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Original Article

Posterior urethral valve: Outcome of antenatal intervention

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Introduction and Aim: Antenatal treatment of obstructive uropathy, although widely performed, remains controversial. This study evaluated the long-term outcome of managing patients with posterior urethral valves (PUV), highlighting the effect of antenatal vesicoamniotic shunt placement for patients who underwent fetal surgery.

Methods: The medical records of 58 patients with PUV were retrospectively reviewed from June 1998 to June 2004. On the basis of prenatal assessment of sonographic findings and serial urinary electrolytes and protein measurements, patients were divided into two groups: group 1 comprised patients who had antenatal vesicoamniotic shunt placement whereas group 2 comprised patients who underwent postnatal surgical correction of PUV. Their outcomes and long-term results were evaluated.

Results: Patients were followed up from 6 months to $6^1/_2$ years (mean 3.9 years). Group 1 included 12 patients who had vesicoamniotic shunt placement and were confirmed postnatally to have PUV. Four patients out of 12 died (33.3%); three out of the eight living patients had perinatal complications. Of the eight living patients, three (37.5%) underwent valve ablation and five (62.5%) underwent urinary diversion (three vesicostomies and two cutaneous ureterostomies). Renal function returned to normal in only four patients (50%). Radiological abnormalities (hydronephrosis and/or reflux) resolved in three (37.5%) patients, was downgraded in one (12.5%) patient and persisted in four patients (50%). Group 2 included 46 patients who were treated postnatally. Thirty-five patients (76%) underwent primary valve ablation, while 11 (24%) underwent urinary diversion (seven vesicostomies, four cutaneous ureterostomy and one pyelostomy). Renal function returned to normal in all patients who underwent valve ablation, except in three, while renal function returned to normal in only three of 11 patients who underwent urinary diversion. Radiological hydronephrosis and/or reflux resolved in 28 patients (60.9%), was downgraded in six patients (13%) and persisted in 12 patients (26.1%).

Conclusions: Antenatal vesicoamniotic shunt placement makes no difference to the outcome and long-term results of patients with PUV and debate about its efficacy on renal outcome remains. Primary valve ablation is the keystone of treatment for patients with PUV that might achieve the primary goal of nephron preservation. The lowest creatinine concentration in the first year of life is the most appropriate predictor of future renal function.

Key words antenatal, urinary diversion, valve.

Introduction

Posterior urethral valves (PUV) are the most common congenital abnormalities causing bilateral renal obstruction.[1] The mortality rate secondary to PUV ranges from 24-54%.[2–5] Primary valve ablation and temporary vesicostomy with delayed valve ablation are alternative initial management procedures in neonates and infants with PUV.[6]

The widespread use of prenatal ultrasonography has contributed to an increased awareness of PUV and the detection of hydronephrosis in up to 1% of fetuses.[1,2] There is a substantial prognostic discrepancy between those cases diagnosed prenatally and those not detected until after birth, because the more severe cases do not survive the immediate postnatal period.[7] Fetal surgery for obstructive uropathy due to PUV has been attempted since the early 1980s by open fetal surgery then percutaneous vesicoamniotic shunt placement to ensure bladder drainage.[7,8]

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Despite improvements in the technique and selection of patients, there is little evidence of the efficacy of prenatal intervention and the treatment remains controversial.[2,7,9,10] The fate of the kidneys seems to be unchanged despite adequate drainage through the vesicoamniotic shunt. Renal failure has been reported to occur in about 19-64% of males diagnosed with PUV prenatally and in 25-40% of infants diagnosed postnatally.[8]

Our study aimed to evaluate the long-term outcome of patients with PUV, highlighting the effect of antenatal vesicoamniotic shunt placement for patients who underwent fetal surgery.

Methods

Medical records of patients with PUV were retrospectively reviewed from June 1998 to June 2004. On the basis of prenatal assessment of sonographic findings and serial urinary electrolytes and protein measurements, patients were divided into two groups.

