Exposure to Diazepam during Pregnancy Alters the Breathing Control in Post-Natal Life

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Introduction: Breathing is an important motor behavior that contributes to the maintenance of homeostasis. This behavior depends on the proper development of respiratory network located in brainstem that generates and controls the respiratory rhythm during the embryonic and post-natal ages. The development of this network can be affected by the use of psychiatric medications prescribed to mothers to treat general anxiety or panic disorders. One of the most common drugs prescribed is Diazepam (DZP), a benzodiazepine that binds to gamma-aminobutyric acid ($GABA_A$) receptors enhancing the permeability of chloride channels. However, it is still unknown if the administration of DZP during pregnancy could have deleterious effects on breathing control during post-natal life.

Objective: To understand the consequences of intrauterine exposure to DZP on the ventilatory responses of newborns rats,

Material and Methods: We administered DZP (1mg/Kg) or its vehicle, via osmotic pump, to pregnant rats during whole pregnancy (21 day). We used newborns rats (male and female) at post-natal day 0 (P0) and P12. Ventilation (V_E), tidal volume (V_T), respiratory frequency (fR) and oxygen consumption (VO_2) were measured by using head-out plethysmograph during 20 minutes of normocapnia, hypercapnia (7% CO_2) and hypoxia (10% O_2).

Results: At P0, females treated with DZP had an attenuation of V_T during hypoxia. At P12, males and females presented a decrease on V_E during hypoxia and V_E/VO_2 was lower in DZP-treated animals. At this age, hypercapnic ventilatory response was also reduced in DZP groups due to an attenuation of V_T.

Conclusions: DZP during pregnancy promotes a decrease in ventilatory responses to CO_2 and O_2 in males and females, and this disturbance occurs at P12 that is considered the critical period for breathing control.

Keywords: Diazepam, pregnancy, breathing control, animal

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