Vesicoamniotic shunting for fetal lower urinary tract obstruction: an overview

R K Morris, K S Khan, M D Kilby

Efficacy and complications of prenatal in utero treatment

Lower urinary tract obstruction (LUTO) is a heterogeneous group of pathologies, most commonly urethral atresia and posterior urethral valves (PUVs)¹ that accounts for one third of renal tract anomalies detected at autopsy after termination for ultrasound-diagnosed fetal anomaly.² The affected fetus is typically male unless associated with bladder hypoperistalsis syndromes which carry a worse prognosis. PUV accounts for about half of the cases presenting with ultrasonic features of LUTO³ in some case cohorts. In 2005, data from the Northern Region Congenital Anomaly register were reported. Over a 14-year period, 113 cases of LUTO were identified, giving an incidence of 2.2 in 10 000 births.⁴

PATHOPHYSIOLOGY

The importance of LUTO in terms of perinatal outcome lies in its clinical course, with long-term urethral obstruction being potentially associated with cystic renal dysplasia, abnormal renal (glomerular and tubular) function leading to severe oligohydramnios, pulmonary hypoplasia and positional limb anomalies.⁵ Animal studies have shown a causal link between the distal renal tract obstruction in the fetus and these abnormalities. The fetal phenotype has been variously described as the effects of potential in utero treatment.

Fetal LUTO, if untreated, carries a mortality of up to 45% mainly due to the severe oligohydramnios in the mid-trimester⁶ being associated with pulmonary hypoplasia. Even in those that survive the neonatal period, up to one third may develop end-stage chronic renal impairment, necessitating dialysis or transplantation.⁷ Congenital obstructive uropathy accounts for up to 60% of all paediatric renal transplants.⁸ It is therefore a morbid condition, although data informing this comes from small, uncontrolled selected series. For this reason, prenatal in utero treatment has been considered in "selected" cases in an attempt to bypass the congenital urinary tract obstruction, modify pathogenesis and attenuate the secondary developmental complications.

Prenatal counselling in this situation is, however, difficult as the modalities used to assess fetal renal function have uncertain prognostic value and the effectiveness of the treatment remains to be established.

ANTENATAL DIAGNOSIS AND ASSESSMENT

The detection of fetal LUTO using ultrasound has good accuracy,^{9,10} partly because the anomalies of the renal tract and kidneys are also associated with secondary findings, such as oligohydramnios. Assessment of the fetal genitourinary tract forms a part of all routine screening ultrasound examinations (usually at 20 weeks), and when abnormalities are detected this should lead to a detailed assessment focusing on amniotic fluid volume, renal size, parenchyma, collecting system and bladder size. Ultrasonography may help in the differentiation of obstructive and non-obstructive causes of megacystis, with the association of increased echogenicity and oligohydramnios in the presence of bladder distension being predictive of an obstructive aetiology in about 87% of cases¹⁰ (fig 1). However, it is of limited

value differentiating PUV from other causes of LUTO.^{10,11}

It is important to differentiate true urethral obstruction from the megacystis—mega-ureter—microcolon syndrome, a rare disorder characterised by a functional intestinal obstruction/hypomobility and an enlarged non-obstructed bladder. It is more common in female fetuses and has a poor prognosis. As it can be difficult to differentiate on ultrasound, it is important to consider this diagnosis carefully in a female fetus with LUTO but normal liquor volume. It is, as a generalisation, not beneficial to consider in utero shunting for these pregnancies.

It is mandatory to perform a detailed anomaly scan, determine fetal sex and offer fetal karyotyping (owing to the high incidence of karyotypic abnormalities), in cases of obstructive uropathy. Allocation of fetal sex may allow diagnosis to be further elucidated. PUVs and urethral atresia have a high prevalence in the male fetus. If there is severe oligohydramnios, amnio infusion may occasionally need to be used to allow accurate evaluation of fetal structures. If a normal karyotype is confirmed in a fetus with LUTO and no other congenital anomalies, then consideration may be given to in utero treatment. Other prognostic indicators would be assessed from ultrasound, such as kidney appearance and liquor volume. Consideration should also be given to assessing kidney function. Several methods have been used including analysis of fetal urine, serum or amniotic fluid and, finally, renal biopsy.

Assessing fetal renal function in early pregnancy has been used to select fetuses before performing in utero treatment. There are many published studies evaluating the use of fetal urine metabolites in evaluating fetal renal function, but no

Figure 1 An ultrasound image of a fetal bladder in a baby with lower urinary tract obstruction. The dilatation of the proximal urethra gives the bladder a classic "keyhole" appearance.

consensus seems to have been reached as to the overall efficacy.

TREATMENT

Percutaneous vesicoamniotic shunting is the method most commonly used to relieve urinary tract obstruction. It involves the placement of a double pig-tailed catheter (either Rodeck/Rocket or Harrison shunts) under ultrasound guidance and local anaesthesia, with the distal end in the fetal bladder and the proximal end in the amniotic cavity to allow drainage of fetal urine (fig 2). Amnio infusion is often recommended before shunt insertion in cases of severe oligohydramnios to allow space for insertion. Numerous small studies on the effect of fetal urinary shunting have been reported, each using different criteria for fetal selection, different surgical techniques and different outcome measures. In 2003, Clark *et al*¹² published a systematic review and meta-analysis of the literature on prenatal treatment for bladder outflow obstruction. The review showed a lack of high-quality evidence to reliably inform clinical practice relating to prenatal bladder drainage in fetuses with ultrasound evidence of LUTO, mainly owing to considerable heterogeneity in the studies and imprecision due to small sample size. In the controlled studies, vesicoamniotic drainage in utero (either open, fetoscopic or percutaneous procedures) seemed to improve overall perinatal survival as compared with the non-drainage group (odds ratio (OR) 2.5; 95% CI 1 to 5.9; $p < 0.03$). However, subgroup analysis indicated that this improved survival was predominantly noted in fetuses with a defined "poor prognosis" (defined on ultrasound appearance or fetal urine analysis), where there seemed to be marked improvement (OR 8; 95% CI 1.2 to 52.9; $p < 0.03$).

