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ORIGINAL ARTICLE

Metabolic consequences and tubular function after augmentation cystoplasty in children with neurogenic bladder

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Abstract

Background: While many studies have reported the renal outcomes and metabolic consequences of augmentation cystoplasty (AC), few have focused on changes in renal tubular function. This study investigated the prevalence of metabolic disturbances, renal tubular function, and 24-hour urine chemistry, aiming to evaluate the association between metabolic alterations and urolithiasis after AC.

Methods: We investigated serum biochemistry, blood gas, and 24-hour urinary metabolic profile of children who underwent AC between January 2000 and December 2020. The assessed outcomes included metabolic complications, tubular function, and magnesium status. Associations between 24-hour urinary metabolic parameters and urolithiasis formation were also examined.

Results: A total of 25 patients with a mean follow-up period of 13.8 ± 5.7 years were enrolled. The mean age at AC was 7.5 ± 4.4 years, and 22 and 3 patients underwent AC using the ileum and colon, respectively. There were no abnormalities in serum levels of sodium, potassium, chloride, and calcium. Hypomagnesemia (magnesium <1.7 mg/dL) due to renal loss was observed in one patient (4.0%). Six (24.0%) patients had increased urinary β2-microglobulin levels and normal serum levels. The ratio of the maximum rate of tubular phosphate reabsorption to the glomerular filtration rate was low in three (12.0%) patients. Four (16.0%) patients had normal serum magnesium levels but urinary magnesium excretion <40 mg/d. Urolithiasis occurred in 11 patients (44.0%). The most common 24-hour urine metabolic abnormality was hypomagnesiuria (72.0%). No urinary metabolic parameters or daily protein intake were associated with urolithiasis.

Conclusion: AC for children is safe and does not significantly impact the metabolic profile. Excretions of 24-hour urinary calcium, uric acid, magnesium, and the sodium-to-potassium ratio were not associated with urolithiasis. However, a high prevalence of 24-hour urine magnesium excretion <88 mg/1.73 m^2 was noted. Further prospective studies are needed to investigate longitudinal changes in renal tubular function and 24-hour urine metabolic profiles, particularly magnesium status.

Keywords: Augmentation cystoplasty; Children; Magnesium; Neurogenic bladder; Renal tubular function

1. INTRODUCTION

Augmentation cystoplasty (AC) is a surgery performed in children with low capacity, poor detrusor compliance, or refractory overactive bladder who have failed previous conservative treatments. AC is effective in achieving urinary continence, preserving the upper urinary tract, and improving quality of life.[1,2]

The ileum is the most commonly used segment in AC.[3] Exposure of the ileal or colonic mucosa to urine can lead to hyperchloremic metabolic acidosis due to the absorption of ammonium chloride and secretion of sodium bicarbonate and potassium.[4–6] Acidosis can then induce bone to release calcium, carbonate, and phosphate, leading to hyperphosphatemia. In response, the kidneys adjust their function to maintain the acid-base and electrolyte homeostasis by increasing renal phosphate excretion. In addition, patients with AC have increased excretion of oxalate, which may increase the risk of stone formation.[7,8]

Resection of the terminal ileum can result in vitamin B12 deficiency. In addition, the ileum is the major site of magnesium absorption, with some in the colon.[9] Loss of the distal ileum and colon can also affect bile salts reabsorption, and the continued

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CA9_V88N2_Text.indb 156 14-Feb-25 12:18:01 PM

loss of bile salts can lead to fat malabsorption, steatorrhea, gallstones, and loss of calcium and magnesium.[7] Consequently, hypomagnesemia is a potential side effect in patients receiving ileocystoplasty, sigmoid cystoplasty, or cecocystoplasty.

Magnesium is a mineral that plays an important role in bone formation and mineralization, and magnesium deficiency can thus increase the risk of electrolyte imbalance, neurologic and musculoskeletal disorders, osteoporosis, and a number of chronic diseases such as diabetes mellitus, hypertension, and hyperlipidemia.[10,11] Magnesium homeostasis is regulated by the intestine, bone, and kidneys,[12] and more than half of magnesium in the body is stored in bone. Magnesium deficiency can be difficult to diagnose by clinical symptoms alone, because they are generally absent and nonspecific.[13] The strong compensatory response of magnesium excretion in the urine to maintain magnesium homeostasis means that measurements of serum magnesium may fail to detect normomagnesemic magnesium depletion.

