Influence of dietary components on the risk of urinary tract stones

Authors:
Marek Miśkiewicz
Wojewódzki Szpital Podkarpacki im.Jana Pawła II w Krośnie
miskiewiczkeram@gmail.com
https://orcid.org/0000-0002-3691-343X

Michał Głodzik
Przychodnia Bracka Bielszowice, Ruda Śląska
glodzikmichal@gmail.com
https://orcid.org/0009-0009-4751-1784

Katarzyna Stencel
Specjalistyczny Zakład Opieki Zdrowotnej "MULTIMED" Sp. z oo
katarzynastencel96@gmail.com
https://orcid.org/0009-0006-9574-9277

Karina Stelmaszak
SPZOZ Okręgowy Szpital Kolejowy w Katowicach
stelmaszak1259@gmail.com
https://orcid.org/0009-0006-3877-2753
Monika Wojtasik
Przychodnia Wielospecjalistyczna w Mikołowie
monika.wojtasik95@gmail.com
https://orcid.org/0009-0008-6723-3841

Aleksandra Ogieło-Kowalczyk
SPZOZ Okręgowy Szpital Kolejowy w Katowicach
aleksandra.ogiełko@gmail.com
https://orcid.org/0009-0008-8773-7123

Julia Samborska
SPZOZ Okręgowy Szpital Kolejowy w Katowicach
julia.samborska.med@gmail.com
https://orcid.org/0009-0001-2157-7015

Paweł Więckowiak
Śląski Uniwersytet Medyczny w Katowicach
pawew36@gmail.com
https://orcid.org/0009-0004-6610-1792

Martyna Łęcka
Szpital Murcki Sp z o.o. Katowice
martyna.lecka@gmail.com
https://orcid.org/0009-0007-1473-8400

Katarzyna Żak
Uniwersyteckie Centrum Kliniczne w Gdańsku
lek.katarzyna.zak@gmail.com
https://orcid.org/0009-0000-7056-1960
Abstract
Urinary tract stones are a common condition that significantly reduces quality of life. A proper diet is an important factor in the prevention and treatment of lithiasis and, for this reason, dietary interventions have become an essential part of treatment.
In our review of the literature, we analysed the individual components of diet in terms of the risk of developing urinary tract stones.
A number of dietary guidelines have been developed to reduce lithogenic factors in the urine, such as calcium oxalate, calcium phosphate and uric acid. Current guidelines recommend increasing the intake of fluids, increasing the intake of fruit and vegetables, using a balanced calcium supplementation and limiting the supply of sodium and especially animal protein. Based on these recommendations, a vegetarian diet containing dairy products combined with calcium supplementation appears to have the lowest risk of developing urinary stones. However, there are still many uncertainties in this area, and research needs to continue and be expanded to include the influence of diet type on the risk of lithiasis. This will allow us to gain a better understanding of the factors influencing the disease process and to create clear guidelines in the field of urolithiasis in the future.

Key words: “kidney stones”; “diet”; “stone risk”; “nephrolithiasis”

Introduction
Urinary tract stones are an increasingly prevalent illness in the population. There has been an increase in the prevalence of this condition over the decades [1].
Urolithiasis results in a reduced quality of life, reduced income generation for patients and increased health care expenditure. This creates a need for a better understanding of this disease entity and preventive information campaigns.
The aim of this work is to review current knowledge on the effects of specific dietary components on the risk of urinary tract stones

Epidemiology
Many research papers estimate the prevalence to be between 10% of the population in both sexes [2],[3]. In addition, there is an increased incidence in countries with hot climates which, in an era of global warming, may be a predictor of an increased incidence of urinary tract
stones [4]. There are also genetic conditions in which the incidence of urinary tract stones increases [5].

