Studies on Closure of the Ductus Arteriosus in Perinatal Rats

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ABSTRACT. Measurements of the inner diameters (calibers) of the ductus arteriosus (DA) and pulmonary artery (PA) were made in late fetal rats and newborn rats, the latter being obtained by spontaneous or caesarean delivery. The fetal and newborn pups were frozen instantly with an acetone-dry ice mixture. The chests of these whole-body frozen pups were shaved with a surgical knife gradually from the back toward the ventral side to expose the DA and PA for measurements of their calibers. As a result, it was revealed that the DA was almost closed 180 min after birth, but that the closure and shirinkage of the DA were accelerated to some extent by caesarean delivery. On the other hand, there was no remarkable change in the PA throughout the postnatal period observed, regardless of the type of delivery, spontaneous or caesarean.

---KEY WORDS: ductus arteriosus, perinatal rat, pulmonary artery.


The ductus arteriosus (DA) conducts most of the blood from the pulmonary artery (PA) to the aorta during the fetal period. This vessel, different from the PA and the aorta which are both elastic in type, is equipped with the media abundant in smooth muscles as a type of muscular arteries [8]. After birth, with the beginning of respiration, the DA is rapidly closed and transformed into a fibrous cord.

Powell and Cochrane [10] observed the time of normal closure of the DA in the rat using their freezing method and reported that the DA was completely closed by 85–98 min after birth. However, their results were based on macroscopic estimation, not on morphometric data.

The present work was designed to observe chronologic changes in the inner diameters of the DA and PA from the late fetal to the early neonatal period in the rat, by comparing the pattern of closure of the DA between neonatal pups of spontaneous delivery and those of caesarean delivery. Observation was made by a method of shaving whole-body frozen pups with a surgical knife and observing them under a dissecting microscope.

Female Wistar rats, 12–15 weeks old at the time of mating, were used in this work. They were maintained on a commercial diet (Labo MR Breeder) and tap water ad libitum and were kept at a room temperature of 22±3°C and a relative humidity of 55±10%. The females were placed with males overnight and examined the next morning for the presence of sperm in the vaginal smear. The day on which sperm was found was designated as day 0 of gestation, and the females were caged individually from this time.

Male fetuses and newborn pups were used. Observation and calibration of the DA and PA before birth were performed on days 18, 19, 20 and 21 of gestation. As regards observation after birth, neonatal pups were picked up at the time of witnessed delivery. They were used for observation 10, 30, 60, 90 or 180 min later. Those pups which were cyanotic and did not breathe were excluded. Besides, in order to observe changes in premature newborn pups, some pregnant rats were subjected to caesarean section on day 21 of gestation. The way of observation in these caesarean newborn pups was the same as in the spontaneous newborn pups. All the pups were kept in a chamber at 37°C prior to observation.

Exposure of the DA and PA was carried out as follows: Each fetus or newborn pup was instantly immersed in an acetone-dry ice mixture. The frozen animals were stored for a few days at −20°C prior to observation. The calibers of the DA and PA were determined by the method described by Arishima et al. [1]. Briefly, under a dissecting microscope the chest of each frozen pup was shaved with a surgical knife from the back toward the ventral side to expose the exact site where the DA was completely separated from the aorta (Fig. 1). At this site, the DA was calibrated with an ocular micrometer. By further shaving beyond the DA, the left and right branches of the PA joined together. At this site, the PA was calibrated (Fig. 1).

Analyses of the data between two adjacent experimental stages were made with Student’s t test. A P value less than 0.05 was considered to be significant.

The data are summarized in Fig. 2. During gestational period, the DA was steadily increased in caliber from days

---Fig. 1. Diagrammatic representation of a chest, showing the level (broken line) at which the DA was observed and the level (solid line) at which the PA was observed. E=esophagus; H=heart; T=thymus; TA=thoracic aorta.
18 to 21 (Figs. 3–6). On days 20 and 21, the DA was situated close to the thymus (Figs. 5, 6). The PA was also constantly increased in caliber until day 21, and its caliber appeared about the same as that of the DA.