Group 1: patients diagnosed antenatally with obstructive uropathy were selected for vesicoamniotic shunt placement, with postnatal diagnosis of PUV based on voiding

cystourethrogram and cystoscopic findings. Vesicoamniotic shunting was performed using a double pigtail catheter placed in the bladder and amniotic cavity. Indications for prenatal intervention included bilateral hydronephrosis with distended bladder, oligohydramnios, isolated urinary tract abnormalities, and normal male Karyotype with good predictive outcome based on serial (three) percutaneous needle bladder drainage (vesicocentesis) performed at 48–72 h intervals. The threshold indicative of a favorable prognosis was defined by urine sodium of less than 100 mmol/L, chloride less than 90 mmol/L, osmolarity less than 200mOsm/L, calcium less than 2 mmol/L, and β-2 microglobulin less than 508 mmol/L.

Group 2 included patients with PUV diagnosed postnatally or antenatally but not fulfilling the criteria for antenatal intervention. These patients underwent postnatal correction of PUV either endoscopically (primary valve ablation) or surgically (urinary tract diversion).

The outcome and long-term results of all patients were analyzed and focused on mortality, antenatal complications, surgical procedures, renal function, bladder function based on voiding pattern and urodynamic studies if available, and persistence of radiological abnormalities (hydronephrosis and/or vesicoureteric reflux).

Results

Fifty-eight patients were included in our retrospective study. Patients were followed up for a mean of 3.9 years (range 0.5–6.5 years).

Group 1 consisted of 12 patients diagnosed antenatally with obstructive uropathy and they fulfilled all criteria necessary for antenatal intervention. A vesicoamniotic shunt was inserted between the 19th and 29th weeks of gestation and postnatal investigations (voiding cystourethrogram and cystoscopy) confirmed the presence of PUV.

Only one patient suffered vesicoamniotic shunt displacement and subsequent urinary ascites, which was treated successfully by repositioning the catheter. Four out of 12 patients died (33.3%), two due to pulmonary hypoplasia, one due to postnatal sepsis and one from extreme prematurity and extensive necrotizing enterocolitis (Table 1).

Three of the remaining eight living patients had perinatal complications. One patient had urinary ascites due to intraperitoneal displacement of the shunt. One patient developed herniation of the bowel at the site of vesicoamniotic shunt insertion which necessitated surgical repair after delivery, and the last patient developed only omental herniation which required surgical repair postnatally (Table 1). Of the eight living patients, three (37.5%) underwent primary valve ablation and five (62.5%) underwent initial urinary diversions (three vesicostomies and two cutaneous ureterostomies) followed by valve ablation (Table 2). Indications for urinary diversion were persistently elevated serum creatinine in three patients, despite urethral catheter drainage, urosepsis and elevated serum creatinine in one patient and a small caliber urethra that precluded primary transurethral valve ablation in one patient. The serum creatinine level returned to normal in four patients (50%); three treated with primary valve ablation and one with vesicostomy. One patient had renal insufficiency with a serum creatinine level of 120 μmol/L and three patients had renal failure.

Hydronephrosis and vesicoureteric reflux were present in three patients. Vesicoureteric reflux was present in two patients and hydronephrosis in three patients. Hydronephrosis resolved in two patients, persisted in three and was downgraded in one patient. Vesicoureteric reflux (VUR) resolved in two patients and persisted in three patients. Globally, radiological abnormalities resolved in three patients (37.5%), was downgraded in one (12.5%) and persisted in four patients (50%) (Table 3).

One patient underwent renal transplantation concomitant with augmentation cystoplasty and bilateral reimplantation and the Mitrofanoff procedure for clean intermittent catheterization (CIC). Two patients were scheduled for the renal transplantation program. One patient who had renal insufficiency received conservative treatment. Augmentation cystoplasty with the Mitrofanoff procedure was performed for one patient with valve bladder syndrome.

Urodynamic studies were carried out in only three patients in group 1 and this revealed detrusor overactivity

Table 1 Causes of death in group 1

Cause of mortality	No.	Cause of morbidity	No.
Pulmonary hypoplasia	2	Bowel prolapse	1
Extreme prematurity and extensive NEC	1	Omental prolapse	1
Postnatal sepsis	1	Dislodgement of V-A shunt and urinary ascitis	1

Table 2 Surgical intervention

Primary	Group 1	Group 2
Primary valve ablation	3	35
Vesicostomy	3	7
Cutaneous ureterostomy	2	3
Ureterostomy and pyelostomy	0	1
Delayed		
Augmentation cystoplasty	2	9

Table 3 Group 1 radiological abnormalities

Type of anomaly	No.	Returned to normal	Persisted	Downgraded
VUR + HN	3	1	2	0
VUR only	2	1	1	0
HN only	3	1	1	1
Total (%)	8	3 (37.5)	4 (50)	1 (12.5)

HN, hydronephrosis; VUR, vesicoureteric reflux.