Pathophysiology
The process of urinary tract stone formation is influenced by a variety of factors that disrupt the balance between inhibitors and promoters of urinary tract stone formation. Urinary supersaturation is an important factor in urinary stone formation. In addition, bacterial infections, epithelial damage or urinary stasis also affect stone formation. Factors inhibiting stone precipitation include citrate, uromodulin and magnesium. Stone development begins with the formation of crystals in supersaturated urine, which then adhere to the epithelium of the urinary tract. The biological processes that anchor the crystals in the urinary tract epithelium are not fully understood. They grow, causing erosion of the urinary tract epithelium, forming a nucleus for the deposition of calcium oxalate. Low or high urinary pH is a factor promoting stone formation. Calcium phosphate and struvite are less soluble at higher pH; therefore, in alkaline urine these components are predisposed to stone formation. In contrast, uric acid and cystine are less soluble at lower pH, making their stones more prone to form in acidic urine [6],[7]. The disruption of the components that make up the balance is influenced by many factors that can include age, gender, genetic factors, infections and many others. A factor that has a great influence on the described process in new and recurrent stones is diet [8],[9].

Methods
In this paper, we review the current knowledge on the influence of dietary components on the occurrence of urinary tract stones. We selected articles with an unlimited search period in several databases, including PubMed, Google Scholar, and Web of Science. We included in the review only articles written in English and with full text available. No restrictions were made based on article type.

Fluids
Fluid intake is one of the key elements in urolithiasis. It is recommended that the correct fluid intake should be between 2 and 2.5 liters of water, which helps prevent the recurrence of lithiasis [10,11]. The results of a large UK BioBank study have recently been published. It was found that drinking extra fluid (200ml) consumed daily reduces the risk of urinary stones by 13% (risk ratio [HR] = 0.87, 95% confidence interval [CI] 0.85-0.89) [12].
However, the type of fluids affects urinary tract stone formation to varying degrees. The effect of water was investigated by a team led by Borghin, in a prospective study. Patients burdened with idiopathic stones were divided into two groups. In the study group, patients took an increased amount of water, sufficient to produce at least 2l of urine per day. The second group remained as a control. No specific diet was implemented. Over the 5-year study period, the risk of stone recurrence in the study group was half that of the control group (12.1% vs. 27%, respectively, p = 0.008) [13]. However, it is uncertain whether each type of water affects urinary stone formation in the same way. Mineral waters contain higher concentrations of ions, including calcium and magnesium, than tap water. In addition, drinking water varies in ion composition depending on geographical location [14]. There are studies that have examined the effect of increased ion concentrations in water intake on urine composition. High ion content resulted in increased calcium excretion [15] but also citrate excretion [16]. However, no studies investigating the synergistic effect of these phenomena on clinical outcome have emerged.

The effects of coffee and tea were initially considered to be stone-forming. Large studies by a team led by Curhan : Nurses' Health Study I [17] and Nurses' Health Study II [18] and a study by Littlejohns [12] found a protective effect of coffee and tea consumption on urinary stone formation. Regular consumption of adequate amounts of tea can reduce the risk of developing stones by approximately 8-14%. Similar reports have been reported by researchers in China [19]. This effect may be related to an increase in the urinary excretion of citrates, oxalates and also an increase in the volume of urine excreted [20]. The protective effect of regular coffee consumption in urinary stones has been linked to an increase in urine excretion and may reduce the risk of developing stones by 8% [12],[21]. Sweetened carbonated drinks contain an average of 150 calories per 350 ml and often with added fructose. Fructose can increase the excretion of calcium, oxalate, which is associated with a higher risk of kidney stones [22],[17],[18].

Other liquids whose effects on lithiasis have been studied in the literature are fruit juices. In this paper, we discuss the juices that have been most frequently evaluated in the literature for their effect on urinary tract stones. Apple and grapefruit juices are thought to be non-protective. It was initially thought that lemonade might have a beneficial effect in the prevention of urinary tract stones. After careful analysis, it turns out that the citrates contained in lemon juice are neutralised by the hydrogen ions contained in the juice. In contrast, orange juice, like lemonade, contains a large amount of citrates, but is devoid of excess hydrogen ions, which does not neutralise the desired citrates. In addition, orange juice
contains significantly less fructose compared to apple juice, which is another beneficial aspect of this juice. However, long-term studies are needed to confirm the usefulness of this juice in the prevention of urinary tract stones [23],[24].

