

Urinary stone disease and obesity: Different pathologies sharing common biochemical mechanisms

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Abstract

The prevalence of urolithiasis is increasing in parallel with the escalating rate of obesity worldwide. It has previously been speculated that obesity is a potential risk factor for urinary stone disease. The possibility that common biochemical mechanisms underlie both obesity and urolithiasis is remarkable. Better understanding of possible common mechanisms of these diseases could potentially lead to a better management of urinary stone prevention. The prevention of urinary stone formation gives clinicians an acceptable reason to encourage lifestyle modification and weight loss through a regular diet. In this review, the association of obesity with urinary stone disease, possible common biochemical mechanisms, effects of dietary habits and weight loss on stone formation, as well as difficulties in surgical management of obese individuals with urolithiasis are discussed.

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Key words: Urinary stone disease; Obesity; Biochemical mechanism; Weight loss; Body mass index

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INTRODUCTION

The prevalence of urolithiasis requiring medical or surgical treatment is 5%-10% and increasing worldwide^[1]. Urolithiasis is a multifactorial disease and it has previously been speculated that there is an association between urolithiasis and obesity^[1-5]. Recently, a common pathophysiology has been advocated for both diseases, since several investigations have mentioned that the prevalence of urolithiasis has been increasing in parallel with obesity^[2,3,6].

Various lithogenic risk factors, including increased body mass index (BMI), low urinary volume, hypercalciuria, hyperoxaluria and hyperinsulinemia, are associated with obesity^[7]. A recent trial found that 98% of obese patients had at least one lithogenic risk factor in a 24 h urine sample and 80% had 3 or more factors^[8]. As the possible biochemical mechanisms related with obesity and urinary stone disease are clearly identified, management will potentially be more effective.

In this review, the association of obesity with urinary stone disease, possible common biochemical mechanisms, effects of dietary habits and weight loss on urinary stone formation, as well as difficulties in surgical management of obese individuals with urinary stone disease will be discussed.

OBESITY AND URINARY STONE FORMATION

Little is known about the biochemical mechanisms that explain the association between obesity and urinary

stone disease. Recent investigations have mentioned that obesity is related with changes in the biochemical components of urine, including phosphate, oxalate, uric acid and citrate^[2,3,5,9]. These biochemical changes may explain the association between obesity and urinary stone disease. In a recent study, uric acid and oxalate were found to be significantly higher in the urine samples of obese patients^[5]. The authors demonstrated no significant increase in urinary calcium, magnesium and citrate levels. In another study, a positive relationship was observed between BMI and urinary excretion of oxalate, calcium, uric acid, citrate, sodium, phosphate and potassium^[10]. The authors also observed a significant decrease in urinary pH level with increased BMI. Similarly Siener *et al*^[11] found a positive relationship between BMI and urinary levels of sodium, ammonium, uric acid and phosphate, as well as an inverse relationship between urinary pH and BMI. In a retrospective study, it has been found that patients heavier than 120 kg with urolithiasis excreted more oxalate, calcium and uric acid in urine compared to patients weighing less than 100 kg^[9]. In this trial, urine samples were observed to be more acidic in obese patients. Ekeruo *et al*^[12] studied the effect of BMI on urine biochemistry and noted a significant association between increasing BMI and urinary levels of calcium, oxalate, sodium, phosphate and uric acid, as well as urinary pH. The authors also observed that protective factors, including urine volume and urinary citrate excretion, increased with an increasing BMI. Maalouf *et al*^[13] have found that in urinary stone patients, urinary pH had a strong graded inverse association with BMI. In contrast, Nouvenne *et al*^[14] demonstrated no significant change in urinary pH with increasing BMI for both patients with urolithiasis and a healthy control group.

Several studies including patients with urolithiasis showed that higher BMI is significantly associated with a lower urinary pH level^[1,5,9,12]. The reasons for a progressive decline in urine pH with increasing BMI in urolithiasis patients are not well defined. Insulin resistance is one of the possible reasons^[1]. Hyperinsulinemia and insulin resistance are more frequently observed in obese patients due to higher incidence of diabetes mellitus^[3]. Insulin resistance may potentially result as a defect in ammonium production in the kidney and ability to excrete acid load, thus affecting urinary pH level^[1,3]. It has previously been advocated that hyperinsulinemia could possibly lead to decreased urinary citrate level as well as increased lithogenic factors in urine, including calcium, uric acid and oxalate^[1,3,15]. Another important factor causing a significant decrease in urinary pH level in obese patients might be increased risk of hyperuricosuria, resulting in increased uric acid excretion and thus acidic urine^[1,3,15].

