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УРОЛОГІЯ

Are there seasonal variations of renal colic in calcium oxalate stone formers in Germany?

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SUMMARY

Seasonal variations of renal colic have been described by many authors throughout the world for different countries. No such evaluation has yet been made for Germany. We have collected data to analyse whether such seasonal variations of renal colic are relevant in Germany as well.

Prospectively, we have studied n=1049 calcium oxalate stone formers with symptoms of renal colic treated in our department. We have divided them into four groups according to the quarters of the year. For stone analysis, x-ray diffraction / polarizing microscopy was used. Furthermore, the following general parameters have been examined in all patients: age, BMI, blood pressure, stone frequency, diabetes mellitus; blood: creatinine, glucose, uric acid, calcium, sodium and potassium; urine: pH, volume, calcium, uric acid, citrate, ammonia and urea. Using the statistic programme Prism 5 (GraphPad), significant differences between the four groups were calculated by the Kruskal-Wallis-test.

In Germany no seasonal variations of renal colic in calcium oxalate stone formers have been found. We have also not found seasonal variations in metabolic parameters or urine composition. Low temperature fluctuations could be a potential explanation. However, there are countries with similar climate conditions showing seasonal variations of acute stone episodes. Another possible explanation for the missing variation in colic is the constant urine composition throughout the year. This was shown for other regions with a constant frequency of acute stone episodes. Further investigations are required to support this hypothesis.

INTRODUCTION

Вступ

Urolithiasis affects an estimated 5% of the population and the lifetime risk of passing a stone in the urinary tract is estimated to be 8-10% (Scales et al. 2012; Johnson et al. 1979). Urinary calculus formation is highly variable and certain risk factors such as age, gender, anatomic abnormality, and metabolic diseases have been identified. The prevalence of kidney stones in the United States as well as Germany (Hesse et al. 2003) has risen over the past 30 years. There is a general expectation that the gradual and long-term increase in ambient temperatures due to global warming via greenhouse gases will induce a corresponding rise in urolithiasis-related morbidity (Brikowski et al. 2008; Chen et al. 2008). Increasing ambient temperatures may increase urinary stone risk by increasing the urinary excretion of calcium and leading to the supersaturation of calcium oxalate and calcium phosphate in the urine.

However, the trend of increasing prevalence of urinary stones in hot climates is not necessarily universal. The incidence of urinary stones is quite low in Nigeria (Esho 1978), but extremely high in the Middle Eastern Gulf States, such as Kuwait, the United Arab Emirates, and Saudi Arabia (Robertson 2012).

The tendency for increasing incidence of renal colic in parallel with the rise in ambient temperature and seasonal variations has been well documented in many countries (Lo et al. 2010; Scales et al. 2012; Fujita 1979; Basiri et al. 2011; Sirohi et al. 2014; Fukuhara et al. 2016), yet no such investigation has been made for Germany. We have chosen to investigate the prevalence of renal colic in Upper Franconia divided into the four quarters of the year.

MATERIALS AND METHODS

Матеріали і методи дослідження

Prospectively n=1049 consecutive patients calcium oxalate urolithiasis patients (CaOxU) with symptoms of renal colic treated in the Department of Urology and Paediatric Urology at the Regiomed-Klinikum Coburg, Germany were studied. Patients with primary hyperparathyroidism, hyperoxaluria and distal renal tubular acidosis were excluded. Stone analysis was performed by polarization microscopy and x-ray diffraction.

Patients have been divided into four groups according to the quarter of the year they have been treated for their renal colic episode.

Furthermore, a detailed history including the number of stone episodes was recorded. Arterial blood pressure (RR) was measured according to the

recommendations of the World Hypertension League sitting after 5 minutes at rest.

The following parameters were determined in all these patients: Urine pH profiles on three consecutive days at morning (fasting), noon (postprandial) and evening (postprandial). For urine pH measurements, dipsticks were used which allow pH measuring in 0.1 steps (Madaus GmbH, Cologne, Germany). The mean urinary pH was calculated in every patient.

