Apgar scores and the UV and UA propofol levels, I–D and U–D of either phase 1 or phase 2.

Maternal and neonatal blood gas tensions and acid-base status at delivery were within the normal clinical limits in both phases (table 7). No relationship was found between the neonatal propofol levels and umbilical cord acid-base status.

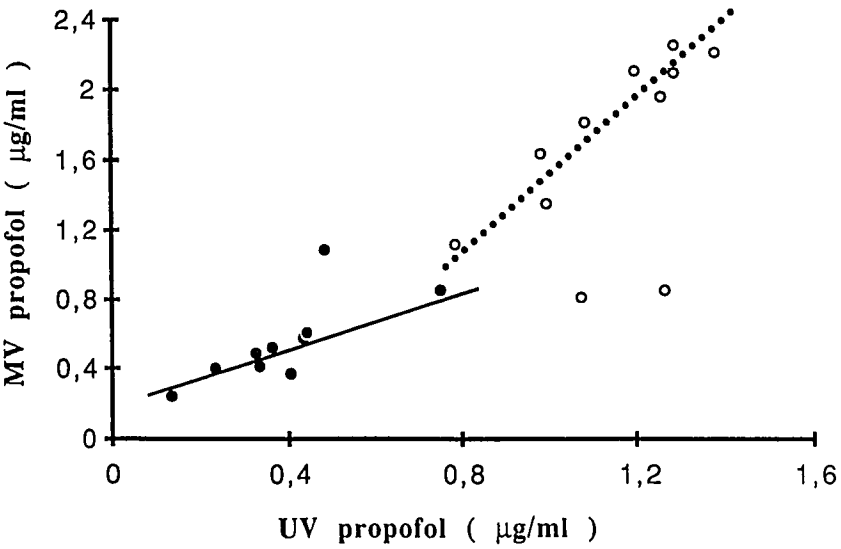

FIG. 2. The plot of propofol levels in maternal venous blood (MV) against propofol levels in umbilical cord venous (UV) in μg/ml in both phases. ●●● Phase 1: r = 0.75, $P < 0.01$; ○○○ Phase 2: r = 0.55, $P < 0.05$.

TABLE 5. Propofol Concentration in Milk/Colostrum Samples (μg/ml)

	Time of sampling		
	4 h	8 h	
Phase I			
Patient number			
2	0.14	0.089	
8	0.14	0.11	
9	0.24	0.19	
10	NS	0.16	
	4 h	6 h	24 h
Phase II			
Patient number			
1	0.74 (5 h)	NS	0.048
4	0.33	NS	NS
5	NS	0.036	NS

NS: No sample taken.

TABLE 7. Blood Gas Tension and Acid Base Values at Delivery

	Phase 1	Phase 2
Maternal artery	n = 10	n = 11
P_{O_2} (mmHg)	194.3 (9.1)	179.5 (1.6)
P_{CO_2} (mmHg)	34.1 (1.12)	32.3 (.15)
*p*H	7.41 (.01)	7.41 (.01)
BE (mmol/l)	−1.2 (.2)	−3.2 (.5)
Umbilical vein	n = 10	n = 11
P_{O_2} (mmHg)	37.6 (2.9)	31.1 (2.7)
P_{CO_2} (mmHg)	49.1 (2.7)	46.0 (2.6)
*p*H	7.32 (.01)	7.32 (.01)
BE (mmol/l)	−.9 (.3)	−4.0 (.3)
Umbilical artery	n = 6	n = 11
P_{O_2} (mmHg)	21.6 (.73)	20.8 (3.0)
P_{CO_2} (mmHg)	57.9 (4.02)	55.3 (3.6)
*p*H	7.26 (.02)	7.27 (.07)
BE (mmol/l)	−2.2 (.6)	−4.1 (.3)

Values are mean SEM.

The neurobehavioral status of the newborn at 30 min, 2 h, and 24 h are shown in table 6. For all neonates in both phases, NACSs improved over the assessment period. In phase 1, the NACS was not assessed at 24 h in one case because the baby was transfered to a special care unit as a result of a clonic convulsion 3 h after birth. In phase 2, the neonate who was noted sleepy at delivery had the lowest NACS (20) at 30 min, but achieved a score of 38 2 h after birth. There was no correlation between NACS at 30 min and I–D or U–D in phase 1, but a correlation was found in phase 2 between NACS at 30 min and I–D ($r = -.546$, $P < .05$). In both phases, no correlation was found between neonatal propofol levels and NACS.