OBESITY AND URINARY STONE TYPES

The correlation between urinary stone type and increasing incidence of urolithiasis, as well as the biochemical mechanisms underlying this relationship, are not clear in

obese individuals. In a recent study by Chou *et al*^[3], the authors investigated if obesity was related to the formation of every kind of urinary stone. Although they demonstrated a higher risk of calcium oxalate and uric acid stone formation in obese patients, no significant increase was noted for calcium phosphate stones. There is increasing evidence that obese patients have a higher risk of uric acid stone formation^[4,16]. Previously, it has been demonstrated that 63% of stones in obese patients were composed of uric acid compared to 11% in the non-obese group^[12]. Increased urinary uric acid excretion is also a potential risk factor for calcium oxalate stone formation, since calcium oxalate stones may develop from heterogeneous nucleation of calcium oxalate in a hyperuricosuria environment^[1,3]. Urinary pH decline in obese patients leads to a decrease in calcium phosphate crystal production, resulting in a relative increase in the formation of calcium oxalate stones^[3].

It has previously been shown that although urinary excretion of oxalate and uric acid increased in obese patients, there was no significant change for calcium^[5,17]. Chou *et al*^[3] mentioned that the formation of calcium phosphate stones is frequently associated with metabolic factors, including hyperparathyroidism, and thus may explain why the incidence of calcium phosphate stones is not significantly higher in obese patients.

EFFECT OF DIETARY HABITS ON URINARY STONE FORMATION IN OBESE PATIENTS

High dietary sodium causes obese patients to be more susceptible to worsening calciuria due to natriuresis^[4,5]. Obese patients' diet may possibly be deficient in potassium, magnesium and citrate, resulting in increased risk of calciuria^[4]. Obese patients have urinary compositions reflecting a higher protein diet^[10]. High dietary animal protein has been shown to be a risk factor for urinary stone disease, since this type of diet causes increased excretion of uric acid and calcium as well as decreased excretion of citrate, and a lower urinary pH level, thus making urine more lithogenic^[4,18,19].

The effect of dietary intake of oxalate on urinary stone formation is controversial. In a previous study, Lemann *et al*^[20] demonstrated that urinary oxalate excretion was significantly associated with BMI. In another retrospective study, Taylor *et al*^[10] did not find an association between increased oxalate excretion and obesity. It has been advocated that adoption of a lower sodium diet with increased vegetables, fruits and foods including lower concentrations of fat might be useful to prevent urinary stone formation^[4].

EFFECT OF WEIGHT LOSS ON URINARY STONE RECURRENCE

In a previous study, patients in both obese and non-obese

groups demonstrated a significant decrease in new stone formation rates following dietary and medical therapy^[12]. In contrast, Curhan *et al*^[21] noted no reduction in stone risk following weight loss. Natarajan *et al*^[22] mentioned that the effects of long term weight loss are not as immediately apparent for urinary stone formation in obese patients. There are conflicting results for the effect of bariatric surgery on urinary stone formation in obese patients in the literature^[23-26]. In a previous study, 35 morbidly obese patients who underwent biliopancreatic diversion surgery were included^[23]. Authors found decreased urinary excretion rates of calcium and citrate as well as an increased urinary oxalate excretion 1 year postoperatively. In a further study, authors compared urine compositions of urolithiasis patients who underwent gastric banding or by-pass surgeries for weight reduction with other urinary stone formers who were not treated with bariatric surgeries^[24]. Patients who were treated with surgical procedures for weight loss demonstrated a significantly increased incidence of hyperoxaluria. In another trial, Sinha *et al*^[25] studied 60 patients who had urinary stones following a Roux-en-Y gastric bypass procedure and found a significantly increased calcium oxalate supersaturation with significantly decreased uric acid supersaturation. In contrast, in a similar study, no association was demonstrated between a Roux-en-Y gastric bypass procedure and risk of urolithiasis in a group of morbidly obese patients^[26].

DIFFICULTIES IN SURGICAL MANAGEMENT OF OBESE PATIENTS WITH UROLITHIASIS

Extracorporeal shock wave lithotripsy may be a suboptimal treatment for obese patients since positioning of the patient for an optimal stone fragmentation is a limiting factor^[7]. Most lithotripters have a maximum skin to stone distance of 12-14 cm for their focal point and thus can restrict the acquired distance for complete stone fragmentation in obese patients^[7,27]. Similar difficulties may also decrease the success rate of a percutaneous nephrolithotomy (PCNL) procedure in an obese patient with nephrolithiasis due to difficulties in percutaneous access, as well as limitations in the use of normal sized instruments and higher risk of anesthetic complications in prone position^[7]. In contrast, El-Assmy *et al*^[28] showed that PCNL in obese patients is a safe method with similar success rates, morbidity and operative time.

Natalin *et al*^[7] retrospectively compared stone free rates of ureteroscopic treatment between normal, overweight and obese patients with ureteral and renal stones. The authors concluded that flexible or semirigid ureteroscopy with holmium:yttrium-aluminum-garnet laser lithotripsy in obese and overweight patients is an acceptable treatment modality with success rates comparable to non-obese patients.

CONCLUSION

Obesity is associated with an increased risk of urinary

stone disease. Further studies will better demonstrate the biochemical mechanisms connecting urinary stone disease and obesity. Given the significant association of obesity with urinary stone disease, clinicians should encourage obese patients with urolithiasis to reduce weight through a regular diet and recommend a dietician for further weight loss management. A balanced diet including moderately sized meals with more vegetables, fruits and less fat should be encouraged.

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