Magnesium deficiency has been reported to increase the risk of calcium oxalate calculi, and magnesium supplementation may prevent the formation of renal stones by decreasing the intestinal absorption of oxalate and increasing urinary citrate excretion.[14,15] Patients undergoing AC are at high risk of both the development and recurrence of urolithiasis.[16] It is therefore critical to elucidate the magnesium status and association between urinary excretion of magnesium and calculi formation after AC. However, the effects of magnesium status and tubular function compensation on metabolic consequences after AC have not yet been fully elucidated. Therefore, in this study, we investigated metabolic disturbances, especially magnesium status, long-term renal tubular function as evaluated by 24-hour urine collection, and bone mineral density, and compared urinary metabolic profiles between children with and without urolithiasis.

2. METHODS

2.1. Study population and postoperative follow-up

We retrospectively reviewed children (age <18 years) who underwent AC for neurogenic bladder at our center between January 2000 and December 2020. Patients without complete records (with <50% of the required information) and those who were lost to follow-up were excluded. Demographic data, length of bowel resected, and clinical characteristics including age, sex, augmentation type, medications (diuretics, proton pump inhibitors, and nephrotoxic drugs) were recorded. Postoperatively, all patients received clean intermittent catheterization. The patients were regularly followed up at our multidisciplinary spina bifida clinic where they received renal function tests and neo-bladder and renal ultrasound to monitor urinary tract dilation and formation of urinary tract calculi. At the last follow-up with a mean duration of 13.8 ± 5.7 years after surgery, the patients underwent comprehensive biochemical investigations including blood urea nitrogen, creatinine, sodium, potassium, chloride, phosphate, calcium, uric acid, intact parathyroid hormone (iPTH), venous blood gas, serum and urine β2-microglobulin levels, and tubular function as assessed by 24-hour urine collection. Metabolic acidosis was defined as a venous pH <7.35 and bicarbonate concentration <22 mmol/L, and hyperchloremia was defined as a chloride level >110 mmol/L. Hypophosphatemia was defined as a serum phosphate concentration <2.5 mg/dL, and hyperphosphatemia was defined as a serum phosphate level >5 mg/dL in adults or >7 mg/dL in children or adolescents. Hyperammonemia was defined as an ammonia level >80 μg/dL. This study was approved by the Institutional Review Board of Taipei Veterans General Hospital (2024-05-006BC).

2.2. Proteinuria and tubular function evaluation

Microalbuminuria and macroalbuminuria were defined as a spot urine albumin/creatinine ratio of 30 to 299 and >300 mg/g, respectively. Samples of 24-hour urine were collected for biochemical analysis, including protein, sodium, potassium, chloride, phosphate, calcium, and uric acid. We classified the patients into mild proteinuria (<0.5 g), moderate proteinuria (0.5-3.5 g), and severe proteinuria (≥3.5 g) groups based on 24-hour urine protein results. Tubular function was evaluated by venous blood gas analysis, glucosuria, urinary β2-microglobulin, fractional excretion of uric acid (FeUA), fractional excretion of phosphate, tubular reabsorption of phosphate (TRP), ratio of the maximum rate of tubular phosphate reabsorption (TmP) to the glomerular filtration rate (GFR) (TmP/GFR), and urinary anion gap (UAG).[17] The renal fractional excretions of electrolytes were calculated using standard formulas. TmP/GFR was calculated as follows: if TRP ≤0.86, TmP/GFR = TRP × serum phosphate; or if TRP >0.86, TmP/GFR = serum phosphate × 0.3 × TRP/[1–(0.8 × TRP)]. TmP/GFR values below the age-dependent reference values indicated renal phosphate wasting. TmP/GFR values <2.8[17,18] and <2.5 mg/dL[19,20] were considered low for patients under 15 and ≥15 years of age, respectively. UAG was calculated as [(urine sodium + urine potassium) – (urine chloride)]. A positive UAG value indicated normal ammonium excretion. Urinary β2-microglobulin was considered to be increased if the result was >300 ng/mL. Hypouricemia with increased FeUA was defined as a serum uric acid concentration ≤2.0 mg/dL with FeUA >10%.

