THE TRANSMISSION OF MEPERIDINE ACROSS THE HUMAN PLACENTA

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Quantitative data on the transmission of certain anesthetic and analgesic drugs from the maternal to the fetal circulation have been cited. Such information is of value to the obstetrician and anesthesiologist for a better understanding of the effects upon the newborn baby of drugs administered to the mother during labor.

Hitherto, such knowledge was unavailable with regard to meperidine (Demerol). This drug has been used with increasing frequency for the relief of labor pain because it is said to produce little or no effect upon the respiration of the newborn baby when employed in this manner. Because of the important place meperidine has in the management of labor, the current studies of the pattern of its placental transfer from mother to fetus were undertaken.

Methods

Nine healthy pregnant women at term were used for this study. Two patients were delivered by cesarean section, the remainder spontaneously, with episiotomy. Meperidine in doses of 50 to 100 mg. was administered intramuscularly or intravenously during labor. The average total quantity of drug per patient during labor was 175 mg. and ranged from 50 to 300 mg. The last dose of meperidine varied from 40 minutes to 3 hours and 38 minutes prior to delivery. The first dose varied from 1 hour and 40 minutes to 15 minutes before delivery. The method of drug administration was adjusted to the need of the patient for satisfactory analgesia.

Five patients were anesthetized for delivery with nitrous oxide-oxygen (a minimum concentration of 25 per cent oxygen was given); two with cyclopropane, and one each with low spinal anesthesia and caudal block.

At delivery, samples of blood were drawn simultaneously from the mother and the umbilical cord. The latter was considered representative of the fetal blood. Meperidine in plasma was determined according to a method to be published elsewhere. This method has been shown to be specific in that it included none of the metabolites of meperidine in the measurement.

Results

Plasma levels of meperidine indicate clearly that the drug crossed the placenta in significant concentrations (Table I). These varied from 45 to 106

*Supported in part by the Squibb Institute for Medical Research.
<table>
<thead>
<tr>
<th>PATIENT</th>
<th>TYPE OF DELIVERY</th>
<th>MEPERIDINE (IN MG.)</th>
<th>ROUTE OF ADMINISTRATION</th>
<th>TIME PRIOR TO DELIVERY (IN HR. AND MIN.)</th>
<th>ANALGESIC EFFECT ON MOTHER</th>
<th>DEPRESSANT EFFECT ON INFANT</th>
<th>ANESTHESIA</th>
<th>MATERNAL PLASMA LEVEL (IN MG./L.)</th>
<th>CORD BLOOD LEVEL (IN MG./L.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>He</td>
<td>Vaginal</td>
<td>100</td>
<td>IM</td>
<td>2:00</td>
<td>Good</td>
<td>0</td>
<td>Cyclopropane</td>
<td>0.40</td>
<td>0.22</td>
</tr>
<tr>
<td>Zi</td>
<td>Cesarean</td>
<td>50</td>
<td>IM</td>
<td>1:43</td>
<td>Good</td>
<td>0</td>
<td>Cyclopropane</td>
<td>0.38</td>
<td>0.24</td>
</tr>
<tr>
<td>Po</td>
<td>Vaginal</td>
<td>50</td>
<td>IM</td>
<td>2:40</td>
<td>Good</td>
<td>0</td>
<td>Nitrous oxide</td>
<td>0.29</td>
<td>0.13</td>
</tr>
<tr>
<td>Fr</td>
<td>Vaginal</td>
<td>100</td>
<td>IM</td>
<td>1:15</td>
<td>Good</td>
<td>Moderate depression</td>
<td>Nitrous oxide</td>
<td>0.45</td>
<td>0.38</td>
</tr>
<tr>
<td>Ni</td>
<td>Vaginal</td>
<td>75</td>
<td>IM</td>
<td>4:08</td>
<td>Poor</td>
<td>0</td>
<td>Nitrous oxide</td>
<td>0.50</td>
<td>0.39</td>
</tr>
<tr>
<td>St</td>
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<td>75</td>
<td>IM</td>
<td>2:00</td>
<td>Poor</td>
<td>0</td>
<td>Nitrous oxide</td>
<td>0.76</td>
<td>0.55</td>
</tr>
<tr>
<td>St</td>
<td>Vaginal</td>
<td>50</td>
<td>IV</td>
<td>0:43</td>
<td>Poor</td>
<td>0</td>
<td>Nitrous oxide</td>
<td>0.76</td>
<td>0.55</td>
</tr>
<tr>
<td>Pa</td>
<td>Cesarean</td>
<td>100</td>
<td>IM</td>
<td>15:00</td>
<td>Good</td>
<td>0</td>
<td>Low spinal</td>
<td>0.73</td>
<td>0.76</td>
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<td>Bu</td>
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<td>IM</td>
<td>4:52</td>
<td>Good</td>
<td>0†</td>
<td>Nitrous oxide</td>
<td>0.76</td>
<td>0.55</td>
</tr>
<tr>
<td>Al</td>
<td>Vaginal</td>
<td>100</td>
<td>IM</td>
<td>3:38</td>
<td>Good</td>
<td>0</td>
<td>Caudal</td>
<td>1.02</td>
<td>0.72</td>
</tr>
</tbody>
</table>

*Spontaneous breathing early. Aspirated meconium. No sequela.

†Difficult to evaluate. Delivery was complicated by impaction of the shoulders of the fetus in the birth canal. A difficult delivery was followed by fetal anoxia requiring 20 minutes of intratracheal oxygen insufflation. Fetal recovery was satisfactory.
per cent (average 77 per cent) of the levels measured simultaneously in the
maternal blood.
Satisfactory analgesia for the mother was achieved in all but one patient.
In only one instance was there a clearly demonstrable depression of fetal respi-
ration, presumably due to meperidine. Even so, the fetal plasma level of 0.38
mg. per liter was not the highest encountered. There were two other compli-
cations in the newborn. One was attributable to early intrauterine respiration
and aspiration of meconium; the other to a difficult delivery caused by shoulder
impaction of the fetus. Neither complication was harmful to the baby.

Comment

With the aid of a sensitive method for its estimation, it was demonstrated
that meperidine enters the fetal circulation relatively freely after parenteral
administration to the mother. It also appears that doses of the drug which
can produce satisfactory analgesia in the mother do not necessarily cause signifi-
cant depression of respiration in the newborn baby. The rate of transplacental
movement of the drug is unknown.

Summary

1. Meperidine crosses the human placenta in significant concentrations.
2. In therapeutic doses administered to the mother, meperidine appears
to cause little or no depression of respiration of the newborn child.

References