Comparison of the Protective Effect of Dapagliflozin and Empagliflozin on Cisplatin-Induced Ovarian Toxicity in Female Rats

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Introduction

- Cisplatin is a widely used chemotherapeutic agent known for its gonadotoxic effects due to oxidative stress and inflammation. SGLT2 inhibitors, including dapagliflozin and empagliflozin, exhibit antioxidant, anti-inflammatory, and antiapoptotic properties that may mitigate these effects

Aim

- To compare the protective effects of dapagliflozin and empagliflozin against cisplatin-induced ovarian toxicity in female rats using biochemical, molecular, and histopathological markers.

Study Design

Control Group:

Rats in this group received dimethyl sulfoxide (DMSO) at a concentration of 2% orally once daily for 14 consecutive days. This group served as a negative control to account for any potential effects of the vehicle (DMSO) used in the treatment groups.

Cisplatin Group (CP only):

- Animals received a single intraperitoneal (IP) injection of cisplatin at a dose of 7 mg/kg on day 14 of the experiment. This group was used to induce ovarian toxicity and serve as a positive control for cisplatin-induced damage.

Study Design

- Dapagliflozin + Cisplatin Group:
- Rats were administered dapagliflozin orally at a dose of 1 mg/kg once daily for 14 days. On the final day (day 14), they received a single IP injection of cisplatin at 7 mg/kg. This group was designed to assess the potential protective effect of dapagliflozin against cisplatin-induced ovarian toxicity.

- Empagliflozin + Cisplatin Group:
- Animals received empagliflozin orally at a dose of 10 mg/kg daily for 14 days, followed by a single dose of cisplatin (7 mg/kg, IP) on day 14. This group aimed to evaluate the potential protective role of empagliflozin in cisplatin-induced ovarian damage

Biomarkers Evaluated:

- Oxidative stress (MDA, GSH)
- Inflammatory cytokines (IL-6, TNF-α via RT-PCR)
- Hormones (FSH, Estradiol, Progesterone)
- Apoptotic markers (Caspase-3, by Western blot)
- Histopathological examination of ovarian tissue

Results

- **Ovary Weight**: Cisplatin reduced ovarian weight, while both dapagliflozin and empagliflozin preserved it, with dapagliflozin showing slightly better results.
- **Oxidative Stress**: MDA levels increased and GSH levels decreased in the cisplatin group. Treatment with both drugs improved these markers, especially dapagliflozin.
- **Inflammation**: TNF-α and IL-6 were upregulated with cisplatin but reduced with treatment, with a more notable effect from dapagliflozin.

Results

- **Hormones**: Cisplatin reduced progesterone and estradiol levels and elevated FSH. These effects were reversed by both drugs, indicating protection of ovarian function.
- **Apoptosis**: Caspase-3 expression increased in the cisplatin group. Both drugs reduced their levels, with dapagliflozin showing a stronger antiapoptotic effect.
- **Histology**: Ovarian damage was evident in the cisplatin group. Treated groups showed improved tissue structure and reduced degeneration

Conclusion

- Both **dapagliflozin** and **empagliflozin** have attenuated cisplatin-induced ovarian damage. Their antioxidant, anti-inflammatory, and antiapoptotic properties suggest potential as **protective** agents in chemotherapeutic ovarian toxicity, with dapagliflozin showing a slight better efficacy.


THANK YOU