2.3. Assessment of 24-hour urinary magnesium excretion

Fractional excretion of magnesium (FeMg) was calculated as: FeMg = 100 × (urine magnesium × serum creatinine)/[(0.7 × serum magnesium) × urine creatinine]. Hypomagnesemia was defined as a serum magnesium concentration <1.7 mg/dL based on an increased risk of cardiovascular disease compared to those with a higher magnesium level.[21] In the presence of hypomagnesemia, renal magnesium wasting was defined as FeMg >4% in patients with an estimated GFR (eGFR) >30 mL/mL/1.73 m^2. Normomagnesemic magnesium depletion not from renal loss with appropriate renal magnesium conservation was defined as a magnesium level between 1.7 and 2.4 mg/dL with 24-hour urine magnesium excretion <40 mg/d/1.73 m^2.

2.4. Assessment of urolithiasis and 24-hour urine chemistry studies

Acute symptomatic and asymptomatic urolithiasis were confirmed by computed tomography or routine surveillance ultrasonography. To identify urinary risk factors for urolithiasis, 24-hour urine metabolic profiles including calcium, uric acid, magnesium, sodium, and potassium were measured. Abnormal urine biochemistry findings for urolithiasis were defined as follows: hypercalciuria, urine calcium >4 mg/kg/24 h; hyperuricosuria, urinary uric acid excretion >815 mg/24 h/1.73 m^2; and hypomagnesuria, urinary magnesium excretion <88 mg/24 h/1.73 m^2. Sodium to potassium ratio was calculated as sodium (mmol/L) divided by potassium (mmol/L).

2.5. Estimation of protein intake

We estimated protein intake based on the amount of 24-hour urine urea nitrogen excreted, as follows: [urine urea nitrogen (g/d) + 0.031 × body weight (kg)] × 6.25.[22] Protein intake was expressed as g/kg of body weight.

2.6. Bone mineral density

Bone mineral density of the lumbar spine at the L1 through L4 level was assessed using dual-energy X-ray absorptiometry

CA9_V88N2_Text.indb 157 14-Feb-25 12:18:01 PM

postoperatively. For young adults and children, Z-score of ≤–2.0 without a history of fracture was defined as low bone mineral density.

2.7. Statistical analysis

Continuous variables were presented as mean ± SD, and categorical variables were presented as counts and percentages. The Mann-Whitney *U* test was used to compare continuous variables, and the chi-square test or Fisher's exact test was used to compare categorical variables. All statistical analyses were performed using SPSS version 21.0 (IBM Inc., Armonk, NY). A p value <0.05 was considered significant.

3. RESULTS

3.1. Demographic and clinical characteristics

A total of 25 patients underwent AC and were enrolled, of whom 8 were male and 17 were female. The mean age at AC was 7.5 ± 4.4 years, and the leading cause of neurogenic bladder was spina bifida (88.0%). The ileum was used in 22 cases and the sigmoid colon in 3 cases. The lengths of the resected ileum and sigmoid colon were 21.2 ± 3.5 and 18.3 ± 2.9 cm, respectively, depending on native bladder capacity and desired final capacity. The mean age at last follow-up was 21.3 ± 6.9 years. None of the patients were using diuretics, proton pump inhibitors, or nephrotoxic drugs. Twenty (80.0%) patients had constipation, however none of the patients had steatorrhea or chronic diarrhea.