Table 4 Urodynamic studies in both groups

Findings of urodynamic study	Group 1	Group 2
Normal	1	4
Poor compliance	0	4
Detrusor overactivity	1	8
Poor compliance and detrusor overactivity	1	3
Total	3	19

Table 5 Group 2 radiological abnormalities

Type	No.	Normal	Persisted	Downgraded
HN + VUR	24	16	4	4
VUR	7	4	2	1
HN	15	8	6	1
Total	46	28	12	6

HN, hydronephrosis; VUR, vesicoureteric reflux.

in one patient, poor compliance and detrusor overactivity in one, and normal activity in one patient (Table 4).

Group 2 consisted of 46 patients who were documented postnatally to have PUV on the basis of voiding cystourethrography and cystoscopy and were treated postnatally. Twenty-one of the patients were diagnosed antenatally to have hydronephrosis and obstructive uropathy. Nine had mild to moderate oligohydramnios and were candidates for an A-V shunt, but after parental counseling fetal surgery was refused.

Thirty-five patients (76%) underwent primary valve ablation, seven of whom needed two sessions to ablate the valve. Three patients required secondary urinary diversion through vesicostomy due to persistently elevated serum creatinine in one patient and repeated attacks of sepsis in the other two, despite successful valve ablation. Eleven patients (24%) underwent primary temporary urinary diversion, seven of whom had a vesicostomy, three had cutaneous ureterostomy and one patient had left cutaneous loop ureterostomy and right pyelostomy (Table 2).

Renal function (serum creatinine) returned to normal in all patients, except three, who underwent primary valve ablation. One patient had renal insufficiency with a serum creatinine level of 135 μmol/L and the other two had renal failure (one on dialysis and the other had renal transplantation).

Renal function returned to normal in only three out of 11 patients who underwent primary urinary diversion (three patients had renal insufficiency and the other five had renal failure). Nine patients had oligohydramnios; four underwent urinary diversion and five had impairment of renal function (three underwent diversion and two had valve ablation).

Radiologically, in group 2, 31 patients had VUR and 39 were found to have hydronephrosis (24 patients had both VUR and hydronephrosis, seven had VUR only while 15 patients had hydronephrosis only). Vesicoureteric reflux resolved in 20 patients, persisted in six and was downgraded in five. Hydronephrosis resolved in 24 patients, persisted in 10 and was downgraded in five. Radiological abnormalities resolved completely in 28 patients, persisted in 12 and were downgraded in six patients (Table 5).

Renal function improved in two out of three patients with urosepsis and elevated serum creatinine that underwent secondary urinary diversion after primary valve ablation, and remained high in one patient who developed end-stage renal failure.

Table 6 Comparison of radiological results

	Group 1	Group 2
Returned to normal (%)	3/8 (37.5)	28/46 (60.9)
Downgraded (%)	1/8 (12.5)	6/46 (13)
Persisted (%)	4/8 (50)	12/46 (26.1)

Urodynamic studies were carried out for 19 patients in group 2, denoting detrusor overactivity in eight patients, poor compliance in four, poor compliance and detrusor overactivity in three and normal activity in four patients (Table 4).

Discussion

PUV are the most common congenital abnormalities causing bilateral renal obstruction in males.[1,11] In the past few decades, the mortality rate associated with PUV has declined from 50% to less than 5%. Hemodialysis, excellent broad spectrum antibiotics and improvements in neonatal intensive care units have contributed equally to the decline in mortality.[1,12] Despite all these advances, 24-45% of patients will have renal insufficiency during childhood.[13–16] Unfortunately, prenatal diagnosis of PUV has not improved this rate. Some believe that prenatal intervention holds promise for improved outcomes by preventing progressive tract damage and permitting drainage of urine into amniotic space, minimizing pulmonary hypoplasia or postnatal pulmonary insufficiency. Although controversial, prenatal intervention is technically difficult and the ethical dilemma associated with it precludes its use in many surgical centers worldwide.[1]

