of the cervical cord in two cases.1 Hausbrandt and Meier reported spinal cord lesions in 30 of 103 cases of neonatal deaths.3 From this evidence alone, the significance of spinal injury at birth is considerably more important than is recognized clinically.

**Generic and Trade Names of Drug**

Iophendylate injection—Mulsopaque, Pantopaque.

**References**


**Atropine Sulfate vs Atropine Methyl Bromide**

**Effect on Maternal and Fetal Heart Rate**

*Constance B. dePadua, MD, and Joachim S. Gravenstein, MD*

Effects of atropine sulfate and atropine methyl bromide on maternal and fetal heart rates were observed in 12 women at term. Both drugs were given in graded doses to a total dose of 0.8 mg/70 kg body weight. Both drugs caused significant acceleration of the mothers' heart rates, but only atropine sulfate accelerated fetal heart rates. We assume that atropine methyl bromide, because of its charge, did not penetrate the placental barrier as readily as atropine sulfate.

MANY DRUGS easily cross from the blood into the brain or a fetus; others do so only slowly or not at all. For example, atropine sulfate quickly penetrates into the brain and obviously also through the placenta into the fetus since it can elevate heart rates both in mother and fetus.1 Atropine methyl bromide, a quaternary ammonium derivative of atropine, is a charged molecule (Fig 1) that apparently does not cross the blood-brain barrier appreciably.2 We therefore hypothesized that atropine methyl bromide would fail to cross the placental barrier and that it would accelerate the heart rate of the mother, but leave the fetal heart rate unaffected. We tested this hypothesis in pregnant women at term.

**Methods**

Twelve pregnant women who were at or near term and had no known disease were observed two hours prior to elective cesarean section. The patients were not in labor. They were arbitrarily divided into two groups of six each, one group receiving atropine sulfate, the other atropine methyl bromide. This premedication with atropine constituted the normal preoperative medication for these patients. No other drugs were given. We used commercially available atropine sulfate and atropine methyl bromide, prepared for intravenous injection by our hospital pharmacy. A total dose of 0.8 mg of either atropine salt was injected per 70 kg of body weight. This total dose was divided into four doses with the relationship of 1:1:2:4. Each dose was contained in 2 ml of solution, and was rapidly injected intravenously. The tubing was then flushed with 10 ml of normal saline solution. The injections were made at 15-minute intervals. Two hours before the operation, we placed a large plastic catheter into a vein in the forearm.

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1. Atropine sulfate passes readily from blood of mother into the fetus. Atropine methyl bromide, a quaternary ammonium derivative, carries a charge and does not reach the fetus as easily.
and started a slow drip with a solution of 5% dextrose in water. Maternal and fetal heart rates were counted for full minutes from an electrocardiogram, and with the aid of an ultrasonic Doppler device. The mothers were asked to remain supine and allowed to rest for at least 15 minutes before two control values were obtained and the injections begun. We recorded blood pressures in this position and excluded patients from the investigation who showed a tendency to become hypotensive. All heart rates were counted 1 1/2, 5, and 10 minutes after each drug injection and 20 minutes after the last injection. We computed $t$ tests for statistical analyses.

**Results**

Our results are represented in Fig 2 showing maternal and fetal heart rates with $\pm 1$ standard error of the mean, the time, and the individual and cumulative doses. The injection of the smaller doses of atropine sulfate seemed to decrease rate. This slight bradycardia may have arisen by chance. Both atropine sulfate and atropine methyl bromide caused a significant increase in heart rate in the mothers. With atropine sulfate (a total dose of 0.4 and 0.8 mg per 70 kg body weight), mean heart rates in the mothers increased by 10 and 40 beats per minute, whereas the same doses of atropine methyl bromide accelerated rates by 20 and 47 beats per minute. These differences between sulfate and methyl bromide were not statistically significant. The mothers' blood pressures were not affected by either atropine salt.

Neither atropine salt affected fetal heart rates until the mother had received a total dose of 0.4 mg/70 kg body weight. After 0.8 mg of atropine sulfate had been administered, fetal heart rates rose by 20 beats per minute, but after atropine methyl bromide had been given, the rates increased only by five beats per minute above control values. A $t$ test showed that 10 and 15 minutes after injection of the highest dose, the fetal heart rates were significantly higher ($P<0.05$ for both points) when the mothers were treated with atropine sulfate, as compared to the fetal heart rates when mothers were treated with atropine methyl bromide.

**Comment**

Atropine methyl bromide has a molecular weight of 384.29, atropine sulfate of 694.82, because the sulfate contains two atropine bases, whereas the methyl bromide contains only one (Fig 1). If we had intended to give equimolar amounts of atropine sulfate and atropine methyl bromide, we should have given 10% more atropine methyl bromide than atropine sulfate. In our study equal weights of the two salts were given and the effects of the two drugs on heart rates in the mothers were statistically indistinguishable. However, this was not true for fetal heart rates. Here, atropine sulfate was clearly more effective in accelerating heart rate than atropine methyl bromide. We assume that atropine methyl bromide did not have as ready access to the fetal circulation as did atropine sulfate, and we postulate that atropine methyl bromide, because of its charge, could not cross the placental barrier as readily as atropine sulfate.

The doses tested by us in this study are well within the clinically employed amounts of atropine sulfate or atropine methyl bromide. If larger doses were given, enough atropine methyl bromide might cross the placenta to affect the fetal heart.

When we give atropine to the mother in preparation for anesthesia for a cesarean section or vaginal delivery, or for other reasons, we accept the actions of atropine on the fetus as an undesirable side effect. The fetal bradycardia, an important clinical sign of fetal distress, can be abolished or diminished by atropine sulfate. If future studies confirm that atropine methyl bromide provides the same protection against undesirable cholinergic effects in the mother as atropine sulfate does, without affecting the fetal heart rate, atropine methyl bromide may become the anticholinergic drug of choice for women at term.

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**References**

