

Influence of beta-receptor stimulation on catecholamine and phospholipid concentrations in lungs of fetal rabbits

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It was studied whether the beta-receptor stimulating fenoterol had any influence on endogenous catecholamines in the lung tissue of fetuses. On the 23rd, 27th and 31st days of pregnancy, concentrations of noradrenaline and dopamine in the lung homogenate of mature and immature rabbit fetuses were determined by fluorometry, and the basic surfactant components total phospholipids and lecithin by colorimetry, in a group receiving beta-mimetic treatment and in a control group receiving physiological salt solution. The concentration of noradrenaline decreased with the progression of pregnancy but the concentration of dopamine did not change significantly. Application of fenoterol caused an increase in total phospholipids and lecithin in the lungs of 23 and 27 day old rabbit fetuses and decreased the concentration of catecholamines, especially of noradrenaline. The drug had no such effect in mature (31 day) fetuses.

Insufficiency of surfactant, anoxia and coagulation disturbances are essential factors determining the incidence of idiopathic respiratory distress in premature babies [2, 3, 9, 10, 20, 27]. Anoxia and subsequent tissue acidification inhibit lecithin synthesis [16, 28] on the one hand and on the other evoke a release of catecholamines, especially noradrenaline [20, 21] which increases resistance of the pulmonary vessels [1, 5]. Anoxia and the high circulatory resistance enhance the permeability of blood vessels for proteins and plasma, and result in protein-rich exudate in the lung.

Synthesis of surfactant is realized by stimulation of adrenergic beta-receptors [13, 24], hence all beta-mimetics intensify the process. Clinical and experimental examinations

have confirmed the beneficial influence of beta-receptor stimulating drugs on maturation of the lung tissue [4, 6, 7, 8, 14, 22, 23, 30].

The aim of the present experiments was to clarify the influence of fenoterol on the behaviour of phospholipids and catecholamines in the lungs of fetal rabbits.

MATERIAL AND METHODS

Examinations were carried out on 176 Belgian rabbit fetuses obtained from 22 females. Dead fetuses were excluded from the examinations. Duration of pregnancy was calculated from the date of female covering. Examinations were carried out on the 23rd, 27th and 31st days of pregnancy. The rabbits were divided into two groups (Table I). The experimental group included 11 pregnant rabbits which

TABLE I
Grouping of rabbits

Day of gestation	Examined subjects		Controls	
	Number		Number	
	pregnant rabbits	fetuses	pregnant rabbits	fetuses
23	4	34	4	35
27	4	30	4	31
31	3	22	3	24

received 0.1 mg/kg body weight of fenoterol in intravenous drip infusion. The control group consisted of 11 pregnant rabbits which received physiological solution intravenously. Then 24 hours after administration of the last dose of fenoterol all the fetuses were taken out in general anaesthesia. In this way, 86 fetuses were obtained in the experimental group and 90 fetuses in the control group.

After removing the lungs, they were dried on Whatman paper, weighed, and subsequently homogenized in ice bath.

Total phospholipids and lecithin in extracts of the lung tissue were determined by means of the colorimetric method of Yoshida et al. [31]. Extraction of phospholipids and lecithin from the lungs was carried out by the method of Folch et al. [15]. The obtained results were analysed using Student's *t* test.

Catecholamines (noradrenaline and dopamine) in lung tissue homogenates were determined by the fluorimetric method of Spano and Neff [29] and Chang [11], respectively.

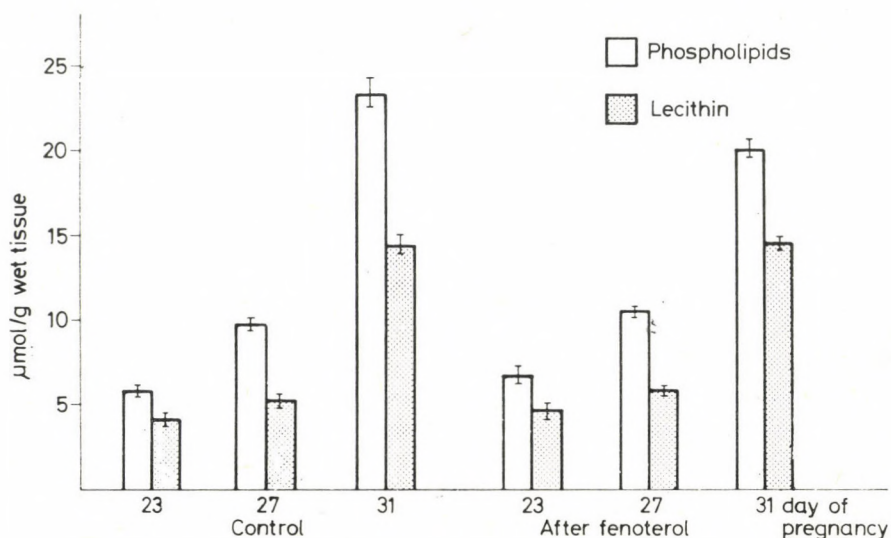


FIG. 1. Concentration of total phospholipids and lecithin in lung homogenates before (control group) and after fenoterol administration

RESULTS

Total phospholipids and lecithin

Concentration of total phospholipids and lecithin in fetal lung homogenates was found to increase with the age of pregnancy (Fig 1).