**Sodium and Calcium.**

Initially, it was thought that dietary calcium restriction should be sought for the prevention of urinary stones. However, a number of studies indicate that limiting dietary calcium supply not only may lead to other conditions, but does not provide protection against lithiasis [17]. In the gut, calcium binding to oxalates inhibits their absorption. With a low-calcium diet, there is an increase in intestinal absorption of oxalates and a subsequent increase in urinary excretion of oxalates which may offset the low dietary calcium binding in the urine. This results in a supersaturation of urine with calcium oxalates resulting in urinary stone formation [25].

A number of studies have further shown that an excessive supply of calcium will be associated with an increased risk of developing urinary tract stones [26],[27],[28]. In a study by Curhan, it was shown that lower calcium intake was associated with a higher risk of kidney stones by more than 50% compared to higher calcium intake [28]. In contrast, a study by a team led by Borghi compared a normal calcium diet (1,200 mg/day), low in salt and animal protein, with a low calcium diet (400 mg/day). In this study, the normal calcium diet group showed a significant reduction in the risk of recurrent lithiasis of approximately 50% compared to the low calcium diet group. In addition, this study confirms the correlations of increased urinary oxalate excretion with a low-calcium diet and lower in patients on a normo-calcium diet [26]. In view of reports on the different effects of calcium on the development of urinary tract stones, current guidelines for the prevention of stones should include a standard calcium diet.

Currently, there is an excessive consumption of sodium in the diet. This causes disturbances of many systems in the human body and also affects the formation of urinary tract stones. Consumption of excessive amounts of sodium chloride causes fluid retention in the extracellular space, which will result in inhibition of calcium reuptake in the renal tubules. This phenomenon will contribute to the increased excretion of calcium in the urine, which may result in the supersaturation of urine with calcium and the onset of stone precipitation [29],[30]. A 6 g increase in daily sodium chloride intake can increase urinary calcium
excretion by 40 mg/day [30], while dietary salt intake >10 g per day correlates with an increased incidence of hypercalciuria compared with recommended values [26]. Clinical trials appear to support the theories. In the NHS I study, patients following a diet with the highest amount of sodium had a 30% higher risk of developing urinary tract stones than patients consuming the lowest amount of sodium [17]. Similar conclusions can be drawn from a study conducted by a team led by Borghi. Patients following a low-sodium diet combined with low animal protein intake and moderate calcium intake had an almost 50% lower risk of stone recurrence compared to patients following a low-calcium diet [26]. Further confirmation can be found in a study investigating the impact of the DASH (Dietary Approaches to Stop Hypertension) diet. The diet consists of low sodium intake and high fruit and vegetable intake. The authors conclude that the DASH diet has a protective effect on the occurrence of urinary tract stones [31].

