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Nephrotoxic effects caused by formaldehyde exposure in rabbits: A histomorphochemical study

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ABS5TRACT

The experiment was conducted to observe the effect of direct exposure of formaldehyde in different concentrations on the physio-anatomy of kidneys. For this purpose, 14 rabbits ageing 3– 6 months were divided into 3 groups; group 1 (n, 6) were exposed to 10% formaldehyde solution for 12 weeks, group 2 (n, 6) to 40% formaldehyde solution for 6 weeks and group 3 (n, 2) served as control. After completion of experimental periods, fresh tissue samples were collected from both the kidneys for the demonstration of enzymes and some part of samples were also preserved in 10% NBF to study histological changes. The present study revealed that after an exposure to 40% formaldehyde solution, there was degeneration of glomeruli and tubular epithelium with necrosis of proximal and distal convoluted tubules. Marked congestion and haemorrhages were also seen in the glomeruli and intertubular blood vessels. There was weak activity of AKPase, ATPase, G-6-Pase, SDH, LDH and G-6-PD, and moderate to strong reaction of NADPH and NADH in the renal glomeruli, proximal and distal convoluted tubules. The alterations in the distribution pattern of phosphatases and oxidoreductases in the rabbit kidney reflects the impairment in the renal functions due to formaldehyde exposure.

Key words: Formaldehyde, Histopathology, Histoenzymology, Kidney, Rabbits

Formaldehyde is a water soluble, colorless gas having pungent and irritating odour. It is widely used chemical primarily in industries and professions including laboratories, hospitals, dispensaries and dentistry (Siegel *et al.* 1983). Anatomists, technicians in embalming and histology laboratories and students during dissection are exposed to formaldehyde. Inhaled formaldehyde is easily absorbed by the upper respiratory tract and is not distributed throughout the body, but its exposure to higher concentration has irritant and allergic potential (Casanova *et al.* 1988). The long term exposure to formaldehyde causes mutagenic effects *in vivo* and carcinogenic effects in experimental animals (Mathur and Rastogi 2007). Although the main target organs of formaldehyde exposure are nasal cavity, trachea, lungs, eyes but chronic inhalation of formaldehyde causes hepatotoxicity (Kamata *et al.* 1997) and nephrotoxicity (Al Ghamdi *et al.* 2003). The present study was undertaken to determine the histopathological and histoenzymic alterations in the kidneys of rabbits exposed to different concentration of formaldehyde for long and short term durations.

MATERIALS AND METHODS

The experiment was conducted on 14 male rabbits of 6–9 months age and were divided into 3 groups; group 1 and group 2 with 6 animals in each group, whereas group 3 had 2 animals as control. These animals were kept in ventilated iron cages and were fed with black gram and green fodder. The rabbits of group 1 were exposed to formaldehyde solution 40% (37– 41% w/v) for 6 weeks and those of group 2 were exposed to 10% formaldehyde solution for 12 weeks. After completion of the experimental periods, both the kidneys from all the animals were collected in 10% NBF solution to examine histomorphological changes. The samples were processed as per acetone-benzene schedule (Luna 1968) and paraffin solution, blocks of sections of 5– 6 µm thickness and were stained with haematoxylin and eosin.

For histoenzymic studies, fresh tissue samples were collected from kidneys and cryostat sections of 10 µm thickness were obtained. The sections were incubated in different substrates for the demonstration of alkaline phosphatase (AKPase), Acid phosphatase (ACPase), G-6-Phosphatase (G-6-Pase) adenosine triphosphatase (ATPase) succinate dehydrogenase (SDH), lactate dehydrogenase (LDH), glucose - 6- phosphate dehydrogenase (G-6-PD), NADPH and NADH ((Barka and Anderson 1963, and Pearse 1972)

