TIME TO DEVELOPMENT OF SYMPTOMATIC URINARY CALCULI IN A HIGH RISK ENVIRONMENT

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ABSTRACT

Purpose: While seasonal variation of stone disease is well described, the time to formation of urinary calculi is unknown. Because southwestern Asia is a high risk environment for stone disease, the date of entry into this region is a definitive beginning to a period of increased risk of urinary calculi. The recent influx of Department of Defense personnel into southwestern Asia provided the opportunity to observe stone disease in a cohort of healthy personnel during a well-defined period of increased risk of stone formation.

Materials and Methods: A database was constructed for all patients presenting with symptomatic urinary calculi to a single military hospital deployed to Kuwait from March through August 2003. Patient demographics, stone characteristics and time to formation of symptomatic urinary calculi were evaluated.

Results: A total of 182 patients were diagnosed with 218 symptomatic stones. Mean time to formation of symptomatic urinary calculi was 93 days with a standard deviation of 42 days.

Conclusions: This study provides unprecedented information about the development of symptomatic urinary calculi in a high risk environment. While unique aspects of the population, environment and medical system created a singular opportunity to study stone disease, the results of this study are applicable to the general population.

KEY WORDS: urinary calculi, ureteral calculi, kidney calculi, physiopathology, military personnel

The phenomenon of the “stone season,” and the link between increased environmental temperatures and increased rates of stone disease is well documented.1 5 While previous publications have reported a 2 to 3-month interval between peak temperatures and peak rates of stone disease, this lag may not be an accurate measurement of time to formation of symptomatic urinary calculi. The majority of published studies are retrospective analyses of environmental and epidemiological data, and because temperatures change gradually through the weeks and months a definitive beginning of the at risk period for stone formation is difficult to define. Without a definitive start point the time to formation of symptomatic urinary calculi cannot be ascertained.

The influx of military and civilian Department of Defense (DOD) personnel into southwestern Asia in support of Operation Enduring Freedom and Operation Iraqi Freedom provided a singular opportunity to observe stone disease in a cohort of healthy people. Aspects of geography, personnel and exposure to risk factors combined to create a cohort that was more standardized than the general population. Southwestern Asia is a high risk environment for urinary calculi where the risk of stone disease developing may be as much as 5 times greater than in other regions of the world.6 9 Therefore, the date DOD personnel entered southwestern Asia began a definitive period of increased risk of urinary stone formation. Military personnel are generally in good health. Before deploying they complete a health questionnaire and are interviewed by a medical provider. Personnel with active medical problems including symptomatic stone disease are treated or excluded from deploying. Finally, deployed DOD personnel are exposed to a similar environment, diet and risk of dehydration. We conducted a historical prospective study to determine the time to formation of symptomatic urinary calculi in patients presenting to a single military hospital in southwestern Asia.

METHODS

Patient accrual. Institutional Review Board approval was obtained to construct a database of patients with symptomatic urinary calculi. All personnel who presented to the 47th Combat Support Hospital (CSH) in Kuwait from March through August 2003 for evaluation, treatment or further evacuation for symptomatic urinary calculi were evaluated by a urologist. The presence of a stone or evidence of a recently passed stone was confirmed by radiographic imaging for all patients in the study. Imaging studies were not repeated if the patient arrived with images adequate to confirm the diagnosis, or was referred by a urologist who included in their medical summary a description of the radiographic findings adequate to confirm the diagnosis and characterize the stone.

Patient demographics and stone characteristics were recorded. Patients were asked the date of the onset of symptoms and medical records, when available, were used for confirmation. Existing military personnel databases were used to verify the date of entry into southwestern Asia. Stone laterality, location, number, size and other pertinent radiographic findings were documented at evaluation. A distant history of stone disease was not exclusionary, but patients...
who had undergone treatment for stone disease in the 30 days before deployment and patients presenting with a second or subsequent stone since arriving in southwestern Asia were excluded from analysis.

Statistical methods. The arithmetic mean and range were calculated for age. Stone size and number were compared using an unpaired Student’s t test with a 2-tailed distribution. Stone locations were compared using the chi-square test of distribution. The interval until symptomatic urinary calculi development was calculated for each patient by subtracting the date of entry into southwestern Asia from the date of symptom onset. Histograms were constructed for the time and date of symptom onset. Standard deviation, mean, median, skew, standard error of skew, kurtosis and standard error of kurtosis were calculated for the interval. The distribution of the interval was evaluated with the Kolmogorov-Smirnov test, which compares the data set to a normal distribution. An insignificant p value from the Kolmogorov-Smirnov test signifies that the data set is not statistically different from the normal distribution. SPSS software (SPSS, Inc., Chicago, Illinois) was used to compute the results.

