ASSOCIATION OF CHANGES IN THE PATTERN OF URINARY CALCULI IN TAIWANESE WITH DIET HABIT CHANGE BETWEEN 1956 AND 1999

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**Objective:** Due to rapid economic development over the past four decades, urinary stone components may have changed in Taiwan. We studied the changes in urinary stone components over time and the possible association with dietary changes during the same period.

**Materials and Methods:** From 1956 to 1999, 9,715 urinary calculi were collected at a single institution and analyzed using polarizing microscopy. Dietary information was obtained from an official national report. Linear regression was used to analyze the possible correlation between the change in stone components with daily consumption of animal protein, vegetable protein, and lipid.

**Results:** Eleven distinct components were identified. Calcium oxalate (Jensen type I stone; found in sterile, acidic urine) was found most frequently (87.3%), and its incidence increased gradually with time. However, the incidence of Jensen type III stone (caused by metabolic abnormality) gradually decreased from 1956 to 1999. The male to female ratio among subjects was 2.3:1, and the modal age was in the forties. Female patients were more likely to suffer from type II stones (found in infected, alkaline urine), whereas type I and III stones were more prevalent in males. Among the dietary components, consumption of animal and vegetable proteins and lipid increased significantly during the same period, and appeared to be coincident with the increased incidence of type I stones during the study period.

**Conclusions:** Patterns of urinary tract stones in Taiwan have progressively changed in the past four decades and are now similar to those in western populations. The incidence of type I stones has increased during the past four decades, which may reflect the Westernization of dietary habits in Taiwanese during the same period.

Urinary tract stone is a disease of antiquity that has afflicted humans from ancient times till now. However, its exact etiology is not fully understood. Both intrinsic and environmental factors are considered to contribute directly to urinary calculi formation [1]. Analysis of urinary calculi is mandatory to design adequate treatment, prophylaxis, and metaphylaxis for urinary tract stone. There is evidence of different stone patterns in industrialized and developing countries [2].

Taiwan has been undergoing transformation from a developing country to an industrialized one in the last three decades, and Taiwanese have Westernized their lifestyles during this period. However, whether the composition of urinary calculi has changed as a result of dietary changes accompanying this transformation remains unclear.

Taiwan is a stone-belt country, and urolithiasis is among the most common urologic diseases. In 1995, it...
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accounted for about one-fourth of the inpatients and 7% of all new outpatients at the urologic clinics of National Taiwan University Hospital (NTUH), a major hospital in Taiwan (J Chen, unpublished data, 1995). The purpose of this study was to determine the type, composition, and anatomic sites of urinary calculi, and their relationships with daily nutrition consumption in patients treated at NTUH during the period from 1956 to 1999.

Materials and Methods

From 1956 to 1999, a total of 9,715 urinary calculi were analyzed at the urinary stone laboratory of NTUH. Most patients (88.79%) were between 20 and 69 years old and the mean age was 48.7 years. The calculi specimens were obtained by either spontaneous passage or surgical removal from 6,973 male and 2,922 female patients (male:female = 2.3:1). There were 4,285 renal stones, 3,442 ureteral stones, 1,742 vesical stones, and 246 urethral stones. The stone specimens, either as a whole or in fragments, were well cleaned and dried. Roentgenography was used to localize the nucleus in larger stone specimens. Thin sections of stone specimens including the nucleus were examined by polarizing microscopy (Olympus BH-2 model, Tokyo, Japan) [3]. When the specimens were powder-like, such as when harvested from the urine after extracorporeal shock wave lithotripsy, sand-like fragments were dried. Roentgenography was used to localize the nucleus in the stone specimens. Thin sections of stone specimens including the nucleus were examined by polarizing microscopy (Olympus BH-2 model, Tokyo, Japan) [3]. When the specimens were powder-like, such as when harvested from the urine after extracorporeal shock wave lithotripsy, sand-like fragments were directly mounted with Canada balsam and examined using polarizing microscopy. One gross and one microscopic photo was maintained as a record for each patient.

Identification of the stone components was performed by one author using two methods. First, components found in the stone specimens were calculated directly. Second, stone compositions were classified according to Jensen’s classification system [4]. Based on its major composition, each stone specimen was counted only once in one of the three categories. Type I stones were defined as those found in sterile and acidic urine, type II stones in infected and alkaline urine, and type III stones resulted from metabolic abnormalities.

The changes in stone composition with time were analyzed and were compared between male and female patients. Dietary information was obtained from the Taiwan food balance sheet (1956–1999) [5]. The correlation between daily consumption of protein and lipid in the general population and the changes in stone components during each 5-year interval from 1956 to 1999 were analyzed using linear regression.

