

## INSULIN-LIKE GROWTH FACTOR TREATMENT OF PREGNANT GUINEA PIGS DURING EARLY PREGNANCY PROMOTES FETAL GROWTH

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Insulin-like growth factor (IGF)-II is an important regulator of growth in many tissues and is abundantly expressed in the placenta during pregnancy. Gene ablation studies performed in mice have shown that IGF-II deficiency results in both impaired fetal and placental growth, whereas deficiency in IGF-I reduces fetal growth only. Conversely, maternal IGF supplementation in early pregnancy in the guinea pig increases placental and fetal size by mid pregnancy. This study aimed to determine whether these anabolic effects persist into late pregnancy after cessation of treatment. On Day 20 of pregnancy, mothers were anaesthetised and a mini osmotic pump was implanted subcutaneously, to deliver 1mg/kg/day IGF-I ( $n = 7$ ), IGF-II ( $n = 9$ ) or vehicle ( $n = 7$ ) for 17 days. Guinea pigs were killed on Day 62 of pregnancy (term ~67 days). Fetal and placental weights, and maternal and fetal body composition, were measured. Total litter size was unaffected by IGF treatment; however, IGF-II increased the number of viable fetuses by 26% ( $P = 0.01$ ). After adjusting for the number of viable pups per litter, maternal IGF treatment increased fetal growth by increasing abdominal circumference, crown-rump length and fetal weight (fetal weight: IGF-I  $79 \pm 2.5$  g; IGF-II  $78 \pm 2.6$  g; vs vehicle  $68 \pm 2.5$  g,  $P = 0.02$ ). IGF treatment did not alter absolute or relative fetal organ weights. IGF-I reduced placental weight by 9% and IGF-II increased it by 9%, but not significantly. IGF-I increased the fetal weight : placental weight ratio ( $19 \pm 0.9$  vs  $15 \pm 0.9$ , respectively  $P = 0.043$ ). IGF treatment did not affect maternal weight gain during pregnancy nor net carcass weight; however, IGF-I reduced maternal lung and adipose tissue weights. In conclusion, maternal IGF-II treatment during early pregnancy improved fetal growth into late gestation, possibly by modulating placental efficiency. As poor placental development is implicated in fetal growth restriction, increasing maternal IGF abundance in early to mid pregnancy may be a potential therapeutic approach to placental insufficiency.