Int. J. Morphol.,
33(3):962-970, 2015.

The Effects of Progesterone on Hypoxic Ischemic Injuries in the Cornu Ammonis (CA) Region of the Hippocampus of Neonatal Rats

Efectos de la Progesterona en Lesiones por Hipoxia Isquémica en la Región Cornu Ammonis (CA) del Hipocampo en Ratas Neonatas

Aaijaz Ahmed Khan[*]; Norhida Binti Ramli[**] & Zulizhar Mohd. Ismail[*]

KHAN, A. A.; RAMLI, N. B. & ISMAIL, Z. M. The effects of progesterone on hypoxic ischemic injuries in the cornu ammonis (CA) region of the hippocampus of neonatal rats. ***Int. J. Morphol., 33(3)***:962-970, 2015.

SUMMARY: Hypoxia-ischemia (HI) is a major cause of brain damage in the newborn. Several studies elicited the neuroprotective effects of progesterone in adult rats but there is very little literature available on neonatal rats. Therefore the present study is undertaken to see the effect of progesterone in hypoxic ischemic brain injury in neonatal rats, using an established neonatal HI rat pup model. Seven-day-old rat pups were subjected to right common carotid artery ligation and then 60 minutes hypoxia. The first dose of progesterone to treatment group was administered by peritoneal injection (4 mg/kg), after 10 minutes of exposure and subsequent doses were given by subcutaneous injection at 6 h, 24 h and 48 h intervals. Control group was also exposed to HI and was given only the vehicle (peanut oil) through the same route and intervals as that of treatment group. After 96 h, the pups were perfused with 10% formalin and brains were sampled and stained with toluidine blue. Cells density and number of pyramidal cells of the hippocampal Cornu Ammonis (CA) regions were examined by stereological methods. The histomorphometric assessment of the effects of progesterone showed minimal but no significant protective value in the volume, cells density and total number of pyramidal cells of hippocampal CA region of the treatment and control groups ($p>0.05$) after HI. Our results concluded that 4 mg/kg of PROG had no significant neuroprotective effect in HI model of the neonatal rat's hippocampus.

KEY WORDS: Cornu Ammonis; Hippocampus; Hypoxia; Ischemia; Neonatal rats; Neuroprotective; Progestrone; Pyramidal cell.

INTRODUCTION

Birth asphyxia occurs when there is inadequate oxygen supply to the neonate just before, during and after birth. Hypoxic ischemic encephalopathy is the outcome of severe birth asphyxia which subsequently may lead to permanent irreversible neurological damage. Current protocols for managing this problem are mostly supportive and treatment is carried out only for its complications. Several neuroprotective agents are still under studies and most of the studies were done on animal.

Progesterone is a steroid hormone with known effects on woman reproductive system. Recent advances have revealed its neuroprotective effect against brain injury in adult rats (Jiang *et al*., 1996, Chen *et al*., 1999; Shear *et al*., 2002; Sayeed *et al*., 2007; Cai *et al*., 2008). In these studies, progesterone was proved to reduce the cortical infarct volume, brain edema and even functional deficit in the rats with induced brain injury. One particular clinical trial on human has actually proven that there is a significant protective effect of progesterone in traumatic adult brain injury (Wright *et al*., 2007).

Despite the new current technology in medical field, birth asphyxia is still one of the leading causes of neurodevelopmental abnormalities and permanent handicap (Volpe, 2008). Thirty percent of them develop seizures and twenty percent of them with moderate encephalopathy develop cerebral palsy (Volpe). The mortality and morbidity

[*] Department of Anatomy, School of Medical Sciences, Universiti Sains, Penang, Malaysia
[**] University Malaysia Sarawak, Sarawak, Malaysia.
The study was carried in Department of Anatomy, PPSP, USM, Kempus Kesihatan, Kubang Kerian- 16150, KotaBharu, Kelantan, Malaysia in the year 2010-11 with the help of short term grant (304/PPSP/61310033) from Universiti Sains Malaysia.