3.2. Serum biochemistry, metabolic acidosis, renal function, iPTH, and proteinuria

The biochemistry parameter data are shown in Table 1. The sodium, potassium, chloride, calcium, phosphate, and uric acid levels were 141.7 ± 2.0 mmol/L, 4.1 ± 0.3 mmol/L, 105.2 ± 2.4 mmol/L, 9.4 ± 0.5 mg/dL, 3.8 ± 0.9 mg/dL, and 5.3 ± 1.5 mg/dL, respectively. Blood tests showed an ammonia level of 32.8 ± 17.3 μg/dL. None of the patients had hyponatremia, hypokalemia, hyperchloremia, hypocalcemia, hypouricemia, or hyperammonemia. The serum creatinine level, cystatin C level, eGFR, and creatinine clearance rate were 0.9 ± 0.8 mg/dL, 1.0 ± 0.5 mg/L, 101.3 ± 37.7 mL/min/1.73 m^2, and 107.3 ± 36.5 mL/min/1.73 m^2, respectively. Chronic kidney disease stage ≥3 developed in four patients (16.0%) during follow-up. At the time of last follow-up, serum pH, sodium bicarbonate, and CO_2 were within normal ranges in all but two patients. These two patients had an eGFR <60 mL/min/1.73 m^2 and metabolic acidosis, and were receiving long-lasting oral sodium bicarbonate therapy. The mean iPTH concentration was 74.2 ± 143.7 pg/mL, and one patient had secondary hyperparathyroidism due to chronic kidney disease stage 5. Twenty-three patients had some degree of proteinuria. Microalbuminuria, macroalbuminuria, proteinuria of 0.5 to 3.5 g/d, and proteinuria ≥3.5 g/d occurred in 13 (52.0%), 3 (12.0%), 5 (20.0%), and 1 (4.0%) patients, respectively.

3.3. Tubular function

Tubular function parameters are given in Table 1. Increased values of urinary β2-microglobulin were observed in 11 (44.0%) of the patients. Of these 11 patients, 6 had normal serum β2-microglobulin levels. None of the patients had glucosuria or negative UAG. No cases were hypouricemia with increased FeUA. The mean TmP/GFR was 3.6 ± 1.0 mg/dL, and three (12.0%) patients had a low TmP/GFR (defined as <2.8 mg/dL and <2.5 mg/dL for patients under 15 years and ≥15 years of age, respectively). One patient had intermittent hypophosphatemia with low TmP/GFR. None of the patients with normal renal function had hyperphosphatemia.

Table 1

Serum biochemistry, proteinuria, and tubular function in the children receiving augmentation cystoplasty

Variable	Mean ± SD or n (%)
Serum biochemistry	
Sodium, mmol/L	141.7 ± 2.0
Potassium, mmol/L	4.1 ± 0.3
Chloride, mmol/L	105.2 ± 2.4
Calcium, mg/dL	9.4 ± 0.5
Phosphate, mg/dL	3.8 ± 0.9
Magnesium, mg/dL	2.0 ± 0.2
Hypomagnesemia (<1.7 mg/dL)	1 (4.0%)
Uric acid, mg/dL	5.3 ± 1.5
Blood urea nitrogen, mg/dL	20.5 ± 16.5
Creatinine, mg/dL	0.9 ± 0.8
Cystatin C, mg/L	1.0 ± 0.5
β2-microglobulin, ng/mL	1868.7 ± 1385.8
pH	7.3 ± 0.0
Bicarbonate, mmol/L	24.8 ± 2.2
Carbon dioxide, mmol/L	22.9 ± 2.5
Ammonium, μg/dL	32.8 ± 17.3
Albumin, g/dL	4.5 ± 0.4
iPTH, pg/mL	74.2 ± 143.7
Microalbuminuria	13 (52.0%)
Macroalbuminuria	3 (12.0%)
Proteinuria, g/24 h	0.6 ± 0.8
Normal	2 (8.0%)
Mild (<0.5 g/24 h)	17 (68.0%)
Moderate (0.5-3.5 g/24 h)	5 (20.0%)
Severe (≥3.5 g/24 h)	1 (4.0%)
Tubular function	
Urinary β2-microglobulin, ng/mL	1671.9 ± 4881.6
Urinary β2-microglobulin (>300 ng/mL)	11 (44.0%)
Hypouricemia with FeUA >10%	0 (0.0%)
Glucosuria	0 (0.0%)
FeP, %	12.8 ± 11.6
TmP/GFR, mg/dL	3.6 ± 1.0
Low TmP/GFR	3 (12.0%)
Negative UAG	0 (0.0%)

Data are presented as mean ± SD or n (%).
FeP = fractional excretion of phosphate; FeUA = fractional excretion of uric acid; iPTH =intact parathyroid hormone; TmP/GFR = ratio of the maximum rate of tubular phosphate reabsorption to the glomerular filtration rate; UAG = urine anion gap.