Blood was drawn to measure creatinine (Jaffé reaction, Dade Behring Marburg, Germany), potassium (atomic absorption), calcium (indirect ion sensitive electrode), glucose (postprandial; hexokinase-glucose-6-phosphatase dehydrogenase method, Flex Siemens Healthcare Diagnostics Newark, DE, USA) and uric acid (modified uricase method, Dade Behring Marburg, Germany). A 24 h-urine specimen was collected to determine the excretion of citrate (citrate lyase method, Boehringer Mannheim, Germany), creatinine (Jaffé reaction, Dade Behring Marburg, Germany), calcium (indirect ion sensitive electrode), uric acid (modified uricase method, Dade Behring Marburg, Germany), ammonia (modified glutamate dehydrogenase method using NADPH, test kit Ammonia Flex, Dade Int., Newark, DE, USA) and urea (urease-glutamate dehydrogenase, Dade Behring Marburg, Germany) as a marker for protein intake].

General parameters, blood and urine values were also grouped according to the quarters of the year.

For statistical analysis means and standard deviations were calculated. Significant differences between the four groups were assessed using the Kruskal-Wallis-test.

Differences were called significant in case of $p < 0.05$. For these analyses, the programme Prism 5 (GraphPad Software, San Diego, CA, USA) was used. Calculations were performed on a personal computer.

RESULTS AND DISCUSSION

Результати та їх обговорення

Figure 1 shows the number of patients treated with renal colic in the four quarters of the year. As we can see there is no big difference in the four groups, as the number of patients with renal colic does not show a significant variety.

Tables 1-3 show the results for general, blood and urine parameters of our patients divided according to the four quarters of the year. Using the Kruskal-Wallis-test we have found no significant differences throughout the four quarters of the year with any of the above parameters ($p > 0.05$).

This is the first study that has been conducted to analyse seasonal changes in the occurrence of renal colic in Germany. It is a mono-centric study

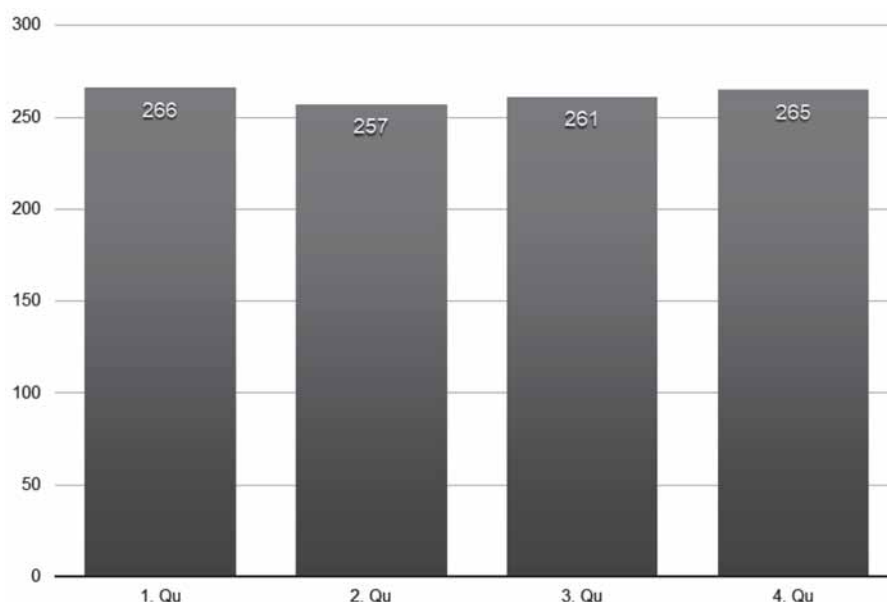


FIGURE 1. Distribution of CaOxU patients presenting with renal colic according to the four quarters of the year. No significant difference ($p > 0.05$).

TABLE 1. Variations of general parameters according to the four quarters of the year. No significant differences ($p > 0.05$)

	1 Quarter	2 Quarter	3 Quarter	4 Quarter
Age	53.6 ± 13.9	51.1 ± 15.7	52.7 ± 15.3	51.7 ± 14.4
BMI	28.0 ± 4.8	28.3 ± 5.5	28.3 ± 5.5	28.7 ± 5.4
Diab. mellitus	16.2 %	14.8 %	13.0 %	14.0 %
Stone episodes	1.7 ± 1.0	1.7 ± 1.1	1.7 ± 1.3	1.7 ± 1.1
BP sy	138 ± 15	137 ± 17	136 ± 17	138 ± 116
BP dia	82 ± 8	82 ± 10	83 ± 11	82 ± 9

TABLE 2. Variations of blood parameters according to the four quarters of the year. No significant differences ($p > 0.05$)

