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RETINOL DEFICIENCY AND URINARY STONE DISEASE : CLINICAL EVIDENCE IS MISSING

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Abstract

Serum retinol levels were studied in : (a) 95, 56 and 43 normal subjects belonging to lower, middle and upper socio-economic groups respectively, (b) 35 adult males suffering from night blindness, (c) 27 subjects with low retinol levels, (d) 8 retinol deficient subjects (e) 17 male infants suffering from overt retinol deficiency, (f) 43 radiologically confirmed stone patients and (g) age and sex matched controls (infants 20; adults 120). The subjects included in groups b to f were clinically and radiologically examined for stone disease. Some inhibitors and promotors of stone disease were estimated in urine in groups b to g. It was found that 68 % of subjects in lower socio-economic group had serum retinol levels between 10 and 19 ug%, and 4% below 10 ug%, but none of them showed any symptoms of retinol deficiency. The subjects included in groups b to e did not show any significant difference in their urine chemistry although oxalate excretion was slightly but not significantly higher in comparison to controls. None of them showed radiological evidence of urinary stones. Thus, our results do not support an association between retinol deficiency and urolithiasis in the population studied.

Key Words: Retinol, nutritional deficiency, stone formers, night blindness, mucoprotein, oxalate.

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Introduction

Nutritional deficiency of retinol has long been suggested in the genesis of urinary calculi and the notion continues that retinol deficiency causes sloughing of epithelium which might serve as a nidus for stone formation (Nath et al.1984; Valyasevi and Dhanmitta, 1977). This claim, though frequently repeated, remains unsubstantiated. Ravi Kumar and Anasuya (1988) observed that rats fed high calcium plus retinol devoid diet developed calcium oxalate predominant bladder calculi as compared to 20% rats consuming high calcium diet. The former group also had lower urinary inhibitory activity and raised excretion of oxalate and uric acid. Some workers have proposed that retinol deficiency increases calcium absorption in the intestine and decreases calcium reabsorption from renal tubules (Bichler et al. 1984; Ferrando et al. 1979). In recent years, some other changes have also been proposed in retinol deficiency such as increased production of acid mucopolysaccharides and uromucoids (Bichler et al. 1984). However, conclusive evidence about the relationship between stone disease and clinical or subclinical retinol deficiency is critically missing from literature, and to the best of our knowledge, the relationship between urinary stone risk factors and retinol deficiency in humans is unexplored thus far. The present paper reports data in these respects.

Material and Methods

Selection of subjects. Seven categories of subjects were selected for this study: (a) Ninety five (18-57 years), 56 (18-50 years), 43 (18-50 years) normal subjects belonging to lower, middle and upper socio-economic groups respectively, with no retinol deficiency symptoms or history/complaints of stone disease, (b) Thirty five adult males (18-50 years) suffering from night blindness, (c) Twenty seven adult males (22-38 years) with low retinol levels, (d) Eight retinol deficient adult males (28-38 years), (e) Seventeen male infants (0.5-2 years) suffering from overt symptoms of retinol deficiency, (f) forty three radiologically confirmed upper urinary tract stone patients

TABLE 1 : Serum Retinol Level and Urine Chemistry of Adults with Low Retinol Level, Retinol Deficient Adults and Patients Suffering from Night Blindness and Comparable Controls

Parameters	Control (n - 120)		Adults with low Retinol Level (< 20 µg/dl) (n - 27)		Retinol Deficient Adults (< 10 µg/dl) (n - 8)		Patients Suffering from Nightblindness (n - 35)		Stone Patients (n - 43)	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Serum Retinol (µg/dl)	24.8	0.6	17.3	0.3*	9.4	0.16*	17.1	1.1*	21.2	2.3
Urine (mmol/g Cr)										
Oxalic acid	0.46	0.06	0.49	0.02	0.52	0.04	0.62	0.05	0.63	0.04*
Calcium	4.02	0.39	3.76	0.08	3.74	0.12	4.15	0.33	4.63	0.24
Phosphorus	28.2	2.73	23.5	0.65	21.8	0.97	23.8	2.01	17.83	1.66*
Uric acid	3.43	0.55	2.76	0.13	2.46	0.17	1.89	0.15	5.28	1.94
Magnesium	3.10	0.36	2.94	0.15	2.51	0.13	2.86	0.34	2.75	0.27
Citric acid	3.49	0.44	2.82	0.21	2.82	0.16	1.99	0.21	1.23	0.14*
Mucoprotein (mg/g Cr)	98.9	7.06	93.8	3.25	113.5	18.05	280.2	44.5	108.32	11.54

* P < 0.001; Cr - Creatinine

(32 males, 11 females; 25-30 years) and (g) age and sex matched controls comparable to groups b to f (infants 20; adults 120).

