Research Article

Histological changes in the hippocampus of adult male albino rats following aluminum chloride administration: evidence of aluminum induced neurotoxicity

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Abstract
Background: Aluminum (Al), one of the metals with easily gain access to the nervous system through its presence in a lot of manufactured foods, medicines and drinking water.
Aims: This study was designed to demonstrate the effects of Aluminum chloride ($Alcl_3$) administration on rat hippocampus. **Materials and Methods:** The control group received distilled water orally while the $Alcl_3$ group received 100 mg/kg body weight/day of $Alcl_3$ orally for 42 days. Hippocampi were prepared for histological assessments using hematoxylin and eosin (H&E) stains. **Results and Discussion:** $Alcl_3$ group showed histopathological changes in rat hippocampus including pyramidal neurons degenerative changes with congestion of the blood capillaries. **Conclusion:** This study provides strong evidence for the neurotoxic action of $Alcl_3$ on the rat hippocampus.
Abbreviations:
Aluminum chloride: $Alcl_3$, Aluminum: Al, cornu ammonis: CA.
Key words: Aluminum chloride, neurotoxicity, neurodegeneration, hippocampus

Introduction

Aluminum (Al) is considered as the most abundant metal in the earth's crust and ubiquitously present in every food product (Majumdar et al., 2014). Aluminum chloride ($AlCl_3$) is present in many manufactured foods and medicines and is also, added to drinking water for purify-cation purposes (Ghoneim et al., 2015). It is also documented to be one of the ingre-dients of antacid drugs and to present in food additives and tooth paste (Abbasali et al., 2005). The hippocampus is considered as the earliest brain region to be affected by these pathologies (Alawdi et al., 2017).

Materials and methods

Animals:
A total of 12 adult male albino Wistar rats (150-180 gm) were used in this study.

Materials:
Aluminum chloride ($Alcl_3$) was obtained from Sigma Aldrich Company, Egypt.

Experimental protocol:
The protocol of this study has been approved by the ethical committee of Faculty of Medicine, Minia University. In this study 12 adult male albino rats

weighing 150-180 gm and of 6 weeks were housed in clean plastic cages for two weeks before study. They were fed standard laboratory diet and were allowed free access to water.

Animals were randomly divided into two equal groups (6 rats each): **Group I**: received distilled water by a gastric tube for 42 days and served as control. **Group II**: received 100 mg/kg body weight/day of $Alcl_3$ (Lakshmi et al., 2015) which disso-lved in water by a gastric tube for 42 days.

Sampling and histological study:
All rats were sacrificed at the end of this experiment by decapitation, the brains were

obtained then sagittaly divided into 2 hemispheres using a sharp blade in order to obtain the hippocampal tissues for histological studies using hematoxylin and eosin (H&E) (Suvarna et al., 2013).

Results

Control group revealed that the hippocampus showed the pyramidal neurons of the cornu ammonis (CA) region with vesicular nuclei and prominent nucleoli. In addition, it showed the nuclei of sparse neuroglial cells on a pink neuropil background which formed of processes of neurons and glial cells. Longitudinal section of blood capillary was also noticed (figure 1A). $Alcl_3$ group showed marked distortion of the histological structure. Some pyramidal neurons showed marked shrinkage with pericellular haloes and deeply stained nuclei. Others showed marked vaccuolation of their cytoplasm with deeply stained nuclei. Congested blood capillaries with perivascular vaccuolation were also noticed (figure 1B).

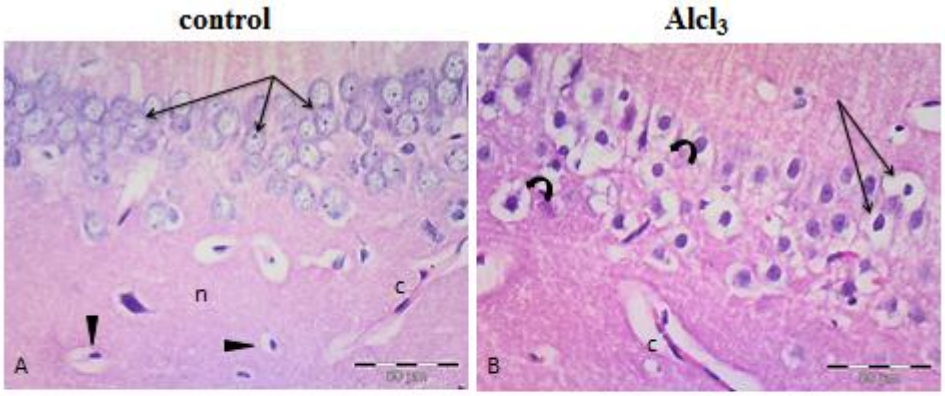

Figure 1: Representative photomicrographs of rat hippocampus showing effect of $Alcl_3$ on the hippocampus:

A) the control group showing pyramidal neurons with vesicular nuclei and prominent nucleoli (arrows), notice the neuropil (n), the glial cells (arrow heads) and the blood capillary (c).

B) $Alcl_3$ group showing shrunken pyramidal neurons (arrows) with peri-cellular haloes and deeply stained nuclei, it also showing swollen neurons with vacuolated cytoplasm and deeply stained nuclei (curved arrows). Notice the congested blood capillary (c) with marked perivascular vaccuolation .

Discussion

Aluminum is found in corn, herbs, tea, yellow cheese, salt, spices, cosmetics, aluminum ware, and containers. It has been reported that Al absorption is enhanced up to four- to five-fold in combination with food or beverage (Majumdar et al., 2014). $Alcl_3$ is thought to have the ability of crossing the blood brain barrier (BBB) (Ekong et al., 2017). $Alcl_3$ is implicated to aggravate oxidative stress and production of pro-inflammatory cytokines and nitric oxide synthase in the central nervous system (Jangra et al., 2015).

In this study, histological examination of rat hippocampus following $Alcl_3$ administration revealed damage of the pyramidal neurons with blood capillaries congestion. These histological results are in agreement with (Qusti et al., 2018) who observed shrunken and deeply stained pyramidal neurons in the hippocampus of rat received $Alcl_3$.

(Ghoneim et al., 2015) reported similar results in addition to blood capillary congestion in rats received $Alcl_3$. These findings provide a strong evidence of chronic inflammation and oxidative damage and (Lynch, 2014). $Alcl_3$ was previously documented to be a potent pro-oxidant which increased lipid peroxides in brain tissues. In addition, it caused disturbance of

iron homeostasis, leading to free iron ions accumulation which consequently lead to oxidative damage which finally cause neurodegeneration. Furthermore, $Alcl_3$ could target mitochondria causing cyto-chrome c release and caspase-3 activation which causing neuronal apoptotic death (Ghribi et al., 2001).

Conclusion

Aluminum chloride has a potent neurotoxic effect on rat hippocampus.

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