## P-356 Oral administration of sodium tungstate to a swine model improves embryo implantation rate

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**Study question:** Does sodium tungstate treatment improve embryo implantation and therefore, fertility in large mammals?
**Summary answer:** Oral administration of sodium tungstate increases embryo implantation and reproductive efficiency in large mammals.
**What is known already:** Sodium tungstate (ST) has shown its capacity to modulate critical molecules in the embryo implantation process. ST showed a positive effect on PCOS-like model to restore ovulation and fertility. Moreover, ST proved to act directly on the endometrium to increase embryo adhesion in *in vitro* assays. There is an inherent difficulty in studying implantation using *in vivo* models due to the close communication between ovary, embryo and endometrium. For the current study, the Large-White swine breed has been selected because of its high efficiency in ovulatory and fertilisation processes, minimising low embryo quality interferences in the implantation process.
**Study design, size, duration:** A randomised, blinded, prospective, placebo-controlled study was performed to evaluate ST effect on fertility, ovulation, and embryo implantation rates in swine, which is characterised by a high fertilisation rate but a limiting implantation rate. Forty-four primiparous Large-White sows (8 months old) were orally-treated with ST or placebo for 44-46 days, from 10 days prior to starting a progestin-based treatment for ovulation induction to gestational days 11th-13th (i.e., the window of implantation in swine). Participants/materials, setting, methods: Animals were randomised in treatment groups based on body weight ranges and housed individually in temperature-controlled conditions. 2.5g ST (diluted in 5ml of distilled water) or vehicle were once-daily orally administered with a syringe. Sows responding to ovulation-induction protocols were inseminated with high-quality sperm from untreated pigs and euthanised at gestational days 28-30 (1st pregnancy trimester) to recover genital tracts. Pregnancy, number of ovulations, number of viable/non-viable implanted embryos and fetal measurements were immediately recorded.
**Main results and the role of chance:** All 44 sows involved in the study responded to ovulation induction and were inseminated, but 4 females were excluded from the study because of uterine anatomical abnormalities (unicornuate uterus) or abnormalities during pregnancy. Hence, 19 ST-treated and 21 placebo sows were eligible.There were no differences in pregnancy rate (pregnancy was observed in 17 ST-treated sows 19 placebo-treated sows; 89.47% and 90.48%, respectively) or number of ovulations (21.5±4.1 vs 21.8±2.9 in placebo and treated animals, respectively; p=0.300). However, implantation rate was significantly improved in ST-treated animals, since the number of implanted embryo was found to be increased by 15% per sow in the ST-treated group; which means two additional good-quality embryos per sow (16.5±3.2 in the ST group vs 14.4±3.9 in the placebo group, p<0.05). The percentage of viable implantations, calculated as the number of viable embryos divided by the total number of viable and non-viable implanted embryos was also increased by the ST treatment (91.6±7.9 vs 96.2±4.7 in treated vs placebo groups, p<0,05). Finally, there were no effects of the treatment on the foetal phenotype, body mass and size.
**Limitations, reasons for caution:** The current study is the first attempt to evaluate ST effect on reproductive outcomes, in healthy large mammals. Having in mind that the selected model is high reproductive efficient, further studies assessing ST effects in infertile and sub-fertile mammals should be performed to elucidate ST activity in suboptimal fertility conditions.
**Wider implications of the findings:** Sodium tungstate treatment proves, for the first time, the improvement of fertility in healthy large mammals. Sodium tungstate treatment improves endometrial implantation and therefore, fertility efficiency. Thus, after subsequent further research, sodium tungstate may become a potential treatment for improving embryo implantation, an unmet medical need.
**Trial registration number:** not applicable