Other treatment modalities previously used include fetal cystoscopy with ablation of PUVs¹³ and open fetal surgery; however, this is no longer common practice owing to the associated maternal and fetal complications.^{14–17}

OUTCOME AND POSTNATAL FOLLOW-UP

As discussed above LUTO is a condition with high perinatal mortality due mainly to pulmonary hypoplasia; however, long-term outcomes are also important. After birth, the neonate must be at least assessed for renal function via plasma creatinine and renal ultrasound. These investigations should be repeated at 6 weeks of age and 1 year; at this later stage, if possible, tubular function should be assessed using renal electrolytes. It is important to also monitor blood pressure, height and weight. At 5 years of age, there should be an assessment of disability and continence by questionnaire administered to the parent.¹⁸ It is known that, as well as long-term complications of end-stage renal failure, these children are at risk of bladder dysfunction (many involving reconstructive surgery), poor growth and male infertility if uraemic.^{19–21} It is thus important when counselling parents to ensure that they are aware of the still considerable uncertainty as to the development of renal failure, but that these children are expected to have normal cognitive abilities and achieve acceptable continence with medical and surgical care, with similar quality-of-life scores to a healthy child.^{19–21}

PLUTO

The University of Birmingham has started recruitment to the PLUTO study, a randomised, controlled trial to investigate the role of fetal vesicoamniotic shunting in moderate/severe LUTO funded by Wellbeing for Women. This is a multi-centre trial in the UK, and will hopefully be extended later to Europe. It is hoped that over a 3-year period, 200 women will be recruited, criteria being singleton, viable intrauterine gestation with diagnosis of isolated bladder outflow obstruction at < 28 weeks (hydronephrosis, megacystis, oligohydramnios < 5 th centile and no other structural or chromosomal abnormalities). Eligible women who consent will be randomised to either vesicoamniotic shunting or conservative observation. Where possible, fetal urine

will be sampled and analysed for calcium, sodium and urinary β_2 -microglobulin. Follow-up will initially be over a 12-month period, with primary outcome measures being perinatal mortality and serum creatinine. Secondary outcome measures will be the degree of reflux on micturating cystourethrography, bladder wall thickness and renal pelvic dilatation on postnatal ultrasound. At 5 years of age, disability and continence will be assessed. Serious adverse events such as miscarriage, premature rupture of membranes, preterm labour and shunt complications will also be collected. At present, the clinical study is only just beginning, with 10 centres having Local Research Ethical Committee/Research and Development approval to randomise and treat patients locally in the UK.

The outcome of this study will allow concerns raised in terms of efficacy and complications of vesicoamniotic shunting by the National Institute for Clinical Excellence to be considered.²²

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Authors' affiliations

R K Morris, K S Khan, M D Kilby, Division of Reproductive and Child Health, Birmingham Women's Hospital, University of Birmingham, Birmingham, B15 2TG, UK

Correspondence to: Dr M D Kilby, Department of Fetal Medicine, Division of Reproductive and Child Health, Birmingham Women's Hospital, University of Birmingham, Birmingham B15 2TG, UK; m.d.kilby@bham.ac.uk

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Figure 2 Percutaneous insertion of vesicoamniotic shunt (Harrison type).

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IMAGES IN NEONATAL MEDICINE.....

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Pneumopericardium in a term infant on nasal continuous positive airway pressure

We report neonatal pneumopericardium in a term infant with gestational age of 39 weeks. The pneumopericardium developed during the second day of postnatal age. There was no evidence of other forms of air-leak. The infant was treated with nasal CPAP delivered for respiratory distress and was not mechanically ventilated before pneumopericardium occurred. His plain chest radiograph showed a halo of air around the heart (fig 1). In the case there was no clinical evidence of cardiac air tamponade and the pneumopericardium resolved spontaneously. The next day, control chest radiograph and echocardiogram showed complete resolution of the pneumopericardium.

Pneumopericardium is a rare form of neonatal air-leak syndrome with high morbidity and mortality. It is almost invariably preceded by other forms of air-leak.¹ Neonatal pneumopericardium is usually a complication of positive-pressure ventilation in premature infants with respiratory distress.² The mechanism by which pneumopericardium is not well understood, but it is probably due to passage of air along vascular sheaths. The clinical signs of pneumopericardium range from asymptomatic to the full picture of cardiac tamponade. Asymptomatic patients should be observed closely with chest radiograph but symptomatic patients should be treated emergently by pericardiocentesis.

Figure 1 Chest x ray film showing a radiolucent halo around the heart in a 2-day-old infant with pneumopericardium.

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Dursun Türkbay

Zekai Tahir Burak Hastanesi, Ankara, 06230, Turkey;
dursun_turkbay@ttnet.net.tr

Correspondence to: D Türkbay, Zekai Tahir Burak Hastanesi, Ankara, 06230, Turkey; dursun_turkbay@ttnet.net.tr

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