3.4. Serum magnesium and urinary magnesium excretion

The mean serum magnesium level was 2.0 ± 0.2 mg/dL (Table 1). One (4.0%) patient was diagnosed with hypomagnesemia (<1.7 mg/dL) caused by renal magnesium wasting. The mean daily urinary magnesium excretion level was 75.0 ± 28.2 mg/d/1.73 m^2 (ranged from 26.5 to 131.8, Table 2). The urinary excretion of magnesium was <40 mg/d/1.73 m^2 in four normomagnesemic patients with normal eGFR.

3.5. Association between 24-hour urine metabolic profile and daily protein intake with urolithiasis

A summary of the 24-hour urine metabolic data and daily protein intake is shown in Table 2. The urinary calcium, uric acid, and magnesium excretion levels were 2.0 ± 1.2 mg/kg/24 h, 579.1 ± 205.3 mg/24 h/1.73 m^2, and 75.0 ± 28.2 mg/24 h/1.73 m^2, respectively. Overall, hypomagnesiuria was the most common urinary abnormality (n = 18, 72.0%) follow by hypercalciuria (n = 2, 8.0%), and hyperuricosuria (n = 2, 8.0%). Eleven patients had urolithiasis at a mean of 9.3 ± 6.6 years post-AC. Compared to the patients without stone formation, those with stone formation had higher urinary sodium to potassium ratio (4.3 ± 1.7

CA9_V88N2_Text.indb 158 14-Feb-25 12:18:01 PM

Table 2

24-hour urine parameters and daily protein intake of the patients with and without urolithiasis

Variable	Total n = 25	Nonurolithiasis group n = 14	Urolithiasis group n = 11	*p* value
Calcium (mg/kg/24 h)	2.0 ± 1.2	2.0 ± 1.3	2.0 ± 1.1	0.870
Hypercalciuria (>4 mg/kg/24 h)	2 (8.0%)	1 (7.1%)	1 (9.1%)	1.000
Uric acid (mg/24 h/1.73 m^2)	579.1 ± 205.3	585.4 ± 137.5	571.1 ± 276.5	0.913
Hyperuricosuria (>815 mg/24 h/1.73 m^2)	2 (8.0%)	1 (7.1%)	1 (9.1%)	1.000
Magnesium (mg/24 h/1.73 m^2)	75.0 ± 28.2	72.7 ± 30.2	78.0 ± 26.5	0.661
Hypomagnesiuria (<88 mg/24 h/1.73 m^2)	18 (72.0%)	9 (64.3%)	9 (81.8%)	0.407
Sodium to potassium ratio	4.0 ± 1.6	3.8 ± 1.5	4.3 ± 1.7	0.477
Protein intake (g/kg body weight)	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	0.584

Data are presented as mean ± SD or n (%).

vs 3.8 ± 1.5), although the difference was not significant (p = 0.477). No significant differences were noted in hypercalciuria (p = 1.000), hyperuricosuria (p = 1.000), and hypomagnesuria (p = 0.407) between the patients with and without stone formation. There was no significant association between protein intake and stone formation (1.1 ± 0.3 vs 1.1 ± 0.3 g/kg, p = 0.622).

3.6. Bone mineral density

The mean bone mineral density was 0.9 ± 0.2 g/cm^2. Reduced bone mineral density was identified in 3 of 21 (14.3%) patients who could walk with or without supportive devices, compared to 2 of the 4 patients (50.0%) who were wheelchair-dependent. Ambulatory status was not associated with decreased bone mineral density (p = 0.584).

