MICE MODEL FOR INVESTIGATION OF THE GONADOPROTECTIVE EFFECT OF THE GNRH ANALOGUES DURING CHEMOTHERAPY: IS IT RELEVANT?
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Background: Thanks to their ability to inhibit ovarian folliculogenesis, Gonadotropin Releasing Hormone analogues (GnRHa) have been proposed to reduce gonadotoxic effect of the chemotherapy. However, their efficiency is still debated and the underlying mechanisms are poorly understood. In this study, we evaluated the relevance of mice model to further study the potential mechanisms of ovarian protective effect of the GnRHa during chemotherapy.

Material and methods: Mice were daily injected with various doses (2, 20, 200 and 500µg/kg) of GnRH agonist (triptorelin) or antagonist (cetrorelix) subcutaneously or intramuscularly for 15 or 21 days. For some experiments, cyclophosphamide (200 mg/kg based on dose response curve) was injected ip on day 14. Mice estrous cycles were daily observed by vaginal smears. The ovarian reserve was evaluated by follicular count. Folliculogenesis was evaluated by calculating growing follicles ratio and by immunohistology (TUNEL, Ki67).

Results: While GnRHa are efficient to inhibit the estrous cycle, they failed to inhibit follicular development whatever the doses and the injection sites. Around 25% of growing follicles were still observed after treatment. Immunohistology confirmed the viability of these follicles. At the chosen dose, cyclophosphamide induced around 45% of follicular depletion as earlier as day 1 and no difference was observed when mice were co-treated with GnRHa.

Conclusion: Theses results suggested that GnRHa don’t inhibit the pituitary-gonadal axis in mice as effectively as in human. Hence, we can wonder if this mice model is appropriate to investigate the indirect mechanisms of protection of the GnRHa on the ovarian function during chemotherapy.