Results

The following components were found in the urinary stones: calcium oxalate dihydrate (weddelite), granular and radiant subtypes of calcium oxalate monohydrate (whewellite), apatite, ammonium magnesium phosphate hexahydrate (struvite), calcium hydrogen phosphate dihydrate (brushite), magnesium hydrogen phosphate trihydrate (newberyite), uric acid in both granular and radiant forms, urates (such as ammonium acid urate and sodium urate), cystine, xanthine, and matrix substances. Among these, calcium oxalate, especially the granular variety, was the most common (in 87.3% of stones). Phosphates were found in 71.8% of stones, with apatite the most common (65.6%), followed by struvite (8.2%), brushite (0.4%), and newberyite (0.3%). Most stone specimens consisted of more than one component. The most common type of urinary stone was a mixture of calcium oxalate and apatite (Jensen type 1, 68.9%). Uric acid and ammonium acid urate were found in 7.5% and 5.3% of stones, respectively. Cystine (0.2%), xanthine (0.02%), and nonmineralized matrix substances (1.1%) were rare in our specimens.

The annual number of cases of urinary calculi increased gradually and the increase in male patients exceeded that in females (Fig. 1). In order to correct for the different numbers of cases in each 5-year interval, we used the percentage of each stone component in the 5-year interval to evaluate the changes in stone composition from 1956 to 1999 (Fig. 2). Among the three main stone components, the percentage of type I stones (calcium oxalate group) gradually increased, whereas that of type III stones gradually decreased during the study period. The percentage of stone composition showed no obvious difference between our data for 1962 and previously reported data for other countries (Table) [3, 6–10]. However, our results for 1999 showed that the percentage of type I stones increased markedly with reduced type III stone percentage.

An analysis of the relationship between stone composition and sex showed that, among the 6,769 male patients, 5,504 had type I stone (89.9%), 606 had type II stone (8.9%), and 686 (10.19%) had type III stone. Among the 2,919 female patients, 2,093 had type I stone (71.7%), 637 had type II stone (21.8%), and 189 had type III stone (6.5%). Female patients had a significantly higher frequency of type II stone and male patients had a significantly higher frequency of type I and type III stones. Fig. 2 also shows the change in stone components in male and female patients during the past four decades. The frequency of type I stone in male patients, and to a
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lesser extent in female patients, increased with time. The change in the frequency of type II stone fluctuated in both male and female groups before 1980. After that, however, the decrease for male patients with time was more obvious than for female patients. The percentage of type III stones decreased with time in both groups.

The location of various stone components in the urinary tract was evaluated from 1956 to 1999. Results were calculated as the number of stones of a particular type at the anatomic site divided by all types of urinary calculi located at that anatomic site during each 5-year period. In kidney, 73.1% of stones were type I, 16.8% were type II, and 10.1% were type III stone. In the ureter, 85.4% of stones were type I, 9.0% were type II, and 5.6% were type III. In the urinary bladder, 58.3% of stones were type I, 20.7% were type II, and 21.0% were type III. In the urethra, 56.8% of stones were type I, 19.7% were type II, and 23.5% were type III.

The average daily consumption of vegetable protein, animal protein, and lipid per person in Taiwan in each 5-year period between 1956 and 1999 is shown in Fig. 3A [5]. The average daily personal intake of animal protein and lipid gradually increased during the study period, especially lipid. Analysis of the mean value of daily, personal consumption of animal protein and percentage of different stone types in each 5-year interval between 1956 and 1998 revealed a positive correlation between type I stone and animal protein consumption ($r = 0.963$, $p < 0.001$; Fig. 3B). No correlation was found between the other two stone types and animal protein consumption. Significant correlations were also found between type I stones and lipid and

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**Fig. 1.** Mean number of cases of urinary calculi in each 5-year period from 1956 to 1999 at National Taiwan University Hospital.

**Fig. 2.** Annual change in stone components of urinary calculi in each 5-year interval from 1956 to 1999 at National Taiwan University Hospital. M = male; F = female. Jensen’s classification of urinary calculi: Type I = stones found in sterile, acidic urine; Type II = stones found in infected, alkaline urine; Type III = stones caused by metabolic abnormality.
Table. Comparison of stone components by Jensen’s classification in various countries with data from Taiwanese patients

<table>
<thead>
<tr>
<th></th>
<th>Type I</th>
<th>Type II</th>
<th>Type III</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CaOx</td>
<td>CaOx+Ap</td>
<td>Total</td>
<td>Apatite</td>
</tr>
<tr>
<td>(%)</td>
<td>(%)</td>
<td>(%)</td>
<td>(%)</td>
<td>(%)</td>
</tr>
<tr>
<td>Herring (USA, 1962) [7]</td>
<td>0</td>
<td>73</td>
<td>73</td>
<td>8</td>
</tr>
<tr>
<td>Prien (USA, 1974) [8]</td>
<td>33.0</td>
<td>34.0</td>
<td>67.0</td>
<td>6.0</td>
</tr>
<tr>
<td>Westbury (Britain, 1974) [9]</td>
<td>39.4</td>
<td>20.2</td>
<td>59.6</td>
<td>13.2</td>
</tr>
<tr>
<td>Herbstein (Israel, 1974) [6]</td>
<td>14.0</td>
<td>64.0</td>
<td>78.0</td>
<td>12.0</td>
</tr>
<tr>
<td>Yoshida (Japan, 1979) [10]</td>
<td>27.5</td>
<td>42.4</td>
<td>69.9</td>
<td>6.3</td>
</tr>
<tr>
<td>Hsu (Taiwan, 1962) [3]</td>
<td>9.1</td>
<td>49.0</td>
<td>58.1</td>
<td>1.6</td>
</tr>
<tr>
<td>Hsu (Taiwan, present study)</td>
<td>19.9</td>
<td>68.9</td>
<td>88.8</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Jensen’s classification of urinary calculi: Type I = stones found in sterile, acidic urine; Type II = stones found in infected, alkaline urine; Type III = stones caused by metabolic abnormality. CaOx = calcium oxalate; Ap = apatite.

