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Changes in Hemodynamics and the Temperature Regime in the Mother-Placenta-Fetus System under the Influence of Some Drugs.

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Key Words: *maternal-placental blood flow; rabbit fetuses; temperature gradient*

At the present time the complicated problem of the physiological regulation of placental blood circulation, being a theoretical basis for the therapeutic improvements of the conditions of fetal vital activity, is being widely investigated. In spite of numerous new data in this field, the influence of the drugs being used for maternal-placental blood flow (MPBF) correction on the temperature homeostasis of the fetus and consequently, on the rate of its metabolic processes has not ben sufficiently studied.

The purpose of the present investigation was to study the physiological correlation between maternal blood circulation, its temperature homeostasis, maternal-placental blood flow and temperature homeostasis of normally developed (ND) and developmentally delayed (DD) fetuses after the administration of rheopolyglucin, trental, and their combination to the mother.

MATERIAL AND METHODS

Two series of experiments were carried out. In the first, in 49 chinchilla rabbit females on the 18th day of pregnancy a placental insufficiency was created by tying about 1/3 of the preplacental blood vessels near each fetus receptacle in one horn of the uterus; the other horn was left intact for control. On the 28th day of pregnancy during a second uterine section under thiopental narcosis, a plastic catheter for venous pressure measurement was inserted into the jugular vein of the female and electrodes were introduced into the spinal muscles of the fetus for the recording of electrocardiograms (ECG). To the collecting veins of both horns of the uterus platinum wire measuring sensors were applied in a plastic sleeve for maternal blood flow registration. The recording of the curves of hydrogen clearance was carried out by the method of polarography [2]. For saturation of the organ with hydrogen the inhalation of the gas by the female via a mask during 1 min was used. The ECG recording of the female and the fetuses was carried out on a Bioskript electroencephalograph. The venous pressure was recorded with a pressure-measuring instrument. A semi-conductor transformer with PDP-21000 MD and PDP-400 tensoresistors developed by the All-Union Research Institute of Medical Instrumentation was used as the pressure sensor.

In the second series of experiments in 47 rabbit females on the 18th day of pregnancy placental insufficiency was created by the method described above. On the 28th day of pregnancy the second uterine section was carried out, during which electrodes for ECG recording and a thermocouple for the continuous registration of the body temperature in the rectum were introduced into the fetuses. On the next day after the operation the multichannel graphic record with an accuracy of 0.01°C was performed of the rectal temperatures of the fetuses and the female with the aid of the recording device, and simultaneously the synchronous record of the ECG of the female and the fetuses was carried out on a Bioskript electroencephalograph.

The preparations were administered to the female in the following dosages: rheopolyglucin 1.7 ml/kg of body weight, trental 20 mg/kg.

RESULTS

A comparative analysis of the two series of experiments conducted showed that the infusion of rheopolyglucin into rabbit females causes an increase in the blood flow rate in the uterus, the degree of the increase being greater in the case of placental insufficiency (14.4±2.1%

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higher in comparison to the initial level). The venous pressure in the female rose on the average by 30.2±6.3% vis-a-vis the initial level (Fig.1). The body temperature rose in some animals and correspondingly their fetuses, while in others it dropped. The temperature gradient (TG) between fetus and mother increased (Fig.2) independently of the tendency of changes in their body temperature, the degree of the increase being greater in the case of DD in comparison with ND (on the average by 11.5±4.1 and by 6.5±2.8%, respectively). In DD fetuses (weighing 33.4±1.45 g) moderate bradycardia was observed whereas in ND fetuses (weighing 39.1±1.4 g) the systolic frequency (SF) did not change reliably.

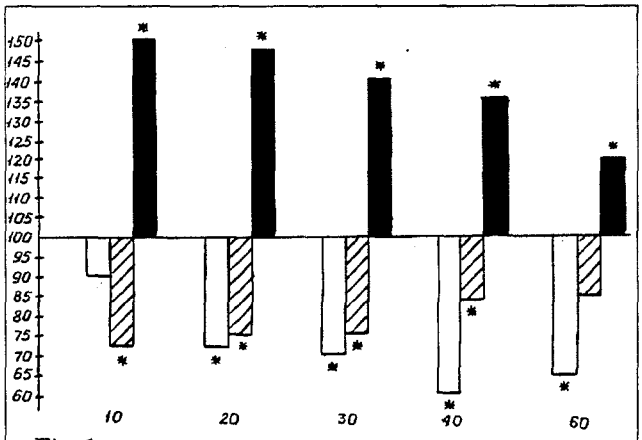

Fig. 1

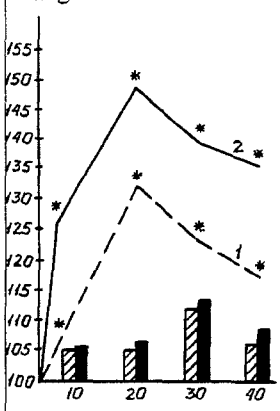

Fig. 2

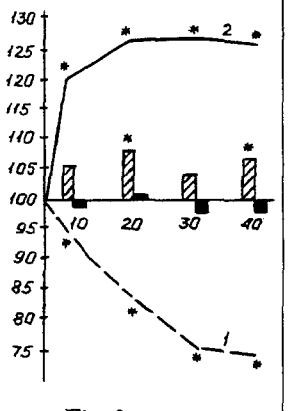

Fig. 3

Fig. 1. Changes of venous pressure after infusion into the females of rheopolyglucin (black columns), trental (white columns), and trental with rheopolyglucin (shaded columns). Ordinate axec: percentage; figures below, time (min). Asterisk marks reliable changes of indicators in comparison with initial level ($p<0.05$).