Although a general consensus among pediatric urologists for antenatal intervention exists, no prospective randomized trials or uniform written guidelines exist that support the therapeutic benefit of antenatal intervention in altering the natural history of obstructive uropathy.[17,18]

The clinical efficacy of vesicoamniotic shunt placement for antenatal treatment of suspected obstructive uropathy and its proper role in therapy are not yet known, and little is known about the postnatal care or long-term outcome for surviving children.[18–20]

Fetal intervention for PUV carries a considerable risk to the fetus with a fetal mortality rate of 43%.[21] In our study, four out of the 12 patients (33.3%) in group 1

died; two due to pulmonary hypoplasia, one due to postnatal sepsis and one due to extreme prematurity and extensive necrotizing enterocoliris (NEC). This outcome is similar to that in a series of patients reported by Freedman *et al*.[7] They reported that 13 of the 34 cases (38%) died and causes of death were pulmonary hypoplasia (six), chorioamnionitis (two), postnatal sepsis (two), intrauterine fetal demize (one), voluntary termination (one), and preterm labor (one).[7] Furthermore, Holmes *et al.* reported six deaths out of 14 who underwent fetal surgery.[21]

Based on fetal electrolytes and ultrasonographic renal cortical findings, Cromleholme *et al*. demonstrated an improved survival rate for candidates of intervention in the good prognosis group (89%) compared to the poor prognosis group (30%).[22] Johnson *et al.* reported eight long-term survivors among 15 fetuses who underwent vesicoamniotic shunts.[9]

Intervention is associated with significant morbidity and mortality even when performed at a tertiary care center. A recent review of the literature demonstrated a complication rate for antenatal intervention of 21-59%.[18,19,23] Several studies reported high complication rates for vesicoamniotic shunt placement, estimated to be 44% in some series.[24] In our series, two patients had evisceration, with bowel prolapse in one and omentum in the other that necessitated immediate postnatal surgical repair with vesicostomy. This complication was also reported by several authors.[24–26] The incidence of vesicoamniotic shunt migration varied in different series. Elder *et al.* reported that it was 19%[18] whereas in our series it occurred in one patient with successful repositioning.

Proper assessment of the effect of prenatal intervention on postnatal renal function is still difficult. Despite advances in the use of fetal urinary electrolytes and proteins, assessment can only estimate presumed prenatal renal injury.[27] In addition, the shunt may become dislodged in up to one-third of fetuses, which limits the time that therapy is effective.[28] Most importantly, in the postnatal period renal injury may be exacerbated by febrile urinary tract infections, residual bladder dysfunction and poorly compliant valve bladder after PUV ablation. Therefore, progressive renal deterioration in some patients with acceptable initial postnatal renal function is probably related to underlying bladder dysfunction and associated risk of infection, and may not adequately reflect antenatal injury or the effect of successful prenatal intervention.[7,29]

While major improvements have been achieved in lowering the mortality of patients with PUV, renal functional impairment remains a significant problem[30] as a considerable percentage (from 24-33%) of patients with PUV still have end-stage renal failure.[31,32] In our series, 50% of patients in group 1 developed renal failure, while in group 2, 23.9% developed renal failure. Of the eight survivors in the Johnson *et al*. series, six demonstrated good renal function and two had poor renal function, which were predicted antenatally by interpretation of bladder urine electrolytes.[9] While in the Holmes *et al*. series, chronic renal disease with abnormal serum creatinine was present in five patients out of eight survivors, two patients had undergone renal transplantation and one was awaiting organ donation.[21]

Patients with an antenatal vesicoamniotic shunt had a 50% improvement rate in both reflux and hydronephrosis. Conversely, the improvement rate in group 2 with postnatal correction of PUVs was 73.9%. This may reflect more severe bladder abnormalities leading to severe upper tract abnormalities, with a higher incidence of renal insufficiency in patients who need antenatal intervention (Table 6).

Some authors demonstrated that postnatal outcome for severe antenatal obstructive uropathy that undergo intervention approaches the outcome of less severe cases of obstructive uropathy detected postnatally, and antenatal intervention may provide an acceptable long-term outcome.[7,17] In our study, nine patients had oligohydramnios and after parent counseling they refused fetal surgery.

