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CORRELATIVE STUDY OF FLUORIDE CONTENT IN URINE, SERUM AND URINARY CALCULI

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ABSTRACT

Fluoride content was measured in 100 urinary stones retrieved by open surgery of stone formers admitted at PGIMS Rohtak and their respective urine and serum and compared with those of healthy individuals. The concentration of fluoride was also measured in the sources of drinking water of these stone formers. The concentration of fluoride was definitely significantly higher in serum ($p>0.01$) and highly significantly higher in urine ($p>-0.001$) of stone formers compared to those of healthy individuals. The content of oxalate in serum and 24 h urine of the stone formers was also measured, which was increased significantly ($p<0.005$ and $p<0.001$) compared to healthy individuals. The concentration of fluoride was probably significantly higher in drinking water of these stone formers than the normal ones. There was a positive correlation between the content of fluoride of urinary stones and urine of stone patients ($r=.88$); stone and serum ($r=.62$); drinking water and stone ($r=.85$) and their urine and serum ($r=.54$); urine and drinking water ($r = .83$) and serum and water ($r = .51$). These results indicate a definite role of fluoride in urinary stone formation.

KEY WORDS

Urolithiasis, Urinary calculi, Calculi, Serum, Urine, Fluoride, Correlation.

Role of fluoride in urolithiasis is a subject of controversy. One group of scientists confirmed its role in stone formation (1, 2), while other denied its any role in urolithiasis (3). A report from New York described that fluoride content vary from nil to 1800 ppm and was not in correlation with stone former's age (4). Li *et al.* from China suggested the inhibitory effect of fluoride on renal stone formation in rats (5). A report from Hyderabad (1) suggested the role of fluoride in the formation of urinary calculi by observing the urinary stone formation in rats by feeding them with high fluoride diet. Verma *et al.* (2) from Rajasthan showed higher concentration of fluoride in serum and urine of stone formers (SF) as compared to non-stone formers (N). A high intake of fluoride provoked nephrolithiasis in tribal higher in endemic area than non-endemic area (6). The aim of the present study is to elucidate the correlation between fluoride content and urolithasis to confirm the role of fluoride in urolithasis.

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MATERIALS AND METHOD

Urinary stones retrieved by surgical operation of 100 urinary stone patients admitted at PGIMS, Rohtak Hospital and their 24 h urine and blood samples and also drinking water consumed by them were collected. 24 h urine and blood samples of 25 apparently healthy adults (non-stone formers as confirmed by their X-ray study) were also collected. The stones, urine and blood samples were pretreated as follow before measurement of their fluoride content.

Pretreatment of stones

Stones were first washed with distilled water, air-dried and powdered in a pestle and mortar. The powder was used for quantitative chemical analysis.

Preparation of stone solution

20 mg of stone powder was dissolved in 2 ml of 6N HCl and the final volume was made upto 5ml with distilled water. The tubes were kept in boiling water bath for 1 h, the tubes were kept undisturbed

for overnight. Supernatant was collected and used for quantitative analysis of fluoride.

Collection and Pretreatment of urine

24 h urine of stone patient and their healthy control were collected in plastic bottles containing 15 ml concentrated HCl and its final pH was adjusted to pH 2.5 and stored at -20°C until use. The pH of urine was adjusted to 7.0 by NaOH at the time of use.

Pretreatment of serum

After keeping at room temperature for half an hr, the blood was centrifuged at 5000 rpm for 15 min and the supernatant was collected and stored at -20°C until use.

Determination of fluoride content

The content of fluoride content in dissolved stone, urine and drinking water was determined by SPADNS colourimetric method (7) and in serum by ion specific potentiometric method (8).

Determination of oxalate content

The soluble oxalate content in serum and 24 h urine was measured by enzymic colourimetric method (9, 10).

The results of fluoride content in urinary stones, serum, urine and drinking water of stone patients were compared with those of apparently healthy persons and correlated using regression equation.