RESULTS AND DISCUSSION

The histopathological and histoenzymic observations were

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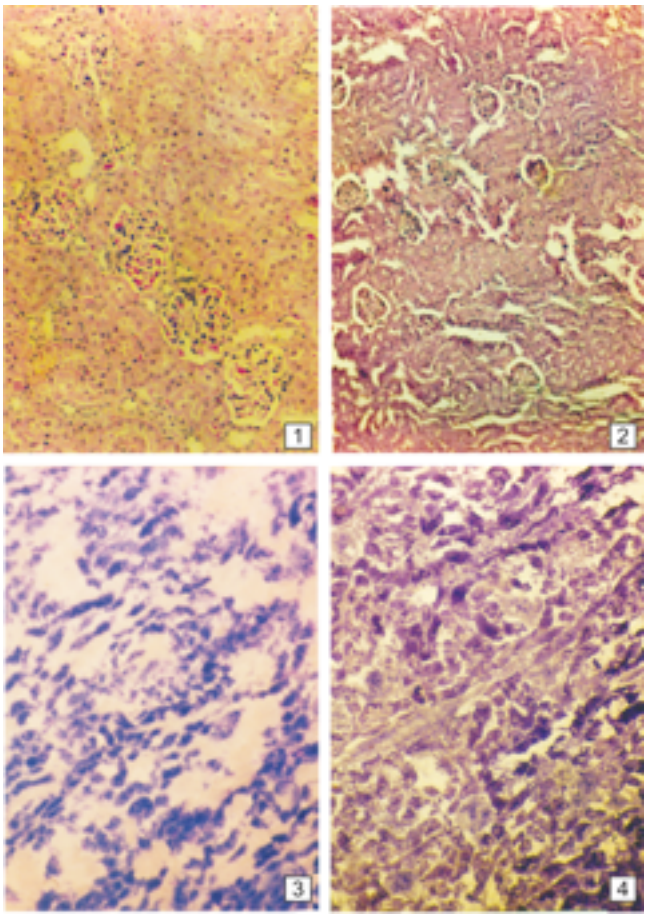

Fig 1. **1.** Degenerative changes in the glomeruli, proximal and distal convoluted tubules of rabbit kidney after an exposure to 40% formaldehyde solution. H & E ×200. **2.** Marked necrosis and lymphomononuclear cellular infiltration in the renal tubules and glomeruli in the animals exposed to 40% formaldehyde solution. Cryostat sections showing H & E ×100. **3.** SDH activity in the rabbit kidney exposed to 40% formaldehyde solution. Nitro BT method × 100. **4.** NADPH activity in the rabbit kidney exposed to 40% formaldehyde solution. Nitro BT method×100.

recorded to correlate the degenerative changes caused by formaldehyde exposure. It was observed that these changes were more remarkable in rabbits exposed to 40% formaldehyde for short duration than those exposed to 10% formaldehyde for longer duration.

Histopathological observations: There was degeneration of glomeruli and tubular epithelium (Fig.1). The congestion and haemorrhages were observed in the glomeruli and intertubular blood vessels and necrosis of proximal and distal convoluted tubules. The capsular space was enlarged due to the degeneration of glomeruli. Lympho-mono-nuclear cellular infiltration was found to be more in the glomeruli than the renal tubules (Fig.2). These changes were observed in group 1, whereas group 2 showed mild degenerative changes in the kidneys. The rabbits of control group showed normal histo-architecture of kidney. Similar changes were observed in the rat kidneys after formaldehyde exposure (Golalipour *et al.* 2009), by cypermethrin toxicity in goats (Tamang *et al.* 1991) and by fenpropathrin toxicity in rats (Bhelonde *et al.* 2004). Kum *et al.* (2010) also noticed the adverse effects of formaldehyde and xylene on the liver and kidneys of rats depending upon the dose and duration of inhalation. It is indicated in the present study that the formaldehyde acted as irritant toxin on the tubular epithelium causing anoxia due to congestion in the blood vessels.

Histoenzymic observations

Phosphatases: There was weak AKPase, ATPase and G-6-Pase activity in the renal glomeruli, whereas ACPase reaction was moderate to strong. The activity of phosphatases was found to be moderate to strong in the proximal and distal convoluted tubules and loop of henle. Histoenzymic localization of different phosphatses showed a more loss of activity in group 1 as compared to group 2. Similarly, Anuradha *et al.* (2004) observed severe loss of G-6-Pase and ATPase activity in loop of henle, collecting tubules and glomerular epithelium in the buffalo kidney due to lead toxicity. The degeneration of cell membrane of renal glomeruli leads to leakage of AKPase into the blood reflecting the loss of enzyme from the glomerular epithelium. The increased activity of ACPase into the degenerating glomeruli may be due to its lysosomal activity.

Oxidoreductases: There was complete loss of SDH, LDH and G-6-PD from the renal glomeruli, however moderate to strong reaction of these enzymes was observed in the proximal and distal convoluted tubules and loop of Henle (Fig.3). The loss of activity was more in group 1 as compared to group 2. The activity of NADPH and NADH was found to be weak in the glomeruli and medullary rays, moderate to strong in the loop of Henle, proximal and distal convoluted tubules (Fig.4). Similar observations have been reported in rabbit kidney after cypermethrin toxicity (Bansal *et al.* 2007). The loss of enzymatic activity from the renal glomeruli may be correlated with its degenerative changes leading to increased cellular permeability which results into the leakage of enzyme into the blood. It was also observed that the toxic effect of formaldehyde was more in the upper segments of renal tubules which may be due to the excretion of toxins and metabolites from the kidney as reported earlier by Nanda *et al.* (1983).

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