Prenatal Detection, Intrauterine Vesico-amniotic Shunting and Postnatal Follow up of Isolated Lower Urinary Tract Obstruction Cases

Thesis
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List of Abbreviations

ACE Angiotensin Converting Enzyme
AGT Angiotensinogen
AGTr1a/b Angiotensin II receptor, type 1a/b
AGTr2 Angiotensin II receptor, type 2
AFI Amniotic Fluid Index
ARPKD Autosomal Recessive Polycystic Kidney Disease
AUD Anterior Urethral Diverticulum
AUV Anterior Urethral Valves
CAKUT Congenital Anomalies of the Kidney and Urinary Tract
CI Confidence Interval
COPUM Congenital Obstructive Posterior Urethral Membrane
CUF Congenital Urethroperineal Fistula
CUTA Congenital Urinary Tract Abnormalities
FBSL Fetal Bladder Sagittal Length
FDA Food and Drug Administration
HDE Humanitarian Device Exemption
ICD10 International Classification of Diseases version 10
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>LUTO</td>
<td>Lower Urinary Tract Obstruction</td>
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<tr>
<td>MCDK</td>
<td>Multicystic Dysplastic Kidney</td>
</tr>
<tr>
<td>MDC</td>
<td>Mullerian Duct Cyst</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>PBS</td>
<td>Prune-Belly Syndrome</td>
</tr>
<tr>
<td>PUV</td>
<td>Posterior Urethral Valve</td>
</tr>
<tr>
<td>RAS</td>
<td>Renin-Angiotensin System</td>
</tr>
<tr>
<td>TOP</td>
<td>Termination of Pregnancy</td>
</tr>
<tr>
<td>UPJ</td>
<td>Ureteropelvic Junction</td>
</tr>
<tr>
<td>US</td>
<td>Ultrasonography</td>
</tr>
<tr>
<td>UTO</td>
<td>Urinary Tract Obstruction</td>
</tr>
<tr>
<td>UVJ</td>
<td>Ureterovesical Junction</td>
</tr>
<tr>
<td>VACTERL</td>
<td>Vertebral anomalies, Anal atresia, Cardiovascular anomalies, Tracheoesophageal fistula, Renal anomalies, and Limb abnormalities</td>
</tr>
<tr>
<td>VCUG</td>
<td>Voiding Cystourethrogram</td>
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<tr>
<td>VUR</td>
<td>Vesicoureteral Reflux</td>
</tr>
<tr>
<td>WMCAR</td>
<td>West Midlands Congenital Anomaly Register</td>
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Abstract
Prenatal Detection, Intrauterine Vesico-amniotic Shunting and Postnatal Follow up of Isolated Lower Urinary Tract Obstruction Cases

**Objectives:** The objectives of the study were to determine whether intrauterine vesico-amniotic shunting for fetal bladder outflow obstruction, versus a conservative non-interventional approach improves prenatal and postnatal mortality, morbidity, and renal functions of isolated lower urinary tract obstruction cases. We aimed to find a prognostic index for cases of fetal lower urinary tract obstruction and to determine the safety and efficacy of the shunting procedure.

**Patients and Methods:** The study included 20 cases of lower urinary tract obstruction (LUTO). Initial ultrasonography was done to all our cases upon detection of the lower urinary tract obstruction and a follow up ultrasounds were performed on 9 cases. The most important indicator to predict renal function was fetal bladder size. Bladder wall thickness, amniotic fluid index and the size of the kidney were of lesser value in the early detection of LUTO. Fetal urine analytes including Sodium, Potassium, Chloride, Calcium, Creatinine and B2 microglobulin were analyzed in 16 cases. In our study of 20 LUTO patients, 6 fell into the intervention group and 14 into the conservative group.

**Results:** The perinatal and neonatal outcomes of the interventional group were 33.3% terminations of pregnancy, 33.3% miscarriage, 16.6% neonatal death and 16.6% alive at 28 days. The conservative group results included 36% terminations of pregnancy, 7% miscarriage, 14% neonatal deaths, 7% alive at 28 days and 36% dropouts.