Investigative protocol. The subjects included in groups b to f were clinically and radiologically examined for the presence of stone disease. Night blindness was clinically examined by a fundus test. Groups c to e were examined for retinol deficiency by various methods (clinical symptoms such as Bitot's spot, Cytology impression and Rose Bengal dye test). 5 ml of blood were collected from all subjects for analysis of retinol in duplicate. Twenty four hour urine samples of stone formers and random urine samples of subjects in group b to e and the respective controls were collected.

Methodology. Serum samples were analysed for retinol (Natelson, 1971). Urine samples were analysed for creatinine, phosphorus, mucoprotein (Natelson, 1971), calcium (Gindler and King, 1972), uric acid (Caraway, 1955), and citric acid (Rajagopal, 1984). Oxalic acid was estimated by colorimetric procedure described by Hodgkinson and Williams (1972) which is comparable to other standard methods (Scurr et al. 1985). Qualitative analysis of stones removed from stone formers was carried out by wet chemical analysis (Lloyd and Oldroyd, 1983).

Statistical evaluation was done by applying student's 't' test.

Results

Figure 1 shows the serum retinol level of subjects belonging to different socio-economic groups, stone formers and retinol deficient infants.

The urine chemistry of subjects in group b to e did not show any significant difference from controls (Tables 1 and 2). The oxalate and mucoprotein excretion was slightly, but not significantly, higher in retinol deficient

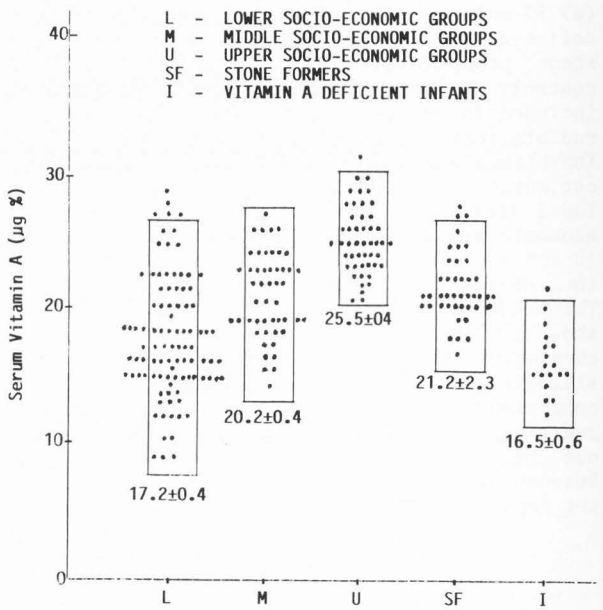

Fig. 1 : Serum Vitamin A Levels in Different Socio-Economic Groups, Stone Formers and Infants with Vitamin A Deficiency.

groups where as in stone formers oxalic acid was significantly higher and citric acid was significantly lower than controls. Table 3 shows the nature of stones qualitatively analysed.

The plain skiagram of KUB region showed that none of the subjects in group b to e had any evidence of stones in the urinary tract.