**Oxylates**

Oxalates in the human body are endogenously produced in the liver and supplied with food. The endogenous production of oxalates is influenced by the vitamin C provided in the diet. In one study, a group of men took excessive amounts of vitamin C (≥1000 mg/day). This was associated with a 41% increase in the risk of stones [32]. Oxalates provided with food are most often of plant origin; foods rich in oxalates include nuts, spinach, chocolate and potatoes [33]. However, between 10 and 15% of the oxalates contained in food are absorbed from the intestines, and this may be altered by short bowel syndrome, bacterial flora disorders or varying bioavailability of oxalates in food [34],[35]. However, the amount of oxalate absorbed does not only depend on the amount of dietary oxalate consumed, but also on calcium intake. Increased dietary calcium intake leads to decreased intestinal oxalate absorption, whereas reduced calcium intake results in increased intestinal oxalate absorption and increased urinary oxalate excretion [25],[36]. The effect of calcium on the amount of oxalate absorbed is dependent on the duration of calcium intake alone. This was confirmed in a study of men who were divided into two groups and given two different calcium supplementation regimes. One group took 1g of calcium carbonate with each meal, while the other group took 3g of calcium carbonate daily before bed and without food at the same time. There was an increase in urinary calcium excretion in both groups; however, urinary oxalate excretion decreased significantly in those taking the calcium preparation with meals, whereas no change in urinary oxalate concentration was observed in men taking the preparation before bedtime. In addition, it was
noted that there was no increase in urinary calcium oxalate saturation in those taking the calcium supplement with meals, while it increased in the other group. This study confirms the beneficial effect of calcium supplementation in reducing intestinal oxalate absorption. It introduces an important condition for the effectiveness of such an intervention and the reduction of urinary oxalate concentrations. [37]

Overall, it is estimated that the proportion of oxalates excreted in urine of exogenous origin is about 50%, with the remainder coming from hepatic metabolism. Depending on the amount of oxalate intake, calcium, vitamin C and other factors influencing absorption and hepatic metabolism, the percentage of urinary oxalate of exogenous origin may vary [35].

At present, it appears that the best way to reduce intestinal oxalate absorption and consequently urinary oxalate concentrations is through calcium supplementation at the same time as food intake [37],[38].

Proteins

Current guidelines in urolithiasis recommend limiting dietary protein intake with particular emphasis on non-dairy, animal protein (eggs, meat) [17]. Unfortunately, there is currently an excessive intake of animal protein which, combined with the low calcium content of the diet and the high acidity of the food consumed, contributes to a decrease in urinary pH, which in turn will inhibit the reuptake of calcium from the urine. In addition, the effect may be a decrease in the urinary excretion of citrate, potassium or magnesium, which are among the inhibitors of urinary stone formation. Such a trend may be a strong reason for the increased incidence of urinary tract stones [39],[40]. However, there are reports in the literature that the hypercalciuriac effect of animal protein is not related to the acidic load of the food [41]. Another effect of animal protein is an increase in purine metabolism, which will result in hyperuricosuria in both urate and calcium lithiasis [42]. There are reports that a high intake of animal protein increases urinary oxalate excretion [43].

Excessive protein intake appears to increase the risk of urinary stones, however, an important aspect is the origin of the protein. It has been noted that proteins of plant origin are not associated with an increased risk of lithiasis. This is confirmed by a large study on 3 large cohorts. The study showed no effect of BMI or thiazide use, and higher potassium intake due to high vegetable intake was an additional protective factor for lithiasis [44].

There are studies confirming a reduction in lithiasis risk with a DASH-type diet, rich in vegetables and low in animal protein, has the lowest risk of lithiasis [45]. An earlier cited study also found that a diet high in vegetables, fruit and low-fat dairy products may reduce
the risk of lithiasis [32]. There is still a lack of definitive clinical data confirming the reduction of animal protein intake to reduce the risk of developing urinary tract stones. Studies led by Curhan found no association between animal protein intake and stone risk [17],[18]. A pooled analysis of studies led by Ferraro assessed animal protein intake and found a small and non-significant increase in the risk of stones in the subgroup with the highest non-dairy animal protein intake. No association was found between vegetable protein intake and risk of lithiasis. In addition, it was noted that in one group, a higher intake of dairy protein was associated with a reduced risk of lithiasis [44].

**Carbohydrates and fats**

In the literature on the effect of carbohydrates on the development of urinary stones, there are studies examining the effect of simple sugars.

The study cited by the Curhan-led team found that higher dietary intake of sucrose was associated with a higher risk of lithiasis. Increased fructose intake was associated with an increased risk of lithiasis between 27% and 37% [17],[18]. Some studies have reported that daily fructose consumption increases urinary oxalate excretion and decreases urinary pH and magnesium [46], while others have shown no change in daily urinary oxalate, calcium or uric acid excretion [47].