**Conclusion:** Fetal urine biochemical analysis results were not in accordance with the ultrasonographic results nor were they useful in predicting severity of disease and neonatal outcome. Fetal bladder sagittal length was the most important sign in early diagnosis of LUTO. Vesico-amniotic shunting did not alleviate the LUTO condition, nor did it affect neonatal mortality or morbidity.

**Keywords:** Lower urinary tract obstruction (LUTO), vesico-amniotic shunt, fetal urine analysis, prenatal diagnoses of LUTO, prenatal management of LUTO.
Introduction
Introduction

Rationale and Background

Fetal congenital anomalies, both treatable and untreatable occur all over the world. This study focuses on urogenital anomalies, specifically isolated fetal lower obstructive uropathies. Fetal lower urinary tract obstruction (LUTO) affects 2.2 per 10,000 births. It is a consequence of a range of pathological processes, most commonly posterior urethral valves (PUV) (64%) or urethral atresia (39%). It is a condition of high mortality and morbidity associated with progressive renal dysfunction and oligohydramnios, and hence fetal pulmonary hypoplasia (Lissauer et al, 2007). Renal function plays a significant role in maintaining fetal metabolic equilibrium. The kidneys contribute to amniotic fluid production, which is needed to stimulate the intrauterine fetal respiratory activity. Intrauterine breathing is essential for lung development; therefore, oligohydramnios is synonymous with pulmonary hypoplasia, which in turn usually leads to neonatal detriment.

There haven’t been any proper statistical data in Egypt as to the incidence of fetal lower urinary tract obstructions, however in clinical practice; one does see a number of neonates born with various obstructive uropathies. The goal of this study is to evaluate whether fetal intervention will improve the prognosis of these cases born with isolated obstructive uropathies.

Trials of intervention, including fetal surgery, fetal cystoscopy with endoscopic surgery, and percutaneous vesico-amniotic
Introduction

Shunting has been performed. A clinical trial covering fetal obstructive uropathy concluded that early bladder drainage before the 24th week of gestation by shunting enables delivery of newborns with a good perinatal outcome, and without pulmonary hypoplasia. This method of therapy limits renal damage and allows time for normal development of the fetal lungs (Szaflik et al, 1998).

Recently it has become possible to decompress the obstruction in-utero via percutaneous vesico-amniotic shunting with relatively good results. A study done in the University of Pennsylvania, school of Medicine, on male children who underwent prenatal bladder shunting, showed that they were neurodevelopmentally normal. Although one third of the surviving babies required dialysis and transplantation, the majority has acceptable renal and bladder function and report satisfactory quality of life (Biard et al, 2005.) This is due to the fact that the intervention happened in the appropriate time to decompress the bladder and ureters. Another study, ongoing until September 2013, is the PLUTO study. In this trial, two groups were randomized; one underwent vesico-amniotic shunting, while the other was conservatively managed. (Kilby et al and Pluto Collaborative study group et al, 2007).

Although all of the above mentioned studies have shown positive results for vesico-amniotic shunting, some show equivocal results. A clinical trial done in Ain Shams University, Egypt compared two groups with Posterior Urethral Valves (PUV); one
group underwent antenatal vesico-amniotic shunting while the other underwent post natal surgical correction of the PUV. Their study concluded that antenatal vesico-amniotic shunt placement makes no difference to the outcome and long-term results of patients with PUV and that primary valve ablation is the keystone of treatment for patients with PUV (Salam, 2006). Another study done in the University of Toronto showed that although vesico-amniotic shunting is effective in reversing oligohydramnios, its ability to achieve sustainable good renal function in infancy is variable (McLorie et al, 2001.)

The hypothesis of this study relies on the fact that fetal lower urinary tract obstruction causes backpressure on the bladder, ureters and kidneys with possible progression to hydroureter and hydronephrosis. Therefore, hypothetically bypassing the obstruction via vesico-amniotic shunting should decrease the back pressure; thus preserving the physiological and functional states of those organs.
Introduction

Objectives of the Study

1. To determine whether intrauterine vesico-amniotic shunting for fetal bladder outflow obstruction, versus a conservative non-interventional approach improves prenatal and postnatal mortality, morbidity, and renal functions of isolated lower urinary tract obstruction cases.

2. To find a prognostic index for cases of fetal lower urinary tract obstruction and to determine the safety and efficacy of the shunting procedure.
Review of the Literature