The Effect of Sulpiride Administration on Maternal and Fetal Plasma Prolactin Levels, and Fetal Growth in Rats

TAKAO FUKAYA, NOBUAKI FURUHASHI, HIDEAKI KONO, OSAMU SHINKAWA, TORU TAKAHASHI and MASAKUNI SUZUKI

Department of Obstetrics and Gynecology, Tohoku University School of Medicine, Sendai 980

FUKAYA, T., FURUHASHI, N., KONO, H., SHINKAWA, O., TAKAHASHI, T. and SUZUKI, M. The Effect of Sulpiride Administration on Maternal and Fetal Plasma Prolactin Levels, and Fetal Growth in Rats. Tohoku J. exp. Med., 1983, 141 (3), 323-326 — Pregnant Wistar rats were daily injected with 5 mg sulpiride into the peritoneal cavity starting on day 14 of gestation. Blood samples were obtained from the maternal carotid artery and fetal axillary vessels on day 20 of gestation. Serum prolactin (PRL) levels were determined by radioimmunoassay using a rat PRL RIA kit. The maternal serum and fetal plasma PRL levels were significantly higher in the sulpiride-treated group than in the saline control group. There was a significant positive correlation between fetal body weight and fetal plasma PRL level. These results suggest that sulpiride which reached the fetus stimulates fetal PRL secretion and that PRL may exert a growth-promoting effect on the fetus. —— prolactin; sulpiride; fetal growth; rat

The roles of prolactin (PRL) during pregnancy still remain unclear, especially the effect on the fetus. The PRL levels in fetal circulation increase significantly after 28 gestational weeks in human (Winter et al. 1975), and fetal growth is promoted markedly after the end of mid gestation. Although anencephalic infants have a low growth hormone level, the growth retardation has not been found in them (Furuhashi et al. 1980). These findings suggest that PRL may have some growth promoting effect on human fetus, and that growth hormone is not essential for fetal growth.

In this study, we investigated the effect of PRL on the fetal growth and the relationship of PRL and fetal body weight using sulpiride-treated pregnant rats.

MATERIALS AND METHODS

Sulpiride (Dogmatyl®) 5 mg or saline (control) was daily injected into the peritoneal cavity of pregnant Wistar rats from 14 days of gestational age. On day 20 of gestation all animals were sacrificed under ether anesthesia and maternal blood was obtained from the carotid artery, and the then all fetuses were exteriorized. Fetal body weight was measured immediately after exteriorization. Fetal blood samples were collected via an incision from axillary vessels using heparinized capillaries. The blood was pooled from fetuses which were taken out from one side of the uterus.
After centrifugation, maternal serum and fetal plasma were stored at -20°C. The levels of maternal serum and fetal plasma PRL were determined by using reagents and methods supplied from NIAMDD.

All values were expressed as mean±s.d. and statistical analysis was performed by using Student's t-test.

**RESULTS**

Maternal PRL levels were markedly higher in the sulpiride-treated group than in the control group; the mean concentration of maternal PRL was 93.7±43.3 ng/ml (n=5, mean±s.d.) in the sulpiride-treated group, and 3.8±0.6 ng/ml (n=4) in the control group (Table 1).

Fetal PRL levels were also significantly higher (p<0.002) in the sulpiride-treated group (10.8±3.5 ng/ml, n=6) than in the control group (4.2±2.0 ng/ml, n=6) as shown in Table 1.

**DISCUSSION**

The treatment with sulpiride had a promoting effect on fetal body weight (Table 1). There was a significant positive correlation (n=16, r=0.539, y=5.346 x-7.18) between fetal body weight and fetal plasma PRL level (Fig. 1).

It is well known that sulpiride stimulates pituitary PRL secretion (Mancini et al. 1976). In this study, maternal and fetal PRL levels on day 20 of gestational age in the control group were rather lower than those reported by other investigators (Reusens et al. 1979; John et al. 1981). We found the elevation of fetal plasma PRL levels in the sulpiride-treated group. Since PRL has been reported not to cross the placenta (Josimovich et al. 1977), it is unlikely that the elevated fetal plasma PRL levels were of maternal origin, but it appears likely that fetal pituitary PRL secretion might be stimulated by sulpiride.

There were many controversies (Winter et al. 1975; Hauth et al. 1978; Leontic et al. 1979) about the role of PRL for the fetus. Our previous report suggests that PRL has some growth promoting effect on the human fetus (Furuhashi et al. 1980). There were a few experimental reports suggesting a somatogenic effect of PRL on

### Table 1. Maternal serum and fetal plasma PRL levels, and mean fetal body weight in the saline control and the sulpiride-treated group

<table>
<thead>
<tr>
<th></th>
<th>Maternal prolactin (ng/ml)</th>
<th>Fetal prolactin (ng/ml)</th>
<th>Mean fetal weight† (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline control</td>
<td>3.8±0.6 (n=4)</td>
<td>4.2±2.0 (n=6)</td>
<td>2.65±0.32 (n=27)</td>
</tr>
<tr>
<td>Sulpiride</td>
<td>93.7±43.3 (n=5)</td>
<td>10.8±3.5 (n=6)</td>
<td>3.02±0.5 (n=37)</td>
</tr>
<tr>
<td>Significance</td>
<td>p&lt;0.01</td>
<td>p&lt;0.002</td>
<td>p&lt;0.002</td>
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</tbody>
</table>

* Fetal plasma PRL was measured in pooled plasma of fetuses which were taken out from one side of the uterus.
† Mean fetal body weight was calculated using fetuses taken out from one side of the uterus.
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the fetus (Bigazzi et al. 1979; Reusens et al. 1979). In this study, we found a significant difference in fetal body weight between the control and the sulpiride-treated group. Moreover, there was a significant positive correlation between fetal plasma PRL level and fetal mean body weight which was calculated from fetuses in each side of the uterus. It was suggested that insulin (Van Asshe et al. 1977) and chorionic somatomammotropin (Kelly et al. 1976) also have a somatogenic effect on the fetus. From the present results it is strongly suggested that PRL may play an important role as one of the somatogenic hormones in fetuses.

Acknowledgment

This work was supported by a grant from the Ministry of Education, Science and Culture, Japan. We would like to thank NIAMDD for providing us a rat PRL radioimmunoassay kit. We acknowledge the technical assistance of Miss M. Okudera.

References


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