Metformin, a biguanide derivative molecule discovered from *Galega Officinalis* (trench lilac) for its hypoglycemia properties. Metformin is a drug used during pregnancy in the treatment of type 2 diabetes and disorders associated with insulin resistance including PCOS (Polycystic ovary syndrome). Few studies have investigated the consequences after an *in utero* exposure to metformin.

**AIM**

The aim of the present study was to assess the effects of maternal metformin administration during pregnancy on the fertility of male offspring mice.

**Experimental design**

- **Offspring birth**
  - Menstrual cycle
  - Metformin treatment at 300mg/kg/d
- **Gonad analysis or mating**
  - D0
  - D25
  - D90
- **Puberty**
- **Adult**

**Fertility of male offspring**

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In *in utero* exposure to metformin resulted in a 25% reduction in male fertility when mated to untreated females (*P*<0.05) n=8.

**Figure 1:** Experimental design Metformin was administered via water at 300mg/kg/d during the entire period of pregnancy. Control mice were provided with untreated water. Fertility analysis was then performed on the male offspring.

**Figure 2:** Number of pups per litter from control and *in utero* metformin exposed males. *In utero* exposure to metformin resulted in a 25% reduction in male fertility when mated to untreated females (*P*<0.05) n=8.

**Figure 3:** Metformin exposed males had a reduction in seminiferous tubule diameter (*P*<0.05) n=225 tubules.

**Figure 4:** Metformin exposed males had a reduction in germ cell number per seminiferous tubule (*P*<0.05) n=40 tubules.

**Figure 5:** Similar phenotype where found between males Sc-AMPK +/- exposed to metformin *in utero* & Sc-AMPK -/- and males exposed to metformin *in utero* had more sperm with a thin head (*P*<0.05) n=7 males.

**Figure 6:** In *in utero* exposed males had lower LH concentrations in the pituitary. Exposed adult males presented with significantly more visceral adipose tissue (*P*<0.05) n=6 males.

**Conclusion**

*In utero*, metformin exposure has consequences on the fertility of male offspring, mainly by affecting testis development, seminiferous tubules diameter, germ cells number & the quality of sperm. Together these results complete Tartarín et al 2012 data which shown a negative effect on ability of fetal murine and human testis explants to secrete testosterone after metformin exposure and complete the *in vitro* results from Bertoldo et al., 2014 which have demonstrated a direct effect of metformin on spermatozoa.