Effect of administration of estrogen to pregnant rabbits on the lipid content and composition of the fetal brain

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Summary. Intramuscular injection of 17 β-estradiol to pregnant rabbits did not produce any significant change in the phospholipid, neutral lipid and cholesterol content of the fetal brains, nor did it cause any significant difference in their wet and dry weights. It may be inferred that use of estrogen in the gestational period to enhance surfactant production and lung maturation in the fetus would not produce adverse effects on the fetal brain lipids.

Administration of estrogen to pregnant rabbits produces significant changes in the phospholipid content and composition of the lung washing and lavaged lung tissue of the fetus[1]. The total phospholipid content as well as the phosphatidylcholine (lecithin) concentration increases while sphingomyelin concentration decreases. These changes enhance pulmonary surfactant production and hence fetal lung maturation. Surfactant is a phospholipid containg-, surface tension-lowering agent which lines the lung alveolar wall and prevents collapse of the alveoli during expiration. Its absence is considered to be the cause of the primary respiratory distress syndrome of the newborn[2]. Because estrogen enhances surfactant production, its use in the prevention and/or treatment of the respiratory distress syndrome of the newborn may be regarded as an alternative among the present regimens. Therefore, it is valuable to study the effects of estrogen on other lipid-containing organs of vital importance such as the brain. In the present investigation, the effect of estrogen injection to pregnant rabbits on the fetal brain lipids was studied.

Materials and methods. 15 pregnant New Zealand white rabbits, whose conception time was known to within 2 h, were used. On the 25th day of gestation (full term is 31 days), 7 rabbits received an i.m. injection of 75 µg 17β-estradiol in 1.5 ml of 0.9% NaCl containing 0.5% ethanol (v/v) and 0.0025% Tween 80 (w/v). The 8 control rabbits received the solvent only. On the 26th day of gestation, the rabbits were killed with sodium pentobarbital (80 mg/kg i.v.) and the fetuses were removed by cesarean section. The newborns were killed with i.p. sodium pentobarbital (32 mg per fetus) and the brains of the fetuses from each doe were pooled and lyophilized. Lipids were extracted with chloroform:methanol (2:1 v/v), and separated into the upper- and lower-phase fractions by the method of Folch, Lees and Sloane-Stanley[3]. The lower-phase lipids were fractionated and quantitatively determined[4]. The upper-phase fraction containing gangliosides was not used in the analysis. The wet and dry (lyophilized) weights of the brains were measured.

Results and discussion. The results are presented in the table. Estrogen administration to the maternal rabbit did not produce any statistically significant change in the wet and dry weights of the fetal brain, nor did it cause any significant difference in the phospholipid, neutral lipid and cholesterol contents. Glycolipid was identified in the brains of the control and test groups, although its quantitative measurement was not attempted. The effects of estrogen administration to pregnant rabbits on the lipid content of the fetal brain are, therefore, different from those on the fetal lungs where significant changes in the phospholipid content and composition are produced[1].

Administration of corticosteroids to mice[5] and rats[6] in the neonatal period reduces the brain weight and causes a small but significant decrease in the cerebral cholesterol content[7]. ACTH injection to infant rats brings about reduction of the brain weight and elevation of the cholesterol content[8]. However, studies dealing with the effects of administration of hormones to pregnant animals on fetal brain lipids are scanty.

Based on the results of the present investigation, it may be inferred that administration of estrogen in the gestational period for prevention or treatment of the respiratory distress syndrome of the newborn would not produce adverse effects on the lipid content and composition of the fetal brain.

However, in this study, whole brain lipids were measured, and although estrogen did not produce changes in the whole brain lipids, local changes in lipid content and concentration could have occurred, especially in the main target area of the estrogen, the hypothalamus. Moreover, a limited number of lipids were examined.

Another point is that even if estrogen administration does not affect brain lipids, estradiol is a potent hormone and is bound to have other effects on the fetus and its differentiation. Until safety of estrogen administration is clearly demonstrated in regard to these points, its use in the gestational period for prevention or treatment of the respiratory distress syndrome of the newborn would be a risky undertaking.

	Control group (mean ± SE)	Estrogen-treated group (mean ± SE)
Wet weight per brain (mg)	684 ± 25	675 ± 23
Dry weight per brain (mg)	72.8 ± 3	63.5 ± 3
Dry weight as percent of wet weight	10.6	9.4
Phospholipid (mg per g dry brain)	112.2 ± 10.6	118.2 ± 4.6
Neutral lipid (as µmole glycerol per g dry brain)	40.3 ± 4.8	50.4 ± 8.7
Cholesterol (mg per g dry brain)	25.2 ± 1.8	27.6 ± 1.1

All comparisons with controls non-significant ($p > 0.05$), Student's t-test.

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