In 23 day fetuses, mean concentration of total phospholipids in the lung amounted to $5.78 \pm 0.319 \mu\text{mol/g}$ and lecithin to $3.93 \pm 0.306 \mu\text{mol/g}$. On the 27th day of pregnancy, the mean value of total phospholipids was $9.51 \pm 0.452 \mu\text{mol/g}$ and of lecithin $5.34 \pm 0.411 \mu\text{mol/g}$. In mature fetuses i.e. on the 31st day of pregnancy, total phospholipids in the lung homogenate amounted to $20.10 \pm 0.876 \mu\text{mol/g}$ and lecithin to $14.50 \pm 0.495 \mu\text{mol/g}$ tissue.

After administration of fenoterol, in 23 day fetuses the level of total phospholipids amounted to $6.84 \pm$

0.553 and the level of lecithin to $4.80 \pm 0.396 \mu\text{mol/g}$. In 27 day fetuses the mean of total phospholipids was 10.66 ± 0.155 and of lecithin $5.97 \pm 0.170 \mu\text{mol/g}$. The increase was statistically significant in both groups. In the mature fetuses, however, fenoterol caused no change, total phospholipids amounted to 20.29 ± 0.598 and lecithin to $14.68 \pm 0.354 \mu\text{mol/g}$.

Catecholamines (noradrenaline and dopamine)

The behaviour of catecholamines was different from that of phospholipids and lecithin. The concentration of noradrenaline in the lung homogenates decreased with the age of pregnancy while the dopamine concentration was unchanged (Fig 2).

On the 23rd day of pregnancy, noradrenaline amounted to 1.27 ± 0.197 and dopamine to 1.09 ± 0.23

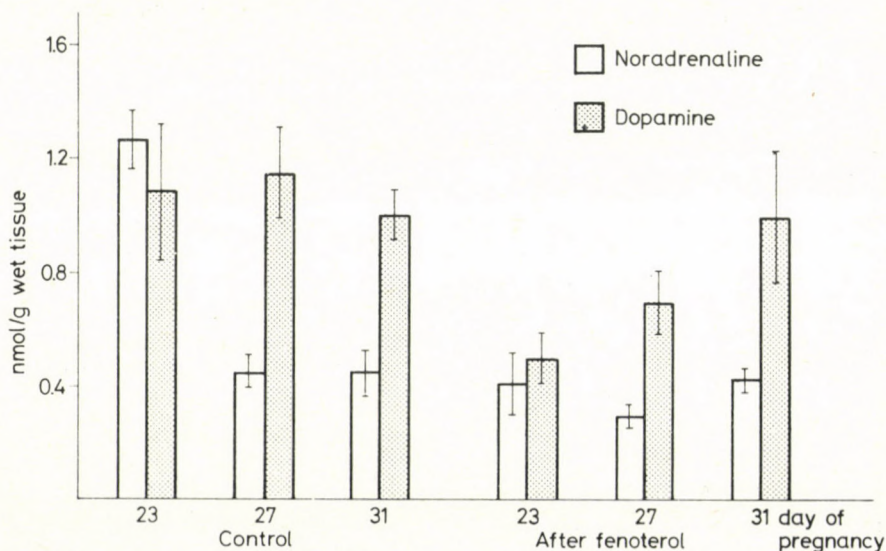


FIG. 2. Concentration of noradrenaline and dopamine in lung homogenates before (control group) and after fenoterol administration

nmol/g. In 27 day fetuses the concentrations were 0.452 ± 0.06 nmol/g and 1.150 ± 0.156 , respectively, while in mature fetuses 0.450 ± 0.06 and 1.0 ± 0.156 nmol/g respectively. After administration of fenoterol, concentration of dopamine and noradrenaline on the 23rd and 27th days of pregnancy was lower than in the control group, while in the lungs of mature fetuses i.e. on the 31st day of pregnancy no significant changes occurred in the concentration of catecholamines (Fig 2).

DISCUSSION

The examinations showed that the concentration of total phospholipids and lecithin increases whereas the concentration of noradrenaline decreases in the lungs of the fetal rabbit in the course of pregnancy. The dopamine content, on the other hand, showed no change. These results have confirmed the findings of other reports on the role of the adrenergic system in maturation of pulmonary tissue [13, 17]. It should be emphasized that our lecithin values did not differ considerably from the data of other workers who used alternative techniques of lecithin estimation [18, 19]. Similar observations were done by Hallman and Raivio [18] and Hayden et al [19] in lungs of rabbit fetuses on the 27th and 30th days of gestation, respectively. Administration of betamimetics was found to intensify the observed changes, i.e. to stimulate the maturation of lung tissue.

Decrease of noradrenaline concentration when the dopamine concentration is relatively high, improves the blood supply to the lungs. Like in the placenta, dopamine decreases the blood vessel resistance and thus increases the pulmonary blood flow [26]. High concentrations of dopamine when the noradrenaline content is low, are observed in placenta and lungs i.e. the organs where the blood flow plays an essential part. Improvement of the blood supply in the lungs ensures the adequate metabolism of the lung tissue which is reflected by an increased concentration of total phospholipids. The decrease of the noradrenaline concentration may be explained by the effect of fenoterol on the endogenous inhibitor of dopamine, beta-hydroxylase [25].

The obtained results confirmed the hypothesis that application of betamimetics in the treatment of prematurity simultaneously serves the prevention of neonatal respiratory disturbances.

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