RESULTS

Patient demographics. From March through August 2003, 182 patients with symptomatic urinary calculi were evaluated by 1 of 2 urologists at the 47th CSH and entered in the database. A total of 14 patients were female, 168 were male and mean age was 33.1 years (range 19 to 59). These findings reflect the younger age and male predominance of the military compared to the general population. United States Army personnel comprised the majority of patients (129) followed by 29 United States Marine Corps personnel, 9 civilians, 8 United States Navy personnel, 2 United States Air Force personnel, 1 United Kingdom Army member and 4 patients whose affiliations were not recorded.

Imaging, stone location, size and laterality. Computerized tomography was the most frequently used imaging modality (105) followed by excretory urography (37), plain x-ray of the kidneys, ureters and bladder (8), and retrograde pyelogram (4). The imaging modality was not recorded for 28 patients. Of the 182 patients with urinary calculi 159 had stones only in the ureter, 5 had stones only in the intrarenal collecting system and/or renal pelvis (renal stones), and 16 had synchronous renal and ureteral stones. Two remaining patients had renal masses in addition to stones. Other findings included a caliceal diverticulum containing stones and contralateral ureteral stone, a ureteropelvic junction obstruction with ipsilateral renal and contralateral ureteral stone, a ureteroceles containing a stone and partial duplication of the ureter with a contralateral ureteral stone.

There were 44 renal and 174 ureteral stones recorded for a total of 218 stones. An additional 8 patients had radiographic evidence of recently passed stones and the location of the ureteral stone was not recorded in 2 patients. There was no side predominance for the renal or ureteral stones. The difference in mean size between right and left side renal stones (9.43 and 6.69 mm, respectively), and right and left side ureteral stones (3.87 and 3.69 mm, respectively) was not statistically significant (p = 0.347 and 0.923, respectively). The difference in size among the locations of ureteral stones (ie ureteropelvic junction, proximal, mid, distal and ureterovesical junction) was also not statistically significant (p >0.1 for all locations). There was a statistically significant predominance of lower ureteral stones. At diagnosis 30% (26 of 86) of right side and 33% (29 of 88) of left side ureteral stones were located in the distal ureter, and 40% (34 of 86) of right side and 45% (42 of 88) of left side ureteral stones were located in the at the ureterovesical junction (chi-square test p <0.05, bilaterally).

Time interval. Of the 182 patients diagnosed with symptomatic urinary calculi 9 were excluded from analysis of the interval. Three were excluded because they were treated for stone disease within the 30 days immediately before deployment, 1 was excluded because he presented with a second stone since arriving in Kuwait more than 2 years earlier, and 5 were excluded because of incomplete dates.

There were 173 patients for whom the date of arrival into theater and the date of symptom onset were known. The time to onset of symptomatic urinary calculi was calculated for these patients and is presented in figure 1. The interval follows a normal distribution with a mean of 93 days, a median of 91 days and a standard deviation of ±42 days. The data are skewed slightly to the right (skew is 0.55, greater than the standard error of skew of 0.372) but are mesokurtic (kurtosis is 0.47, less than the standard error of kurtosis of 0.744). The Kolmogorov-Smirnov test reveals that the time interval approximates a normal distribution (p = 0.2). By comparison the graph of the date of symptom onset follows a random distribution (fig. 2). The histogram of the date of entry into southwestern Asia mirrors the buildup of personnel in support of military operations and is not shown.

To our knowledge this is the first study to determine time to formation of symptomatic urinary calculi in a healthy population exposed to a high risk environment, and it is the only modern study of stone disease in deployed DOD personnel. In our study population the time to formation of symptomatic urinary calculi follows a normal distribution with a mean of 93 days. Standard deviation is a broad 42 days, and it reflects the multitude of factors that influence stone formation and renal colic onset. Because of the unique circumstances of the environment, the influx of personnel, and the military medical and personnel records system, this study provides unprecedented information about the formation of symptomatic urinary calculi.

In this study the period of risk of stone formation is well defined, which allows the accurate calculation of time to formation of symptomatic urinary calculi. The hot, arid climate of Kuwait and Iraq, where daily temperatures are a minimum of 10F higher than the warmest regions of the continental United States, represents a high risk environment for stone formation. Therefore, the date personnel arrive in southwestern Asia is the definitive beginning of a period of increased risk of stone formation. To ensure accurate pay and tax records, deployed personnel are entered into
To facilitate comparison to figure 1 dates are in weekly intervals. Evaluating stone disease in a population and conditions studies. A review of the English literature found 1 article between peak environmental temperature and peak incidence in our study corresponded to the 3-month difference practice forced hydration during training and deployment. Trained in the prevention, recognition and treatment of dehydration tracks heat injuries and the trends are scrutinized at the military places strong emphasis on hydration. The medical system between 77 and 250 ppm. Average to hard with a range of combined Ca++ and Mg++ contents listed on these bottled waters show the water to be soft to an undisclosed desert environment. The authors reported the peak incidence of stone disease (6 of 45 patients) occurred at month 10. From their published data mean interval was calculated as 10.9 months with a standard deviation of 4.96 months. The graphical representation of the data reveals a random distribution. In comparison our study revealed a mean interval of 93 days which corresponds to week 13 or month 3. In our study no patient presented with an interval longer than 35 weeks (approximately 9 months) and only 2 patients presented with an interval of 32 weeks (8 months) or greater. The most likely causes for the difference between the studies are changes in diagnostic capabilities and referral patterns. While the number of personnel in southwestern Asia increased dramatically in the months before hostilities, there were personnel within our referral population who had been in southwestern Asia for 10 months or longer at the initiation of this study. Given a longer observation period we may have acquired patients with longer intervals. Trends in our data suggest that the number of patients with intervals longer than 32 weeks would have remained small and, therefore, unlikely to change the mean significantly.