The DA, 10 min after witnessed delivery, was significantly expanded as compared with that on day 21 of gestation, and 30 min after birth, declined to a size comparable to that on day 21 of gestation. This decline was more marked 60 min after birth in such a way that the wall of the DA was thickened and appeared whitish. In addition, the inner diameter of the DA was clearly decreased rather than that before birth. Thereafter, the DA was further decreased in caliber until 180 min after birth when it was almost closed. On the other hand, there was no remarkable change in the PA throughout the postnatal period observed, regardless of the type of delivery, spontaneous or caesarean.

Following caesarean delivery, the DA was abruptly decreased in caliber until the time 90 min after birth when the DA was almost closed with its thickened wall (Fig. 8). In addition, the inner diameter of the DA was clearly decreased even 10 min after birth. The DA had been completely closed 180 min later.

The foregoing observation revealed that after spontaneous delivery, the DA was still slightly patent at the time 90 min, but that it was almost closed at the time 180 min. However, after caesarean delivery, the DA was almost closed at the time 90 min. Furthermore, the DA was inversely widened in caliber 10 min after spontaneous delivery, whereas it was narrowed 10 min after caesarean delivery. Thus, the closure and shrinkage of the DA seem to be accelerated by caesarean delivery. The reason for this acceleration is unknown at present. Also, the reason why the DA is once widened shortly after birth is unknown. Our observation that the caliber of the DA 30 min after spontaneous delivery was comparable to that before birth is almost in harmony with the finding of Powell and Cochrane [10] in that the DA did not begin closing until 16–20 min after birth. However, according to their observation, the time of closure of the DA was 85–98 min after birth, earlier than our observation showing the closure 180 min after birth. Powell and Cochrane [10] placed animals in an environment at −29°C for 12–25 min, and then opened their chests upon removal from the cold environment and observed the DA directly. Thus, the discrepancy between their result and ours may be due to the difference in the method of freezing and in the way of observation.

Various lines of evidence indicate that the gradual distension of the DA during fetal period is due to the action of prostaglandins [2, 3, 6, 11–13]. Therefore, the cessation of supply of maternal transplacental prostaglandins is seemingly a factor responsible for closure and shrinkage of the DA after birth, if no allowance is given to prostaglandins produced by neonatal animals themselves. In relation to this, it has been reported that corticoids block the process of biosynthesis of prostaglandins [7, 9]. In fact, the treatment of pregnant women near term with glucocorticoids initiates a premature constriction of the fetal DA [14].
Fig. 3. Showing the ductus arteriosus (DA, arrow) of a fetus on day 18 of gestation. The aorta (arrow head) is seen anterior to the DA. × 10.

Fig. 4. Showing the DA (arrow) of a fetus on day 19. × 10.

Fig. 5. Showing the DA (arrow) of a fetus on day 21. The DA is situated close to the thymus. × 10.

Fig. 6. Showing the DA (arrow) of a fetus on day 21. × 10.

Fig. 7. Showing the DA (arrow) of a newborn pup 180 min after spontaneous delivery. The DA is almost closed and its wall is thickened and appears whitish. × 10.

Fig. 8. Showing the DA (arrow) of a newborn pup 90 min after caesarean delivery on day 21 of gestation. The DA is almost closed as seen in Fig. 7. × 10.
Just before and after birth by spontaneous delivery in the rat, there is a great increase in plasma corticosterone concentrations in fetal and newborn pups [4]. Similarly, in premature newborn pups delivered by caesarean section, the plasma corticosterone concentrations are elevated soon after delivery [5]. These results would constitute a hypothesis that the elevated corticosterone concentrations block the biosynthesis of prostaglandins, eventually resulting in the constriction of the DA after birth. However, this hypothesis is lack in preponderance of evidence to be introduced by further proper and discreet experiments.

REFERENCES