	1 Quarter	2 Quarter	3 Quarter	4 Quarter
Creatinine	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3
Sodium	139 ± 3	139 ± 3	140 ± 3	139 ± 3
Potassium	4.2 ± 0.5	4.1 ± 0.4	4.1 ± 0.4	4.1 ± 0.4
Calcium	4.8 ± 0.2	4.6 ± 0.2	4.6 ± 0.3	4.6 ± 0.3
Uric acid	5.8 ± 1.5	5.6 ± 1.5	5.7 ± 1.7	5.5 ± 1.4
Glucose	119 ± 42	120 ± 38	115 ± 36	116 ± 47

TABLE 3. Variations of urine parameters according to the four quarters of the year. No significant differences ($p > 0.05$)

	1 Quarter	2 Quarter	3 Quarter	4 Quarter
pH	6.1 ± 0.3	6.1 ± 0.3	6.1 ± 0.3	6.3 ± 0.8
Volume	2.7 ± 1.3	2.9 ± 1.9	2.7 ± 1.4	2.7 ± 1.3
Calcium	5.4 ± 2.8	5.5 ± 3.0	5.6 ± 3.0	5.3 ± 3.1
Uric acid	3.7 ± 1.5	3.7 ± 1.5	3.5 ± 1.4	3.5 ± 1.2
Citrate	1.9 ± 1.2	1.9 ± 1.4	1.8 ± 1.3	1.8 ± 1.2
Urea	363 ± 133	379 ± 138	359 ± 180	363 ± 136
Ammonia	48 ± 22	44 ± 22	44 ± 28	46 ± 28

with a large patient pool. A close relationship between seasons and the incidence of urolithiasis has been demonstrated in various areas of the world, including Japan (Fujita 1979; Chen et al. 2008), Taiwan (Chen et al. 2008), the United States (Brikowski et al. 2008; Chauhan et al. 2004), New Zealand (Lo et al. 2010), Italy (Boscolo-Berto et al. 2008), and Iran (Basiri et al. 2009), where the four seasons rotate in a year, and the temperature fluctuates widely in between the seasons (Fukuhara et al. 2016). In many countries, seasonal trends in monthly urinary stone attack rates exist, with the incidence peaking in the summer, which corresponds to July–September (Chen et al. 2008) and January–March (Lo et al. 2010) in the northern and southern hemispheres, respectively. These trends have been demonstrated to exist regardless of patients' age, sex (Chen et al. 2008), and race (Lo et al. 2010).

These results however could not be supported by our findings for Germany. We have found no seasonal variations of renal colic in CaOxU and no seasonal variations of metabolic parameters in our patients.

There are some studies coming from the United Arab Emirates and South Australia (Freeg et al. 2012; Rofe et al. 1981; Baker et al. 1993) that have also not found differences in the frequency of renal colic occurrence throughout the year.

Variations in temperature were regarded as the main reason for seasonal variations in stone episodes. However, this explanation is not satisfying as with similar climate conditions different relations regarding the seasonal variations of renal colic were described.

Another possible explanation could be the seasonal variation of urine composition. Authors from the USA (Eisner et al. 2012), UK (Robertson et al. 1975), Finland (Elomaa et al. 1982) and Poland (GBuszek et al. 1978) have described seasonal changes in Ca-excretion, urine volume produced on a daily bases and urine supersaturation. This theory that has also been suggested by Lo and colleagues (Lo et al. 2010) who explain their findings with the increase in the synthesis of 1,25-dihydroxyvitamin D₃ (Vit D) due to sunlight exposure. Increased exposure to sunlight causes increased production of Vit D and increased urinary calcium excretion (Lo et al. 2010). Serum levels of Vit D and urinary excretion of calcium and oxalate have been shown to be significantly higher during May until October than November until April (Elomaa et al. 1982). In addition, the serum Vit D level was significantly higher throughout the year in hypercalciuric than normocalciuric stone-formers (Elomaa et al. 1982).

In contrast to these findings, we did not find fluctuations in the urine composition (metabolic

urinary stone risk factors) throughout the year. This could explain that we did also not observe a variation of renal colic with the seasons. Unfortunately, no data on urine chemistry have been reported in these studies which did also not observe seasonal variations of acute stone episodes as we did (Baker et al. 1993; Freeg et al. 2012).

