HISTOLOGICAL FINDINGS IN KIDNEYS OF MICE FOLLOWING SODIUM FLUORIDE ADMINISTRATION

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SUMMARY: The present study assesses the effect of sodium fluoride administration on kidneys of mice. One hundred adult male Albino mice were fed 10 ppm (Group A), 500 ppm (Group B), and 1000 ppm (Group C) of sodium fluoride for 3 months. Some of the animals from each group were sacrificed at the end of one, two, and three months. The kidneys were removed and stained with hematoxylin and eosin. The most consistent changes in the kidneys were cloudy swelling of the tubular cells. In the higher dosage groups (B and C), sacrificed at the end of three months, we found marked necrosis of tubular cells, atrophy of the glomeruli, and areas of interstitial infiltration of round cells. It is concluded that kidneys are adversely affected by prolonged use of sodium fluoride.

Introduction

Fluorosis, a crippling disease affecting the skeletal system and teeth, is widespread in India and abroad. It occurs from the cumulative action of fluoride consumption over a prolonged period. The most common source is drinking water; others are vegetables sprayed with fluoride-containing insecticides, tea, edible marine animals, drugs, tobacco, detergents, cleansing powder and certain kinds of dust namely, wood, steel, glass, fibre and asbestos (1).

The annual production of fluoride together with the diversity of its use has increased tremendously. Consequently, the hazards associated with it are also increasing. As industrialization progresses, the incidence of industrial fluorosis increases due to deposition of fluoride on the ground, on herbage and due to inhalation of airborne fluoride.

In addition, fluoridation of public water supplies for the reduction of the incidence of dental caries in some Western countries has exposed a large section of the population to fluoride continuously for prolonged periods.

Studies of effects of fluoride on humans have attained, therefore, new dimensions in recent years. The effect of fluoride on hard tissues has been extensively investigated but data on how fluoride affects soft
tissue are lacking. The purpose of the present study was to observe
the effect of fluoride ingestion on the kidney in experimental animals.

**Material and Methods**

One hundred adult male albino mice were divided into four groups,
A, B, C and D, of 25 each. Group A was given drinking water containing
10 parts of sodium fluoride in 1 million parts (ppm) of drinking water
or 10 mg/liter. Group B was given 500 ppm and Group C 1000 ppm. Group
D, as control, received plain drinking water without fluoride.

All animals were sacrificed after 30, 60 and 90 days of fluoride
administration. The animals were anesthetized with chloroform and af-
ter opening the chest cavity were perfused with 10% neutral formalin
through the left ventricle. The abdominal cavity was opened and both
kidneys were taken out. The tissues were freed of their connective
tissue sheet and then sliced to appropriate size and placed in 10% neu-
tral formalin for fixation for one week. The tissues were then washed
under running tap water for 24 hours, dehydrated through ascending
grades of alcohol, cleared in xylene and embedded and blocked in paraf-
fin. Five to 7 micra thick sections were stained with hematoxylin and
eosin.

**Results**

On gross examination the kidneys of the experimental mice (Group C)
appeared shrunken and showed sub-capsular indentation on the surface.
In animals receiving the lowest dosage, the kidneys appeared normal in
shape and color.

On microscopic examination the most constant and characteristic
changes in kidneys were cloudy swelling and degeneration of tubular
cells (Fig. 1). The swollen tubular cells projected into the lumen of
the tubules which reduced the size of the lumen. Some of the tubular
cells showed granular cytoplasm, another indication of cloudy degener-
ation of the tubular cells. Some of the tubules were dilated.

In many areas the edematous tubular cells were broken and their
remnants were seen in the lumen of the tubule (Fig. 1). The nuclei of
most of the edematous tubule were not visible, but those which could
be seen appeared to be pyknotic and were in the process of nuclear de-
generation (Fig. 2). In other areas the nuclei had broken into smaller
fragments or were in the process of being resorbed.

Patchy areas of necrosis of tubular cells were most pronounced in
the highest dosage group (1000 ppm), particularly in the mice which
were sacrificed at the late stages of fluoride ingestion (Fig. 3).

The glomeruli were congested in the lower dosage group (10 ppm),
whereas in the higher dosage animals (500 to 1000 ppm) they appeared
to be atrophic (Fig. 2). In many areas we noted round cell infiltration
of interstitial tissue (Fig. 4). The blood vessels were markedly con-
gested.
Degenerative changes in kidneys were seen in all three groups of experimental animals irrespective of dosage and duration of fluoride administration. Nevertheless the necrotic changes were most marked in the animals fed 1000 ppm fluoride (Fig. 3).
The kidney sections of control animals revealed none of the above-mentioned degenerative changes: The glomerular tuft was normal in shape and structure. Bowmans space was normal. Both distal and proximal tubules were of normal size and structure.

Discussion

The present study confirmed that the kidneys are adversely affected by the fluoride ions. The striking changes were shrunken gross appearance and patchy areas of discoloration. Microscopically, there were areas of cloudy degeneration and necrosis of tubular cells and interstitial areas. The glomeruli were congested, atrophic and hyalinized. The shrunken appearance of the fluorosed kidneys has been described in 1959 by Lindemann et al. (2). Patchy areas of discoloration seemed to result from formation of hemorrhages which were noted microscopically. The microscopic changes seen in the fluorosed kidney in the present investigations are similar to the ones described earlier by Muehlberger (3), Machle (4) and Geiger (5) and subsequently by Roholm (6) and Bond and Murray (7). Certain other investigators (8-11) have also reported necrosis of renal tubular cells and glomeruli, cloudy degeneration and congestion of blood vessels in fluoride-fed experimental rats as observed in the current series.

Infiltration of inflammatory cells in the interstitial tissue of fluorotic kidney has been observed by Phillips (12) in fluorotic dairy cattle, by Ogilvie (9) and Poulson and Ericsson (13) in experimental rats. These lesions are in accordance with the findings of the current investigation which demonstrated round cell infiltration in the interstitial tissue.

Fluoride is excreted through the kidneys (14). Ogilvie noted as early as 1953 that kidneys are severely damaged in fluorotic experimental rats. He presumed that in the presence of toxic levels of fluoride in the blood the tubular structure of kidneys is selectively damaged by its passage. The findings of the present study, showing extensive destruction to the kidneys of fluorotic mice, support the view of the above author and indicate that high blood levels of fluoride are cytotoxic to the tubular cells of the kidneys.

Bibliography


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FLUORIDE BRIEFS

Fluoride induces contractions of isolated coronary arteries of cattle. These contractions are not related to extra-cellular calcium levels. The authors tested a series of pharmacological agents for determination of their spasmolytic action on the contracted vessels.


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