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Dapagliflozin attenuates anxiolytic-like behavior of rats in open field test

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BACKGROUND

- Anxiety disorders, currently the most prevalent psychiatric disorder, cause a high social impact and economic burden. They are often are co-morbid with a variety of medical conditions including neurological and cardiovascular illnesses, with resultant major reduction in quality of life. Until now, benzodiazepines, anti-depressants such as selective serotonin reuptake inhibitors and tricyclic acids are used to treat anxiety disorder, yet, they also produce many systemic side effects associated with their usage.
- Numerous neural pathways are involved in the pathophysiology of anxiety disorders. These pathways include the monoamines: 5-hydroxytryptamine (5-HT), noradrenaline, dopamine and a number of unrelated compounds that are known to provoke anxiety in humans [1,2]. Thus, the search for newer anxiolytic medicines continues to be a priority in drug discovery.
- Sodium-dependent glucose co-transporter 2 (SGLT- 2) inhibitor (canagliflozin) is used for type 2 diabetes. SGLT- 2 treatment has been shown to significantly decreased noradrenalin levels and significantly increased dopamine and serotonin levels in diabetic rats after 4 weeks of treatment. Dapagliflozin is a SGLT- 2 inhibitor and shows similar mechanism of action to canagliflozin [3].

METHOD

- Male Sprague Dawley rats (250-300 g) were divided into Control (distilled water), dizaepam (2 mg/kg), dapagliflozin (1 mg/kg), groups (n= 7-10 in each).
- Open field test (OFT) was applied 60 min after per oral. drug administrations. Rats were placed on the central square and allowed to explore the apparatus for 5 min. The following anxiety-like behaviours were scored: time spent in the central area, exploration (number of line crossing); displacement (number of grooming behaviour); the number of rearings (vertical activity) [1,2,4].
- One-way analysis of variance (ANOVA) was used for statistical analysis followed by Tukey's test.

RESULTS

- Data showed that in comparison with the control group, dapagliflozin (1 mg⁄kg) increased the total time spent in the center of the apparatus, similarly to diazepam ($p < 0.05$). Rats treated with 2 mg/kg diazepam expressed low grooming when compared to the control group ($p < 0.05$), dapagliflozin was also decreased grooming but there were no significant rearing in OFT between groups.
- There were no significant differences in the number of crossing and rearing in OFT between groups.

CONCLUSION

- Our results showed that dapagliflozin and diazepam increased the total time spent in the center and also reduced the total number of grooming in OFT, an indicative of anxiolytic effect.
- Dapagliflozin may be modify various neurotransmitter systems because numerous neural pathways are involved in the pathophysiology of anxiety disorders.
- The present results could be of interest for further studies aimed to investigate the effect of dapagliflozin on relevant behavioral in anxiety in accordance with the efforts for highlighting the molecular mechanisms driven this effect.

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