4. DISCUSSION

The kidneys play a critical role in the maintenance and regulation of electrolytes and acid-base homeostasis post-AC. Chronic exposure of the intestinal mucosa to urine can result in hyperchloremic metabolic acidosis caused by reabsorption of acid and secretion of bicarbonate by the bowel segment. In our study, metabolic acidosis was subtle, which may be due to the optimal intestine length resected to achieve the desired capacity and adaption of the intestine. Previous studies have reported histopathologic changes including mucosal atrophy and loss of microvilli in augmented ileal segments after exposure to urine for 2 years.[23,24] The severity of metabolic disturbance has also been shown to be influenced by the duration of contact between urine and intestinal mucosa and renal function. Kristjansson et al[25] showed that a GFR of >55 mL/min/1.73 m^2 was sufficient to compensate for the acid-base imbalances in patients with colonic urinary reservoirs. In the present study, slight metabolic acidosis with the need for alkaline supplements was noted in two of the four patients with an eGFR of <55 mL/min/1.73 m^2.

It is well known that terminal ileal resection >20 cm can lead to vitamin B12 deficiency. A previous study demonstrated a decrease in urinary magnesium excretion with an increase in the length of resection in patients with Crohn's disease.[26] After AC, except for potential malabsorption caused by loss of absorptive surface after intestinal resection, chronic metabolic acidosis may also contribute to decreased magnesium status. Therefore, children receiving enterocystoplasty with the ileum or colon are susceptible to magnesium deficiency. The definition of hypomagnesemia varies considerably. In this study, taking 1.7 mg/dL as the threshold value of magnesium deficiency, hypomagnesemia was only noted in one patient (4.0%). In our cohort, hypomagnesemia tended to be unrecognized and did not lead to secondary hypokalemia, hypocalcemia, or severe clinical symptoms.

Magnesium acts as a cofactor of many enzymes and is essential for normal neuromuscular function, as well as electrolyte balance. Magnesium homeostasis is dependent on the small intestine, kidneys, and bone. Magnesium is absorbed in the distal portion of the small and large intestine, primarily in the ilium and distal jejunum. As with calcium, approximately 50% to 60% of total body magnesium is stored in the bone, and it can be recruited in conditions of magnesium deficiency. Most filtered magnesium (65%) is reabsorbed in the loop of Henle, particularly in the thick ascending limb. The kidneys are crucial in maintaining magnesium balance.[27] The renal excretion of magnesium varies from 0.5% to 70% depending on dietary patterns, net intestinal absorption, and magnesium status of the body. Due to the physiological compensatory processes of the kidneys and bone, serum magnesium levels tend to remain normal in the early stages of magnesium deficiency. The diagnosis of magnesium depletion based on serum magnesium is considered a convenient but late marker. Under the assumption that urinary magnesium excretion reflects magnesium intake/absorption, decreased urinary magnesium excretion is likely suggestive of decreased intestine absorption in individuals with a nutritionally adequate intake of magnesium. Therefore, 24-hour urinary magnesium or FeMg may be an early indicator of subclinical magnesium depletion.[28]

No standard cutoff value of urinary magnesium excretion has yet been defined to diagnose subclinical magnesium deficiency. Costello and Nielsen[29] and Costello et al[30] suggested that magnesium deficiency should be considered as urinary magnesium excretion <40 to 80 mg/d. Taking into account the circadian rhythm with more magnesium excretion at night, analysis of 24-hour urine magnesium excretion provides an accurate alternative way of assessing magnesium intake and absorption.[31] To date, no previous studies have used 24-hour urinary excretion of magnesium to evaluate potential magnesium deficiency in children following AC. In the present study, four (16.0%) normomagnesemic patients had urinary magnesium excretion <40 mg/d/1.73 m^2, indicating decreased magnesium intake/absorption. In Taiwan, people prefer polished white rice, which has a lower magnesium content compared to polished brown and red rice. However, no previous study has investigated the implication of regular oral or parental magnesium supplementation for the prophylaxis of hypomagnesemia or to treat asymptomatic magnesium deficiency in AC patients. Increasing dietary intake of magnesium-enriched foods such as whole-grain rice, green leafy vegetables, dairy products, and nuts may be a beneficial clinical approach for AC patients with normal renal function. Children with neurogenic bladder caused by spina bifida are also at risk of chronic constipation.[32] Magnesium oxide supplements may be effective in improving both chronic constipation and low magnesium levels.