Discussion

The rate of infusion of propofol for maintenance of anesthesia varies considerably.[3,20,21] In this study, the initial dose chosen for maintenance of anesthesia was 5 $mg \cdot kg^{-1} \cdot h^{-1}$ which was thought to be necessary to obtain a good quality of anesthesia without any maternal awareness during cesarean section.

TABLE 6. Neonatal Assessments

	Phase 1 (n = 10)	Phase 2 (n = 11)
Immediate cry	10	10
TSR (<90 s)	10	10
APGAR score (>7)		
at 1 min	8	10
at 5 min	9	11
at 10 min	10	11
NACS score (percentage of neonates scoring > 35)		
at 30 min	30%	55%
NACS range	32–36	20–37
at 2 h	90%	100%
NACS range	34–38	35–39
at 24 h	100%*	100%
NACS range	38–40	37–40

* One infant was not assessed.

The high incidence of maternal awareness in phase 1 may be attributed to the rapid redistribution of propofol, with rapid recovery of consciousness in the non-premedicated patients and because we discontinued halothane between uterine incision and delivery of the infant. However, only two of the four parturients who experienced awareness had recall of the intraoperative period. Recall was confined to the time of delivery. In contrast, awareness occurred in only one of the 11 patients in whom induction and maintenance of anesthesia were with propofol. For both phases, awareness would certainly be reduced by increasing the induction dose of propofol or maintaining all anesthetic agents throughout anesthesia. Logan *et al.*[22] have demonstrated that in young non-premedicated patients undergoing intense surgical stimulation immediately after induction, the bolus induction dose of propofol might be 3 mg/kg. Our results support that this higher propofol dose should ensure unconsciousness in the mother, while minimizing anesthetic-related depression of the infant.

PLACENTAL TRANSFER OF PROPOFOL

The results show that, in normal patients undergoing elective cesarean section, propofol administered to the mother crosses the placenta to give, at delivery, an UV/MV ratio of 0.70 (phase 1; induction only) and 0.76 (phase 2; induction and maintenance).

In phase 1, arterial concentrations of propofol in the umbilical cord, which would be similar to those entering the fetal brain, were well below the blood propofol con-

centration (1.07 μg/ml) reported by Schüttler *et al.*[23] at the time of recovery of consciousness following a bolus dose to adult volunteers. The apparent decline in propofol concentrations in maternal blood samples with time post-induction is not surprising in view of the reported rapid clearance of propofol from blood. The individual maternal levels observed in this study are very similar to those previously reported for nonpregnant females following a single induction dose.[9,13] The lack of any trend in the UA/UV propofol ratio with time after dose suggests that propofol in the neonatal circulation has reached equilibrium with the supply of propofol from the placenta even by the time of the earliest delivery (13 min). The slightly higher mean umbilical arterial concentration when compared to the venous samples suggests that redistribution of propofol from the neonatal tissues back into the maternal blood is occurring during this period. Data for thiopental[24] indicate that it also crosses the placenta; however, UV/UA ratios for I–D periods of 10–27 min were more variable (1.1–4.7) than those observed for propofol.

In phase 2, the mean maternal blood propofol concentration (1.66 μg/ml) was about 15% lower than the value derived for this infusion regimen (1.94 μg/ml) using the 6.0 $mg \cdot kg^{-1} \cdot h^{-1}$ data reported by Gepts *et al.*[11] This difference is probably a consequence of the drug dose in the present study being based on the patient's body weight prior to pregnancy without taking into account the likely increase in the volume of distribution of propofol during pregnancy. Umbilical arterial concentrations were all lower than those in the umbilical vein samples with a mean difference of approximately 30%. These lower UA concentrations probably reflect both continuing neonatal uptake of propofol at the time of delivery and possibly neonatal metabolism of propofol. Maternal levels in blood samples taken at delivery were consistently higher than those in umbilical venous samples. This suggests that the placenta is acting as a partial barrier to the distribution of propofol. UV concentrations showed no individual value above the lower limit of 1.64 μg/ml that was reported by Schüttler *et al.*[23] as the lower limit blood propofol concentration at which volunteers lost consciousness during an infusion of propofol. Furthermore, even if potentially hypnotic concentrations were achieved in the UV blood, it may not cause fetal depression since a proportion of the UV blood perfuses the fetal liver and would, therefore, be subject to first pass metabolism; that escaping metabolism together with the fraction shunted through the ductus venosus would be further diluted when entering the inferior vena cava before reaching the fetal brain.¶

¶ Finster M, Pedersen H, Morishima HO: Principles of fetal exposure to drugs used in obstetric anesthesia. Drugs and Pregnancy, 101–13, 1984.