We explain the constant urine composition throughout the year in the lack of seasonal variations of our diet. Investigations from the UK, Finland and Poland have all been made in the late 70s or early 80s when globalization has not reached such levels and hence the availability of certain dietary products had indeed depended on their seasonal growth. Nowadays due to hypermarketizing every dietary product is available at all times of the year. So far, unfortunately, no data are available with respect to this question.

CONCLUSIONS

Висновки

The difference in seasonal fluctuations of renal colic between different countries is not completely understood. The most probable explanation for the fact that in some regions there are and in other regions there are no seasonal variations in acute stone episodes is the variation and non-variation respectively in urine chemistry. Further investigations are crucial as due to global warming we expect a rise in mean temperatures and corresponding also a rise in the frequency of renal colic.

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РЕФЕРАТ**Чи існують сезонні варіації ниркової коліки у пацієнтів з оксалатним уролітіазом у Німеччині?**

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Б. Брюкнер

Сезонні варіації ниркової коліки були описані багатьма авторами світу для різних країн. Для Німеччини такого аналізу ще не проводилося. Ми зібрали дані, щоб проаналізувати, чи такі сезонні варіації також релевантні для Німеччини.

Було проспективно проаналізовано дані пацієнтів (n=1049) з сечокам'яною хворобою, каменями з оксалату кальцію та симптомами ниркової коліки, які проходили лікування у нашому відділенні. Ми розділили їх на чотири групи відповідно до кварталів року. Для аналізу складу каменів використовувалися поляризаційна мікроскопія та рентгенівська дифракція. Також було проаналізовано: вік, індекс маси тіла, кров'яний тиск, частоту виникнення колік, наявність діабету, показники крові (креатинін, глюкоза, сечова кислота, кальцій, натрій та калій) та показники сечі (рН, об'єм, кальцій, сечова кислота, цитрат, аміак та сечовина). Різницю між чотирма групами було розраховано за допомогою статистичної програми Prism 5 (GraphPad) за тестом Крускала-Уолліса.

Сезонних варіацій ниркової коліки з каменями з оксалату кальцію для Німеччини встановлено не було. Також не було знайдено сезонних варіацій метаболічних параметрів або складу сечі.

Потенційним поясненням можуть бути незначні флуктуації температури. Однак існують країни з подібними кліматичними умовами, але наявними сезонними варіаціями гострої ниркової коліки. Іншим можливим поясненням може бути постійний склад сечі протягом року. Це було також показано для інших регіонів з постійною частотою епізодів гострої ниркової коліки. Потрібні подальші дослідження для підтримки цієї гіпотези.

Ключові слова: ниркова коліка, сечокам'яна хвороба, оксалат кальцію, сезонні варіації, клімат, хімічний склад сечі, температура, вологість.

РЕФЕРАТ**Существуют ли сезонные вариации почечной колики у пациентов с оксалатным уролитиазом в Германии?**

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Сезонные вариации почечной колики были описаны многими авторами мира для разных стран. Для Германии такого анализа еще не проводилось. Мы собрали данные, чтобы проанализировать, какие сезонные вариации также релевантные для Германии. Были проспективно проанализированы данные пациентов (n=1049) с мочекаменной болезнью, камнями из оксалата кальция и симптомами почечной колики, проходивших лечение в нашем отделении. Мы разделили их на четыре группы в соответствии с кварталами года. Для анализа состава камней использовались поляризационная микроскопия и рентгеновская дифракция. Также были проанализированы: возраст, индекс массы тела, кровяное давление, частота возникновения коллик, наличие диабета, показатели крови (креатинин, глюкоза, мочева кислота, кальций, натрий и калий) и показатели мочи (рН, объем, кальций, мочева кислота, цитрат, аммиак и мочева кислота). Разницу между четырьмя группами было рассчитано с помощью статистической программы Prism 5 (GraphPad) по тесту Крускала-Уолліса. Сезонных вариаций почечной колики с камнями из оксалата кальция для Германии установлено не было. Также не было найдено сезонных вариаций метаболіческих параметров или состава мочи. Потенциальным объяснением могут быть незначительные флуктуации температуры. Однако существуют страны с подобными климатическими условиями, но имеющимися сезонными вариациями почечной колики. Другим возможным объяснением может быть постоянный состав мочи в течение года. Это было также показано для других регионов с постоянной частотой эпизодов острой почечной колики. Требуется дальнейшие исследования для поддержки этой гипотезы.

Ключевые слова: почечная колика, мочекаменная болезнь, оксалат кальция, сезонные вариации, климат, химический состав мочи, температура, влажность.