Fig. 3. A) Average daily consumption of animal protein, vegetable protein, and lipid per person in Taiwan for each year during 1956–1988. B) Cross-sectional correlations between daily animal protein consumption and different stone types (%). C) Cross-sectional correlations between daily lipid intake and different stone types (%). D) Cross-sectional correlations between daily vegetable protein intake and different stone types (%). Data of dietary consumption were obtained from an official national report [13]. (○ = type I calculi; △ = type II calculi; □ = type III calculi).
Discussion

Accurate knowledge of stone composition is important in determining appropriate treatment and preventing stone recurrence. Stone analysis is the only way to determine the compositions of urinary calculi. There are many methods of stone analysis, including chemical analysis, roentgenographic diffraction, infrared spectroscopy, polarizing microscopy [7], and scanning electron microscopy [11]. However, for the routine analysis of urinary calculi, any method should be accurate and sensitive enough to allow the identification of a tiny amount of material from many areas of the stone including its macroscopic nucleus, should deal easily with mixtures of two or more components, should be rapid, simple, and convenient, and should be inexpensive. The results of chemical analysis frequently cannot be interpreted, and this is discouraging to both the technicians and physicians involved. Roentgenographic diffraction is time consuming and expensive, and is not well suited to resolving mixtures of compounds or dealing with small samples. Scanning electron microscopy uses expensive equipment and is less cost effective for routine stone analysis. Thus, we used thin-section optic petrography for routine stone analysis. This method is sensitive enough to permit the identification of tiny amounts of material from all parts of the calculus, it is convenient, rapid, accurate, and relatively inexpensive, and it can provide information about the structure and natural history of the calculus. While training and experience with this technique are required, the results correlate very closely with the findings of roentgenographic diffraction.

In this study, we found that the number of patients with stone diseases increased yearly at NTUH (Fig. 1), and this pattern follows the changes in daily personal diet during the period from 1956 to 1999 in Taiwan (Fig. 3A). Taiwan has developed into an industrialized country and the lifestyle has Westernized gradually since 1980. Accordingly, the incidence of type I stones has increased greatly (Fig. 2). Epidemiologic and metabolic studies have implicated intake of a number of nutrients in the etiology of urinary calculi, including high intake of animal protein [12], refined carbohydrates or sugar [13], ascorbic acid, and oxalate, and low intake of dietary fiber. The increasing incidence of calcium oxalate stones can be attributed to the rapid change in the intake of nutrients, especially the increased intake of animal protein. The consumption of animal protein in Taiwan increased four-fold from 1961 to 1990 [5]. Among animal protein, vegetable protein, and lipid, we found that animal protein intake was more significantly correlated with type I stones \((r = 0.963, p < 0.001; \text{Fig. 3B})\) than lipid and vegetable protein. The lower incidence of type II stones remained steady throughout the 44 years, while there was a dramatic decrease in type III stones after 1970; the increased frequency of type I and III stones may be attributed to advances in public health and to changes in dietary habits. However, this study provides only indirect evidence, and a longitudinal cohort study may be necessary to confirm this association.

As shown in Fig. 1, the yearly increase in the number of male patients was greater than that of female patients. This may be because stone components are different in the two sexes. We also found that male patients were more vulnerable to the development of urinary calculi than females, especially for type I stones. Type II stones were more prevalent in female patients, which suggests that female patients are more likely to suffer from urinary tract infection. In contrast, type I and III stones are more prevalent in male patients, suggesting a higher incidence of metabolic disorders in the male patients in our series.

Conclusion

The urinary stone patterns in Taiwanese are now similar to those in patients from Western developed countries, as the lifestyles and dietary habits of Taiwanese have been dramatically Westernized with industrialization since 1980. Accurate knowledge of the composition and structure of urinary calculi has become important because the successful therapies to treat urolithiasis and to prevent recurrence that have become available since 1980 depend on knowledge of stone composition. Thin-section petrography can delineate the structure and composition of all layers including the nucleus, which may be of different composition to the exterior of the stone. This information may be of value in selection of regimens to prevent recurrence.

References

5. Taiwan Food Balance Sheet (1956–1999). Taiwan: Council of Agriculture, Executive Yuan, ROC.