Dilatation of the Ductus Arteriosus by Diazoxide in Fetal and Neonatal Rats

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Keywords

Diazoxide · Ductus arteriosus · Rat

43.1 Background

We previously reported that ATP-sensitive potassium (K_{ATP}) channels regulate ductal constriction in response to oxygen [1]. Diazoxide is a K_{ATP} channel opener while the usefulness of diazoxide for hyperinsulinemic hypoglycemia is well established. Yoshida et al. reported DA reopening in very low-birth-weight infants [2]. The objectives of this study were to elucidate the effect of K_{ATP} channel openers on the DA in neonatal rats as well as the different effects in preterm and full-term fetal rats [3].

43.2 Methods

Near-term rat pups delivered via a cesarean section were housed at 33 °C. After rapid whole-body freezing, the ductus arteriosus (DA) diameter was measured using a microscope and a micrometer. Full-term pregnant rats (gestational day 21) were

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intraperitoneally injected with diazoxide (10 and 100 mg/kg) 4 h before delivery, and the neonatal DA diameter was measured at 0, 30, or 60 min after birth. The newborn rats were also intraperitoneally injected with diazoxide (10 and 100 mg/kg) at birth or 60 min after birth. DA was measured at 0, 30, or 60 min after injection. In the fetal study, *constricted by COX and NOS inhibition* the *dilating* effects of diazoxide was studied by simultaneous administration of indomethacin (10 mg/kg) and L-nitroarginine methyl ester (100 mg/kg) in gestational day 21 and 19.

43.3 Results

DA closure was delayed in rats exposed to prenatal diazoxide. Both doses of transplacentally administered diazoxide induced significant and dose-dependent inhibitory effect in postnatal DA constriction. Intraperitoneal injection of diazoxide at 60 min after birth induced DA reopening in a dose-dependent manner.

Diazoxide (10 mg/kg) dilated the fetal DA in both near-term and preterm fetal rats. The effect of diazoxide in dilating the DA at preterm was the same as at full-term fetal rats.

43.4 Conclusion

K_{ATP} channel openers attenuate postnatal DA constriction and dilate a closing DA in neonatal rats. If the DA is affected in a similar manner in human neonates, then PDA could be warranted for use with K_{ATP} channel openers to treat infants with hyperinsulinemic hypoglycemia, especially preterm infants.

References

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