No clear clinical data are available to confirm the effect of individual carbohydrates. With the increasing consumption of foods with added fructose or other sugars, which may influence the development of lithiasis. This area requires further research.

It is now thought that polyunsaturated fatty acids may influence urinary stone formation by affecting the amount of calcium and oxalate in the urine. It has been reported that arachidonic acid, which is a component of cell wall phospholipids, may contribute to increased levels of prostaglandins which, in turn, by modulating urine composition, may cause hypercalciuria [48]. In contrast, n-3 PUFAs such as eicosapentaenoic acid and docosahexanoic acid competitively incorporate into arachidonic acid sites reducing urinary calcium and oxalate levels [49],[50]. However, the limitations of these studies are the small study groups and the lack of studies in the literature to confirm reports unequivocally. There are also no studies confirming the benefits of polyunsaturated fats in a clinical setting. This is an area that requires further research to better understand the effect of lipids on the development of urinary tract stones.
Citrates and magnesium

Citrates have a protective effect on urinary stone formation, which has been confirmed in numerous studies. The properties of citrates include inhibition of calcium crystallisation and also counteracts the aggregation of already formed calcium oxalate crystals [51],[52]. Magnesium is also counted among the protective factors in kidney stones. It inhibits the formation of calcium oxalate crystals in the urine by increasing the solubility of oxalates. It has also been noted that magnesium reduces both calcium oxalate and calcium phosphate aggregation in a concentration-dependent manner. There are also reports of magnesium inhibiting intestinal absorption of oxalate. [53],[54].

Conclusions

In our review, we analysed the influence of individual dietary components on the risk of developing urinary tract stones. Dietary modification is a key element in preventing the development of lithiasis regardless of the pharmacotherapy used. Current guidelines agree on the detrimental effects of excess intake of non-dairy animal protein and under-supplementation of calcium in the diet. In contrast, risk-reducing factors include a diet containing high amounts of vegetables and fruit with a combination of low-fat dairy foods. The effect of drinking plenty of fluids, especially water, and the beneficial effects of calcium supplementation in moderation with a low-sodium diet with limited non-dairy animal protein are best known.

For these reasons, it seems that the recommended diet for the prevention of lithiasis and its recurrence should be a vegetarian diet enriched with dairy products and an adequate amount of fluids, with particular emphasis on pure water.

It is worth noting that there is a lack of data in the literature to determine the real impact of individual components on the risk of developing lithiasis. This is due to the difficulty of isolating a single dietary component for a clinical trial with patients. This brings with it many interactions between individual dietary components which may distort their real-world impact. There are still many unknowns in the field of this issue, which brings with it the need to continue research with the need to expand on the impact of diet types on the risk of lithiasis. This will allow us to gain a better understanding of the factors influencing the disease process and produce clear guidelines in the field of urolithiasis in the future.
Author's contribution:

-Conceptualization, supervision and project administration: Marek Miśkiewicz, Michał Głodzik, Julia Samborska

-Methodology: Monika Wojtasik, Aleksandra Ogiegło-Kowalczyk, Martyna Łęcka

-Software, validation, formalanalysis, investigation, resources, writing original draft preparation: Paweł Więckowiak, Karina Stelmaszak, Katarzyna Żak, Katarzyna Stencel

-Analiza formalna: Paweł Więckowiak, Karina Stelmaszak, Marek Miśkiewicz, Martyna Łęcka, Katarzyna Żak, Katarzyna Stencel, Julia Samborska, Monika Wojtasik, Michał Głodzik, Aleksandra Ogiegło-Kowalczyk

- Writing review, editing and visualization: Paweł Więckowiak, Karina Stelmaszak, Marek Miśkiewicz, Martyna Łęcka, Katarzyna Żak, Katarzyna Stencel, Julia Samborska, Monika Wojtasik, Michał Głodzik, Aleksandra Ogiegło-Kowalczyk

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