The decrease in the propofol concentrations in the heel prick blood samples taken approximately 2 h after delivery, compared with the corresponding UA samples taken at cord clamping, suggests that propofol continued to be cleared rapidly from the neonatal circulation postpartum. It has been reported that rates of glucuronidation and hydroxylation do not reach adult values until about 2 yr of age.[25] However, propofol clearance in adults is limited by blood supply to the liver and not hepatic capacity.[12,26] It is not surprising, therefore, that in these neonates, propofol clearance was apparently rapid.

Breast Milk/Colostrum Propofol Concentration

The very limited milk/colostrum data indicate that transfer of propofol into milk/colostrum was only a very minor route of elimination. Similar concentrations of propofol (0.12–0.97 μg/ml) were observed by Schmitt *et al.*[27] in colostrum samples obtained 4–8 h after induction with propofol; anesthesia in these patients being maintained for up to 30 min with an infusion of propofol and supplementary bolus doses. Colostrum produced in the first few days postpartum is only secreted in amounts of 10–20 ml/day. The volume of mature milk at each feeding has been estimated to be about 125–225 ml.[28] Considering the volume of milk consumed given above and as the concentrations of propofol were very low, even in the unlikely event that all of this drug was absorbed from the gastrointestinal tract and escaped first pass metabolic processes, the exposure of the neonate to propofol by this route would be negligible compared to the observed exposure as a result of the placental transfer of the drug. Those conclusions for propofol are identical to those reported for thiopental[24] when given as a single induction dose.

Neonatal Assessment

UV and UA blood gas and acid base levels compare favorably with results published by others workers using established methods of anesthesia.[15–17,29–33] The Apgar ratings recorded in these two series suggest that propofol seems to be well tolerated by the newborn, as demonstrated by the high incidence of Apgar > 7. The low Apgar scores in the two neonates in phase 1 and one in phase 2 are unlikely to be due to aortocaval compression owing to the lateral table tilt,[34] or maternal hyperventilation.[35] The clinical status of these newborns was probably related to a prolongation of the interval between uterine incision and delivery[36] because no consistency was found between propofol concentrations and low Apgar scores.

Neurobehavioral function as tested by the NACS represents a more sensitive indicator of the neonatal effects of maternally administered drugs. Two hours after birth,

NACS can be compared with those of neonates delivered with regional anesthesia that is known to have minimal effects on the infant,[37] especially regarding adaptative capacity scoring, alertness, crying, and motor activity. No neurologic signs of drug depression were found: no mild hypotonia, no mediocre primary reflex responses, nor any poor habituation to repeated stimuli. NACS could not be made 24 h after delivery in the neonate delivered to patient 2 (phase 1) who developed convulsive movements at 3 h and again at 48 h postpartum. Although propofol appears to be temporally related to convulsive episodes in a small number of patients, there is evidence to suggest it is anticonvulsivant in certain circumstances.[38] Furthermore, animal studies have demonstrated no effect on the seizure threshold[39] and there is some evidence that propofol may control epileptiform movements in status epilepticus.[40] The recurrence of convulsive movements in this neonate 48 h after delivery suggests that the event was not drug related.

It can be concluded that in both phases of this study, propofol crosses the placenta but seems to have no apparent major adverse effects on the neonatal outcome parameters. Furthermore, transfer of propofol into milk/colostrum is negligible. These results justify the performance of additional studies of propofol administration during general anesthesia for cesarean section to compare propofol with thiopental and to evaluate the effect of propofol anesthesia on the high-risk neonate.

The authors wish to thank Herve Nicol and Dominique Sparfeld, C.N.R.A.s, for their participation and assistance in data collection; Mr. E. I. Douglas, ICI plc, for performing the propofol assay; the obstetrician team at Maternité de Port-Royal for their cooperation during the study; and Miss Caroline Loyez and Miss Agnès Rivaille, ICI Pharma, France, for their assistance.

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