91 SILDENAFIL CITRATE MODIFIES FETOPLACENTAL DEVELOPMENT IN A RABBIT MODEL OF INTRAUTERINE GROWTH RESTRICTION


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Abstract

The failure of fetuses to achieve their full growth potential is known as intrauterine growth restriction (IUGR). Sildenafil citrate (SC) is a phosphodiesterase 5 (PDE-5) inhibitor, which enhances nitric oxide (NO)-dependent vasodilatation, and may have a potential therapeutic role in the treatment of IUGR. The aim of this study was to evaluate the effect of SC on placental and fetal development in a diet-induced rabbit model of IUGR. A total of 24 rabbits does weighing 4.3 ± 0.49 kg on average were used. At Day 9 of pregnancy, females were randomly allocated into 3 experimental groups: one group was fed ad libitum during pregnancy (Group C; n = 8); the rest of the does had 50% restricted daily intake and were treated or not with 20 mg of SC daily from Day 22 of pregnancy until parturition (Groups SC and R, respectively, n = 8 for both). At Day 28 of pregnancy, half of the pregnant does from each group were euthanised to study fetoplacental development, while the remaining does were allowed to deliver. At Day 28, weight, length, and thickness of fetal and maternal placentas, and fetal weight and size [crown-rump length (CRL), and transversal thoracic diameter (TD)] were assessed. A fetus was considered IUGR when it weighted less than the 10th percentile for its normal gestational weight. Statistical analysis was performed using the PROC GLM procedure. Nutritional restriction induced a higher rate of fetuses IUGR than control group (31.0% vs. 15.1%; P < 0.05). The percentage of fetuses with IUGR was 23% in SC group (no significant differences with groups C and R). However, SC increased the thickness of maternal and fetal placentas compared to group R (0.4 ± 0.02 v. 0.2 ± 0.02 cm; 0.6 ± 0.02 v. 0.3 ± 0.02 cm; P < 0.05 respectively), being similar to group C (0.4 ± 0.02 and 0.5 ± 0.03 cm). Maternal placental weight in group C showed higher values (1.5 ± 0.08 g; P < 0.05) than both restricted groups (1.2 ± 0.07 g). CRL in group SC was larger than in group R (10.5 ± 0.12 v. 10.0 ± 0.12 cm; P < 0.05) and similar to that in group C (10.5 ± 0.15 cm). The neonates in group SC showed higher values for CRL (10.9 ± 0.15 cm) than those from groups R and C (10.5 ± 0.11, 10.2 ± 0.20 cm; P = 0.05). Regarding TD, fetuses in group SC showed higher values than group R (2.3 ± 0.04 v. 2.1 ± 0.03 cm; P < 0.05) and equaled that of group C (2.3 ± 0.03 cm). In conclusion, maternal malnutrition prejudices fetoplacental development, causing IUGR. Treatment with SC in the last third of gestation counteracts fetal growth retardation by favouring placental development and function and, thus, fetal growth. These results confirm that administration of SC may have a potential benefit in pregnancies complicated by placental insufficiency and IUGR.

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