The Effects of Formaldehyde on Histomorphometrical Change of Photoreceptor Layer in Rat


Abstract

Our objective of this research investigate the histological effects of formaldehyde on photoreceptor layer. 20 male wistar rats divided into two groups: 1- control group, 2- experimental group was exposed to the 10% formaldehyde for one dose and 7 days after formaldehyde exposure, the eye enucleated and fixed in 4% gluteraldehyde. Histomorphometrical and histological changes showed that the thickness of photoreceptor layer decreased and the major sign of pathology obvious in experimental group. We concluded that the formaldehyde caused severe damage in photoreceptor layer of retina.

Keywords: Formaldehyde, Histomorphometric, Photoreceptor layer, Rat.

Introduction

The photoreceptor layer of retina is light-sensitive layer and important for sight. Formaldehyde is a main colorless chemical agent commonly used as a fixative and biopsy in medical laboratories. Occasionally, accidental formaldehyde injection occurred in surgery room by surgeon. This injection into the retro bulbar is unusual but sometime, confused formaldehyde with lidocaine in surgery. Many studies reported to provide information on formaldehyde toxicity such as skin sensitization, eye and upper air way irritation (Wietek, 1987), nasal carcinoma (Albert, 1982; Kems, 1982), induce specific IgE (Wantke, 2000), oxidative stress in tissue (Matsuoka, 2010), inhibiting memory performance (Lu, 2008).

In addition, formaldehyde reacts with glutathione and oxidized glutathione-dependent formaldehyde dehydrogenase (Just, 2011) to S-Formylglutathion and hydrolyzed to glutathione and formate (Anderson, 2010). The toxicity of formaldehyde included chromosome damage and cellular apoptosis (Tang, 2011). Also, methanol toxicity was indicated through its metabolic intermediate formaldehyde (Lanigan, 2001). Methanol causes severity damage and sign of pathology to the retina (AllaEl-din and Gaward and Amal, 2011).

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The histological change of photoreceptor layer of retina under the effect of formaldehyde has not been investigated. In this research, we used formaldehyde retro bulbar injection to cause damage on photoreceptor layer and histomorphometrical change studied.

Methodology:

20 healthy male wistar rats aged 2 month (250-300 gr) were used in this research.

Animals were kept in a cyclic light (12hr light: 12hr darkness) and temperature (22-24 °C).

All instructions and care of animals were carried out in compatibility with in the Guide to the CALAM Standards of Veterinary Care (Patricia, 2008).

The rats divided into two groups namely control group (N=10) and experimental group (received 1ml, 10% buffer formaldehyde solution by retro bulbar injection for one dose).

Formaldehyde solution (Merk-Germany were made from 40% formaldehyde diluted in distilled water to make 10% buffer formaldehyde solution. The solution kept at 4 °C until used. The eye removed 7 days after formaldehyde injection. Separation and preparation of the retina was described in our previous research (Esfandiari, 2009; Goodarzi, 2014).

The retina separated near the optic disc and placed in 4% gluteraldehyde for 4 hrs. then processed for semi thin section (Omu3; Reichert, Vienna, Austria). The micrometry was evaluated by light microscope.

Statistical significances were determined by paired samples test using SPSS ver 16. The significance level was set at p≤0.05.

Results:

Clinical observation in seven days after formaldehyde retro bulbar injection contain of eyelid edema, scarring and contracture.

The histological study showed that photoreceptor layer consist of outer segment, inner segment, outer limiting membrane, outer nuclear layer and outer plexiform layer in control group. The outer segment contain of rod and cone outer segment and the inner segment is cytoplasm of photoreceptor cell.

The outer nuclear layer included nuclei of photoreceptor cells with scattered heterochromatin (Fig 1).

The sign of pathology were seen in formaldehyde injected group, such as disappeared outer segment, vacuolization in the inner segment and condensed and pyknotic nuclei in outer nuclear layer.

As examined by morphometric technique of the thickness of photoreceptor layer indicated that significant decreased of thickness occurred in experimental group. The mean thickness of the photoreceptor layer was 83.50±3.42 micron in control group and 72.26±2.11 micron in experimental group.

![Fig. 1: Photograph of semi thin section of photoreceptor layer in control group. Retinal pigmented epithelium (RPE), outer segment (OS), inner segment (IS), outer nuclear layer (ONL) and outer plexiform layer (OPL). (×3000).](image)

Discussion:

This investigation showed that the photoreceptor layer damage in ischemia and oxidative stress of retro bulbar formaldehyde injection.

The accidental formaldehyde injection resulted in severe damage to the eye, as the previous case reported (SoltanSanjari and Hashemi, 2004).

Apoptosis is a programmed cell death including nuclear clumping, DNA condensation, cellular shrinkage and macrophage engulfment (Kerr, 1998; Wyllie, 1997).
Fig. 2: Photograph of semi thin section of photoreceptor layer in formaldehyde group. Outer segment loss (OS loss), vacuolated inner segment (IS), outer nuclear layer (ONL) and outer plexiform layer (OPL). Vacuole (thin arrow), condense nuclei (thick arrows) and pyknotic nuclei (arrowheads). (×3000).

Potential initiating signals of apoptosis in nervous system contain of growth factor absence, nitric oxide synthesis, oxygen free radical production and abnormalities of calcium metabolism.

Increasing the calcium may damage by stimulating catabolic enzymes or oxygen free radical production (Choi, 1988).

Oxygen free radical initially damage the mostly unsaturated lipid cellmembranes of neural tissues. Ischemia could initiate any or all of these apoptotic pathways. Ischemia of the eye prevent normal transport of agent such as growth factors. On the other hand, ischemia increased glutamate release, oxygen free radical, nitric oxide and intracellular calcium levels (George and Cioffi, 2005). In addition, the formaldehyde caused vesselocclusion in the eye such as central retinal artery and opthalmicartery (SoltanSanjari and Hashemi, 2004). As well as, formaldehyde caused increase the reactive oxygen species as a consequence of inflammation (Turkoglu ., 2008; Green ., 1989). Reactive oxygen species may cause cell injury (Turkoglu ., 2008; Good ., 1996; Gassen and Youdim, 1997). Therefore the major sign of pathology of photoreceptor layer in this study that corroborated increase apoptosis of ischemia resulted by retro bulbar formaldehyde injection. The measurement of photoreceptor layer decreased in formaldehyde group with significant difference compared with control group (p< 0.05).

Conclusion:
We concluded that retro bulbar formaldehyde injection caused inflammation and damage in photoreceptor layer. These injury due to ischemia and increase the apoptotic pathway.

REFERENCES