In contrast, several studies have shown that factors, such as the anticipated postnatal diagnosis, fetal bladder urine electrolytes or the degree of oligohydramnios, have no impact on the survival of the fetus and there is no evidence that fetal urine electrolytes facilitate the identification of which fetuses may benefit from intervention.[33] No evidence exits that demonstrates the benefit of antenatal intervention in terms of renal function and only in a select number of cases will this benefit pulmonary function.[34]

Several studies have investigated the role of urinary diversion in the treatment of patients with PUVs; some authors concluded that urinary diversion is not warranted because it rarely affects renal outcome.[11,35,36] This was supported by another study that doubted the benefits of upper tract diversion as 42% of the patients developed end-stage renal disease or renal insufficiency after long-term follow-up.[37] On the contrary, others have shown that temporary urinary diversion protected the kidneys and promoted this approach as a first line of therapy.[38] Some authors believed that secondary vesicostomy in a select group of patients with unrelenting sepsis may stabilize renal function and possibly delay the onset of dialysis, being an end treatment for otherwise refractory urinary sepsis and stasis.[11]

Patients treated with primary valve ablation did not need bladder augmentation as opposed to those treated with urinary diversion. This again indicates that patients who underwent diversion had more severe bladder abnormalities and upper tract changes.[39] In group 1 in our series, augmentation cystoplasty with the Mitrofanoff procedure was performed in two cases, one patient had renal transplantation and two required dialysis. Two children now void spontaneously without additional maneuvers and four need CIC (two with augmentation and two because of postvoid residuals). In the Freedman *et al.* series, four cases with PUV had V-A shunts, three had augmentation cystoplasty, one had renal transplantation, and three cases had more than six attacks of urinary tract infections and remained on prophylactic antibiotics.[7] Holmes *et al.* reported that five out of eight living patients had urinary diversion with vesicostomy, cutaneous ureterostomy or augmentation cystoplasty.[21]

In an attempt to define the role of urinary diversion, Farhat *et al*. reported that renal outcome was independent of the treatment as urinary diversion to salvage renal

function improved the function in 20% of patients with unrelenting sepsis after initial valve ablation. Patients treated only with valve ablation had a 50% improvement rate in both hydronephrosis and reflux. Conversely, no improvement occurred in those patients who underwent diversion.[11,35]

In group 1, five out of eight patients (62.5%) underwent initial urinary diversion to stabilize renal function; three progressed to end-stage renal failure and one had renal insufficiency. In group 2, 14 patients underwent urinary diversion (11 primary and three secondary) and nine of them had renal failure. Overall, renal failure occurred in only two patients out of 35 (5.7%) who underwent primary valve ablation, while it occurred in 13 patients out of 19 (68.4%) who underwent urinary diversion. Consequently, we believe that primary valve ablation should be considered the preferred management option in patients with improved serum creatinine levels after the initial catheter drainage of the bladder, and the role of urinary diversion is limited to patients with continued elevated serum creatinine levels and refractory urosepsis.

A commonly used predictor of future renal function is the lowest creatinine concentration in the first year of life.[40–42] In our study, all patients with a lowest creatinine measurement of more than 115 μmol/L progressed to renal failure and required renal replacement therapy. The group with serum creatinine less that 80 μmol/L contained children with good long-term function, in which only one progressed to renal failure after repeated urinary tract infections and bladder dysfunction.

Therefore, we believe that the lowest creatinine concentration in the first year of life is a highly predictive and more appropriate outcome measure to assess the effects of antenatal intervention on renal function than the most recent creatinine concentration measure, because of the possible exacerbation of postnatal renal damage by persistent lower urinary tract dysfunction and urinary tract infections.

Conclusions

Antenatal vesicoamniotic shunt placement makes no difference to the outcome and long-term results of patients with PUV and the debate about its efficacy on renal outcome remains. Future challenges to improve selection criteria and develop fetal cystoscopic ablation of valves may improve the outcome and long-term results of fetal surgery of obstructive uropathy. Although urinary tract diversion has a role in patients with refractory urosepsis and severe upper tract deterioration, primary valve ablation is the cornerstone of treatment for patients with PUV that may achieve the primary goal of nephron preservation. The lowest creatinine concentration in the first year of life is the most appropriate predictor of future renal function.

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