The largest confounding factor in this study is the unknown effect of combat on stone formation, stone passage and referral patterns. Another potential confounder is that some personnel, despite medical screening, had undetected urinary calculi before deployment. Our study may have been subjected to selection bias because some personnel with renal colic may have been given a trial of outpatient therapy by the unit medical officer and passed the stones spontaneously. While it might be presumed that these stones would be smaller and, therefore, would have had a shorter time until becoming symptomatic, in truth this effect cannot be known.

The effect of acclimatization or lack thereof may also have influenced time to stone formation. It is interesting that the number of patients with stone disease did not increase steadily during the hot summer season (fig. 2), but this pattern may change with longer followup and/or as remaining personnel became acclimatized.

**CONCLUSIONS**

The recent large scale deployment of DOD personnel to southwestern Asia provided an unprecedented opportunity to observe stone disease. Mean time to development of symptomatic urinary calculi in this high risk environment was 93 days. Our study design is unique because the period of onset of stone symptoms and in many instances brought confirmatory medical records. During the 6 months of this study the 47th CSH was the tertiary referral hospital for the military theater and the main evacuation route for southwestern Asia. As a result the majority of renal colic cases requiring definitive diagnosis, subspecialty care, hospitalization or evacuation were treated at the 47th CSH.

The risk factors influencing in vivo stone formation are difficult to control in a general population. Several important aspects of personnel and environment in this study combined to create a cohort more standardized than a general population. Deployed personnel were subjected to similar living conditions and environmental exposures such as heat, sunlight and absence of air conditioning. The overwhelming majority of deployed DOD personnel are military, which is a young, predominantly male, adult population with few confounding medical comorbidities. Pre-deployment medical screening precluded deployment of soldiers with symptomatic stone disease and the few patients treated for stone disease immediately before deployment were censored from the time analysis.

Food and water sources were uniform for the overwhelming majority of personnel deployed to southwestern Asia. Personnel were restricted to food supplied by dining facilities or prepackaged meals. While there is no way to control the diet patients consumed, personnel were provided the opportunity to consume a balanced diet. Therefore, any dietary excesses were volitional. Bottled water was supplied to deployed personnel and in some areas was supplemented by treated water. No data are available about the mineral content of treated water supplies. A poll of 5 camps with large troop populations (2 in Kuwait and 3 in Iraq) identified 3 dominant suppliers of bottled water. The mineral concentrations listed on these bottled waters show the water to be average to hard with a range of combined Ca++ and Mg++ content between 77 and 250 ppm.

It is important for the reader to understand that the military places strong emphasis on hydration. The medical system tracks heat injuries and the trends are scrutinized at the highest levels of command. Military personnel are regularly trained in the prevention, recognition and treatment of dehydration and heat injuries. As a result military personnel practice forced hydration during training and deployment.

Mean interval to formation of symptomatic urinary calculi in our study corresponded to the 3-month difference between peak environmental temperature and peak incidence of stone disease reported in epidemiologically based studies. A review of the English literature found 1 article evaluating stone disease in a population and conditions similar to ours. In 1945 Pierce and Bloom reported on stone disease in American soldiers deployed for 18 months to an undisclosed desert environment. The authors reported the peak incidence of stone disease (6 of 45 patients) occurred at month 10. From their published data mean interval was calculated as 10.9 months with a standard deviation of 4.96 months. The graphical representation of the data reveals a random distribution. In comparison our study revealed a mean interval of 93 days which corresponds to week 13 or month 3. In our study no patient presented with an interval longer than 35 weeks (approximately 9 months) and only 2 patients presented with an interval of 32 weeks (8 months) or greater. The most likely causes for the difference between the studies are changes in diagnostic capabilities and referral patterns. While the number of personnel in southwestern Asia increased dramatically in the months before hostilities, there were personnel within our referral population who had been in southwestern Asia for 10 months or longer at the initiation of this study. Given a longer observation period we may have acquired patients with longer intervals. Trends in our data suggest that the number of patients with intervals longer than 32 weeks would have remained small and, therefore, unlikely to change the mean significantly.

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**REFERENCES**