Discussion

Animal studies have shown that retinol deficiency increases the urinary stone risk, and that in concert with other nutritional

TABLE 2: Serum Retinol Level and Urine Chemistry of Retinol Deficient Infants and Comparable Controls

Parameters	Controls (n - 20)		Retinol Deficient Infants (n - 17)	
	Mean	SE	Mean	SE
Serum Retinol (µg%)	25.2	0.51	16.5	0.60*
Urine (mmol/g Cr)				
Oxalic acid	0.37	0.01	0.40	0.02
Calcium	3.85	0.11	3.53	0.21
Phosphorus	21.23	1.09	20.20	1.29
Uric acid	1.86	0.07	1.75	0.11
Magnesium	7.47	0.36	6.58	0.37
Citric acid	1.45	0.07	1.34	0.08
Mucoprotein (mg/g Cr)	214.7	6.84	245.2	12.7

* $P < 0.001$; Cr - Creatinine

TABLE 3: Qualitative Analysis of Stones

Radicals	Percent Distribution of Radicals		
	+	++	Total
Calcium	32.5	67.5	100.0
Oxalate	34.9	48.8	83.7
Phosphate	62.8	34.9	97.7
Urate	60.4	7.0	67.4
Magnesium	46.5	-	46.5
Ammonium	46.5	-	46.5
Carbonate	23.3	-	23.3
Cystine	-	-	-
Xanthine	-	-	-

+ Radical in Traces; ++ Predominant Radical
(Renal - 33; Ureteric - 7; Renal + Ureteric - 3)

imbalances can produce stones, but so far no evidence is available to prove that retinol deficiency alone can result in stone formation. Even the clinical studies are far from clear. Rahman and Van Reen (1981) observed lower intake of retinol in both stone formers and normal children but did not find any definite evidence of its involvement. Loutfi and Hamid (1977) in Egyptian population and Aurora (1977) in Indian population also did not find any correlation between retinol deficiency and stone disease. On the other hand, Sadre and Ziai (1977) observed significantly lower levels of retinol in stone patients (winter months - 11.2 µg% and summer months - 15.8 µg%) as compared to normal (35.6 µg%).

Nutritional deficiencies are very common in local population. To search out a link, if any, between retinol deficiency and stone disease in this population we have examined different sets of subjects. In our series, none of the affluent subjects had retinol level below 20 µg% but 42.9% and 68.0% of middle and lower socio-economic group subjects had levels below 20 µg% yet none of them showed any signs and symptoms of stone disease, although as per World Health Organization criterion for developing populations, these subjects fell in retinol deficient category. Similarly, patients suffering from night blindness, and retinol deficient infants did not show any radiological evidence of stone in any part of urinary tract. Although 62.9% of night blindness cases and 11.8% retinol deficient infants had levels above 20 µg% but none of them took vitamin supplements as per their or mothers' statement.

The urine chemistry of retinol deficient groups did not show any significant difference from controls but the oxalate and uromucoid (except group c) excretion did fall in the direction that suggested a very mild increase in stone risk. In stone formers, the oxalate excretion was significantly higher. We have observed hyperoxaluria as one of the commonest factor in stone formers from different regions of India (Singh et al. 1990, Hussain et al. 1987, Singh et al. 1987a and 1987b, Singh and Singh, 1987). Both dietary and endogeneous oxalate appear to contibute to urinary oxalate (Singh et al. 1972, Pendse and Singh, 1986 and Singh et al. 1985, Singh et al. 1987a) and higher excretion of oxalate is not related to lower intake of dietary calcium in local population (Singh et al. 1990).

Stones are usually mixed type in local patients but majority of these contain preponderance of calcium oxalate and phosphate (Hada et al. 1989). The present series is no exception to it. Six patients had retinol levels below 20 µg% but their stones did not show any special physical or chemical characteristics.

All the retinol deficient infants and adults included in this study also suffered from varying degrees of malnutrition. We have also observed that the energy and nutrient intake in rural populations especially tribals are surprisingly very low due to economic constraints yet the prevalence of stone disease is comparatively low (Singh et al. 1990).

A single cause, except in case of genetic errors, is rare to initiate the birth and growth of stone. With the advent of modern investigative technology, it is possible to pin point primary and secondary risk factors in the majority of patients. On the basis of our present and past data we are more inclined to believe that nutritional deficiencies including that of retinol may not be the primary cause of stone disease in local populations.Nevertheless, since such deficiencies beyond a certain degree do increase the stone risk, there is a strong possibility of their abettor behaviour in nephrolithiasis.

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Discussion with Reviewers

W.G. Robertson: The mean oxalate excretion of patients with nightblindness is as high as that of the stone-formers. Is there no evidence of increased stone formation in that group ?

Authors: There was no radiological evidence of stone formation in any of the patients with nightblindness.