CA9_V88N2_Text.indb 159 14-Feb-25 12:18:01 PM

Similar to prior studies, we found that stone formation was a common long-term complication in our patients. Stone formation is thought to be secondary to excessive mucus formation,[33] recurrent infection with urea-splitting organisms,[34] urinary stasis, concomitant bladder neck surgery, cloacal malformations, and vaginal reconstruction, all of which can increase the risk of urolithiasis.[35] Other potential factors associated with urolithiasis include hypercalciuria, elevated urine pH, hyperuricosuria, hyperphosphaturia, hypomagnesiuria, hyperoxaluria, and hypocitraturia. A high urinary sodium to potassium ratio has also been associated with an increased risk of developing urinary stone disease.[36] Furthermore, a high protein diet has been associated with increased excretion of calcium and undissociated uric acid due to a reduction in urine pH as well as a reduction in citrate excretion. In addition, patients who undergo bladder reconstruction with ileum are at risk of enteric hyperoxaluria secondary to decreased reabsorption of bile acid and fat malabsorption. Specifically, free fatty acids reach the colon and bind with calcium, thereby lowering the amount of available calcium for oxalate, subsequently resulting in an increase in free oxalate reabsorption in the colon. Hyperoxalemia then leads to increased urinary oxalate excretion and formation of calcium oxalate stones in these patients. However, we did not analyze urinary citrate or urinary oxalate excretion in this study, as these tests are not readily available in Taiwan. Moreover, the compensatory mechanism of renal tubules in decreasing the excretion of magnesium to maintain normal serum levels may also play a role in increasing the risk of urolithiasis. The actual effects of magnesium on stone formation remain unknown. Previous studies have shown that magnesium supplements can decrease the risk of nephrolithiasis by increasing urinary citrate excretion,[14] decreasing urinary calcium oxalate supersaturation by binding to oxalate in the intestine, or by forming a more soluble magnesium-oxalate complex.[37] On the other hand, other studies have shown that magnesium deficiency is not a significant cause of urolithiasis.[38–40] In the current series, 18 and 2 patients had hypomagnesiuria (<88 mg/24 h/1.73 m^2) and hypercalciuria, respectively. However, no significant differences were noted in the metabolic changes of 24-hour urinary excretion and daily protein intake between the patients with and without stone formation. Further studies with a larger sample are needed to better understand the role of metabolic disturbances and metabolic compensation of tubular function, and especially magnesium, in those at high risk of urolithiasis.

To the best of our knowledge, this is the first study to evaluate the effect of AC on 24-hour urine metabolites. The main limitation of this study is the small sample size and the lack of an unaugmented bladder control group, which may hinder the assessment of the true impact of AC interventions on metabolic complications. In addition, we did not precisely assess dietary intake, so we could not confirm whether hypomagnesemia was caused by inadequate dietary magnesium intake or decreased magnesium absorption. In addition, we did not analyze urinary citrate or urinary oxalate excretion, as these tests are not readily available in Taiwan.

In conclusion, we identified subclinical hypomagnesemia or normomagnesemic magnesium depletion due to renal loss, inadequate magnesium intake, or malabsorption in our cohort of patients undergoing resection of the intestine for enterocystoplasty. We suggest that combining measurements of serum magnesium and 24-hour urinary magnesium excretion may provide a more accurate reflection of magnesium status. We also found a high prevalence of 24-hour urine magnesium excretion <88 mg/1.73 m^2. No statistically significant differences were observed in 24-hour urinary metabolite analysis in the patients with urolithiasis, suggesting that supersaturation alone cannot sufficiently explain stone formation in children following AC. Further prospective studies are warranted to clarify the impact of changes in urine metabolic profile.

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CA9_V88N2_Text.indb 160 14-Feb-25 12:18:01 PM

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CA9_V88N2_Text.indb 161 14-Feb-25 12:18:01 PM