Fig. 2. Changes of blood flow rate in uterus and of gradient between temperatures in rectal cavity of fetus and mother after the infusion of rheopolyglucin into the female. Shaded columns: temperature gradient in normally developed fetuses and mother; black columns: temperature gradient in developmentally delayed fetuses and mother. 1) blood flow in intact horn of uterus, 2) blood flow in experimental horn of uterus. Other designations as in Fig. 1.

Fig. 3. Changes of blood flow rate in uterus and of gradient between temperatures in rectal cavity of fetus and mother after combinated injection of trental and rheopolyglucin into the female.

After the administration of trental alone and in combination with rheopolyglucin the blood flow rate in the uterus changed nonuniformly in dependance on its initial level. After the infusion of trental in the case of higher initial values of the blood flow rate (322.4±42.5 ml/100g·min) it dropped on the average by 21.3±3.4%, while in the case of lower values (235.3±27.7 ml/100 g·min) it increased by 23.8±4.4%. After the combined application of trental with rheopolyglucin an analogous dependence upon the initial blood flow was observed (both before and after the injection of trental alone), but the degree of the blood flow increase was 9.2±2.8% higher, and the degree of the blood flow decrease was 10.1±3.2% lower, than in the case of the injection of trental alone. The venous pressure in the female dropped by 18.6±4.4% after the infusion of trental alone as well as after its combination with rheopolyglucin (see Fig. 1). At the same time the TG between DD fetuses and the mother did not change reliably, while in the case of ND fetuses it increased by 7.5±2.2% (Fig. 3). This is because in DD fetuses the rate of the body temperature drop coincides with that of the mother, while in the ND fetuses it is slower. The SF in both groups after the infusion of trental and trental in combination with rheopolygucin rose: in ND fetuses (weighing 40.2±0.8 g) by 5.4±1.3%, and in DD fetuses (weighing 33.6±0.9 g) by 6.3±2.1%.

Thus it was revealed that the changes in the MPBF caused by the infusion of drugs into the female lead to changes of TG between the fetus and the mother, reflecting the rate of the feto-placental blood flow, and therefore the intensity of the heat transfer of the fetus. Under normal conditions the gradient between the body temperature of fetus and mother is more or less constant. It is known that a rise in the body temperature of the fetus and the increase of the gradient between the temperature of fetus and mother are as a rule connected with disturbances in MPBF [3,4].

After the infusion of rheopolyglucin the TG increases, the degree of the increase being greater in the case of developmentally delayed than in normally developed fetuses. The following assumption can be made to explain this difference: the increase of the venous pressure in the female which usually develops after the injection of rheopolyglucin, combines with the increase of the pressure in the maternal part of the placenta. Obviously the difficulties in feto-placental blood flow are connected with this and lead to a decrease of heat transfer in the fetuses, and consequently to higher values of the gradient between the temperatures of DD fetuses and the mother than between ND fetuses and the mother. This is supported by the fact that in DD fetuses moderate bradycardia is noted, typical for hypoxemia [1] and attesting to a relatively poor adaptation

of these fetuses to changes in the hemodynamics of the maternal organism.

The drop of fetal body temperature observed in our investigations after the injection of trental and trental in combination with rheopolyglucin into the female is connected with increased heat transfer due to a boost of the MPBF more moderate than after the injection of rheopolyglucin, not accompanied by a rise of the venous pressure in the female. The increase of the TG between ND fetuses and the mother is related to the fact that in the case of a high initial blood flow rate in the uterus a drop occurred under the influence of trental and trental in combination with rheopolyglucin, i.e., after the combined infusion of trental and rheopolyglucin the effect of trental prevailed. The drop of the fetal body temperature went along with a qickening of the heart 1rate. Thus, after the infusion of rheopolyglucin, trental, and their combined application in the rabbit females, the changes in fetal heart activity depend more upon the changes in the rate of placental blood circulation, than upon the type of fetal temperature reaction (judging by the absence of a direct dependence between fluctuations of the fetal body temperature and heart rate). The changes in temperature gradient between fetus and mother for different influences on the mother can be used as an indication of the changes in the rate of the maternal-placenta l and interrelated fetal-placenta l blood flow.

Thus, the disturbances in temperature homeostasis of the fetuses for the injection of drugs into the female are due mainly to the changes of the rate of the MPBF, and hence in placental defficiency therapy and in the case of developmental delay of the fetus the possible adverse effect of these drugs on the temperature regime of the fetus and consequently on its metabolic processes must be taken into account.

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Effect of Defensin on Platelet Functional Activity

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Defensins comprise a family of nonenzymatic cation proteins accumulated in the phagocyte granular apparatus of mammals [7]. As established, defensins possess a broad spectrum of antimicrobial, antiviral, and cytotoxic activity and modulate hormonal responses [7, 8, 15]. Human defensin HNP-1 is a strong and

TABLE 1. Effect of Human Defensin (40 μg/ml) on Platelet Aggregation Induced by Thrombin, Collagen, and ADP (M±m)

Parameter	Thrombin, 0,5 U/ml (9)		Collagen, 4mkg/ml (7)		ADP, 5 mkM (5)	
	control	defensin	control	defensin	control	defensin
Aggregation amplitude, %	83,0±5,8	43,0±5,1*	51,9±7,6	39,3±9,4*	74,0±2,7	51,5±2,1*
Maximal rate of aggregation, %/min	99,5±12,0	78,7±7,8	74,3±7,5	52,4±6,4*	42,6±6,0	26,8±5,8

Note: Here and in Table 2 figures in parenthesis denote the number of experiments; values with $p < 0.01$ (in comparison with control) are marked with an asterisk.

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