RESULTS AND DISCUSSION

The Table 1 shows the fluoride content in urinary stones, 24 h urine and serum of stone formers compared to normal (apparent healthy). There observations revealed that fluoride content in urine, serum and drinking water was significantly increased as compared to normal. The concentration of fluoride was highly significantly higher in urine ($p>0.001$) and significantly higher in serum ($p>0.01$) and probably significantly higher in drinking water consumed by stone patients ($p>0.05$) as compared to normal. A positive correlation was found between fluoride content in urine and stone (r=0.88), serum and stone (r=0.621), drinking water and stone (r=0.846), urine and serum (r=0.54), urine and water (r=0.831), serum and water (r=0.505).

The maximum fluoride content was found in kidney stones and least in bladder stones in agreement with the earlier report from Udaipur revealing maximum fluoride contents in kidney stones (6) but in contrary with a report from Hyderabad (1), showing maximum fluoride content in bladder stones.

The fluoride contents of urine, serum and drinking water was significantly higher in stone formers as compared to normal. These observations are in agreement with the earlier report from Jodhpur (2), which showed significant increase in fluoride content of urine and serum of stone formers compared to healthy control, but in disagreement with earlier report which showed normal plasma and urinary excretion of fluoride in children having endemic vesicle stones (3). Earlier a significant correlation between fluoride content of urine and renal calculi was also reported (11). Mean fluoride content in stone was 0.501 ± 0.011 mg/g, which agrees with a earlier report from Hyderabad (1) showing 0.36 ± 0.32 mg/g fluoride content in stone (Table 2).

Although the exact mechanism of fluoride action in calculogenesis is still not clear, one strong

Table 1. Fluoride content in urinary stones, urine and serum of stone formers compared to normal

Type	Urine (mg/l)	Serum (mg/l)	Drinking water (mg/l)	Urinary Stone (mg/g)
N (25)	1.04±0.043	0.025±0.001	0.89±0.01	-
S.F. (100)	1.88±001 p < 0.001	1.12±005 p < 0.01	2.3±0.01 p < 0.05	0.5±0.001

Data are Mean ± S.E. p<0.001 - highly significant
p<0.01 - definitely significant p<0.05 - probably significant

Correlation coefficient (r) for fluoride content between

Urine and stone (r=0.88) Urine and serum (r=0.54)
Serum and stone (r=0.6213) Drinking Water and stone (r=0.846)
Urine and water (r=0.831) Serum and water (r=0.505)

Table 2. A comparison of fluoride content in serum, urine and urinary stones from various places in India

Place	Serum (mg/l)	Urine (mg/l)	Stone (mg/gm)	Reference
Jodhpur	N = 0.35±0.09	1.491±0.216		Verma (1990)
	SF = 0.60±0.21	2.481±0.779		
Hyderabad	-	-	SF=0.36±0.032	Anasuya (1982)
Rohtak	N = 0.015±0.003	1.165±0.028	SF=0.501±0.001	Present
	SF = 1.115±0.046	1.788±0.008		

N = Normal; SF = Stone Formers

possibility could be that fluoride being highly reactive anion might be forming insoluble calcium fluoride in the intestine, thereby decreasing the availability of calcium fluoride in the intestine, thereby decreasing the availability of calcium for precipitating as calcium oxalate. This might increase the concentration of soluble oxalate available for absorption. This is supported by a significant increase in soluble oxalate content of serum* (14.95 ± 0.025 µmol/L) and urine** (18.33 ± 0.025 mg/24 h) of stone formers compared to those of healthy individuals (10.72 ± 0.197 µmol/L and 11.74 ± 0.133 mg/24 h respectively) (p* < 0.01 and p** <0.001). The enlarged oxalate pool and fluoride *in vivo* might be synergically acting to increase the oxidative load, which might injured or killed renal epithelial cells providing an opportunity for urinary crystals to attach to the injured site or to be deposited on dead epithelial cells which serves as nidus. Once crystal get an opportunity to aggregate, fluoride would inherently extend its cementing effect (2, 6).

In conclusion, a higher fluoride content in 24 h urine, serum and urinary stones of stone formers and a positive correlation between urine and serum, urine and stone, serum and stone, urine and drinking water, serum and drinking water and stone and drinking water in the present study indicates a definite role of fluoride in stone formation.

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