Can endoscopic balloon dilation for primary obstructive megaureter be effective in a long-term follow-up?


Summary
Background
Ureteral tapering and reimplantation is an established treatment for persistent or progressive primary obstructive megaureter (POM) but may result in complications and morbidity. Use of a less invasive technique involving endoscopic balloon dilation appears very interesting.

Objective
The objective of this report is to determine if endoscopic balloon dilation for POM is effective in the long term as well as to assess complications of the procedure.

Material and methods
A retrospective review was done on 19 patients and 20 ureters treated with the endoscopic balloon dilation by POM from June 2000 to February 2010.

Surgery was performed solely in those cases in which there was persistence of obstruction in the renogram along with one or all of the following conditions: impairment of the differential renal function < 40%, worsening of the renal pelvic dilation, febrile UTI in spite of antibiotic prophylaxis or renal calculi.

The patients comprised 16 boys and 3 girls with a mean age at surgery of 17 months (range 1–44 months). Ten cases were left sided, eight right sided, and one bilateral.

Under endoscopic and fluoroscopic guidance, a 3–5 Fr dilating balloon was inflated to 12–14 atm, or until disappearance of the stenotic obstructive area. A double J stent was positioned and withdrawn 2 months later.

Follow-up recorded the presence of symptoms, number of reintervention procedures registered, and included renal ultrasound and MAG-3 renogram.

Results
There were no perioperative complications. Eighteen ureters showed a non-obstructive pattern on MAG-3 renogram after the first endoscopic dilation, representing a 90% success rate.

One case required a second dilation, which proved successful and two cases of recurrent lithiasis required ureterotomy without instances of obstruction. 2 patients had a febrile UTI and a vesicoureteral reflux was diagnosed in one. Renal function was preserved in 95% of patients.

The mean follow-up was 6.9 years (range 3.9–13.3 years). One patient was lost after the procedure.

Discussion
In an era of minimally invasive techniques, the search for less invasive procedures for treatment of POM has resulted in a variety of surgical options. Angulo et al., in 1998 and our group described the first POM treatment with endoscopic balloon dilation, which is believed to be a definitive, less invasive, and safe treatment. Furthermore, should an endoscopic approach fail, reimplant surgery can be performed.

Few publications have reported short series with good results in the short and medium term.

Torino et al. presented five cases in children aged less than 1 year, none of these showed evidence of obstruction. Garcı́a-Aparicio et al. presented a series of 13 patients treated with a success rate of 84.6%. Christman et al. added laser incision in cases of narrowed ureteral segment 2–3 cm long and used double stenting. Good outcomes were presented in 71%. Romero et al. reported improvement of drainage within the first 18 months after treatment in 69% of patients.

The potential de novo onset of vesicoureteral reflux may be the source of some controversy. We consider that dilation does not significantly alter the antireflux mechanism. In VCUG is not systematically performed because it is an invasive test. This restricts the conclusions that can be drawn from our findings. Nevertheless, some groups continue to systematically perform VCUG.

Conclusions
Endoscopic balloon dilation for POM is a safe, feasible, and less invasive procedure that shows good outcomes on long-term follow-up. However, multicenter studies and prospective trials should be encouraged to provide more definitive evidence on its benefits.
Introduction

The management of progressive primary obstructive megaureter (POM) in children remains controversial. While conservative management is required for the majority of megaureters, most cases of POM resolve spontaneously, or improve without loss of function or appearance of symptoms [1]. Some megaureters are associated with increasing dilation, UTI and deteriorating renal function, and require surgical intervention. Ureteral tapering and reimplantation is an established treatment for persistent or progressive POM; however, reimplantation of a grossly dilated ureter into the small infant bladder is technically demanding and potentially predisposes to bladder dysfunction [2]. Hence, less-invasive procedures have been proposed as alternatives.

Since the first report of endoscopic balloon dilation for POM in children in 1998 by Angulo [3–9], several publications have shown that the traditional open ureteral reimplantation and remodeling is no longer the only approach for this disorder, and that endoscopic balloon dilation is feasible, safe and a less-invasive procedure for very young patients [3–9]. The success rate of this procedure ranges over the short-term and medium-term from 85 to 100%.

The objectives of the present study were to describe the long-term follow-up of endoscopic balloon dilation for POM, to assess its effectiveness in the long-term, and to review the literature concerning this approach.

Materials and methods

From June 2000 to February 2010, a total of 19 patients and 20 ureters were treated with the endoscopic balloon dilation for POM. The patients comprised 16 boys and 3 girls, with a mean age at surgery of 17 months (range: 1–44 months). Ten cases were left sided, eight right sided and one bilateral. Eleven cases were diagnosed prenatally.

Diagnosis of POM was based on the following parameters: dilation of the distal ureter by more than 14 mm, obstructive curve in the renogram, and absence of VUR after performing a VCUG. Ultrasound was employed to measure the diameter of the renal pelvis, the parenchymal thinning and ureteral dilation. The degree of hydronephrosis was defined in accordance with the guidelines of the Society for Fetal Urology. Diuretic renogram was performed according to the guidelines of the Society of Nuclear Medicine: patients were hydrated orally 30 min before the scan and regions of interest (ROIs) were placed around each kidney for the calculation of differential function. Additionally, similar ROIs were placed around both kidneys and the ureters to calculate the diuresis time–activity curve. Good drainage out of the ROIs 30 min after injection of $^{99m}$Tc-mercaptacetyltriglycine (MAG-3) was regarded as evidence of obstruction. If poor drainage was detected, furosemide (1 mg/kg) was administered intravenously, and total urinary drainage was calculated during the 20 min after the injection. A diuretic T1/2 >20 min after furosemide injection was classified as an obstruction.

After diagnosis, conservative management was maintained with antibiotic prophylaxis, with monthly urine cultures taken during the first year of follow-up, ultrasound every three months, and renogram every six months. Most cases of POM required no surgery and resolved spontaneously; however, 12% of the cases that were detected required surgery.

Surgery was performed solely in those cases in which there was persistence of obstruction on the renogram (T1/2 > 69.56 min; range: 37–90 min) along with one or all of the following conditions: impairment of the differential renal function <40% (37%), worsening of the renal pelvic dilation (47%), febrile UTI in spite of antibiotic prophylaxis (31%) or renal calculi (10%). Mean differential function of the affected kidney was 41.26% (range: 22–52%).

Under general anesthesia, and a single dose of antibiotic prophylaxis with cefonicid, 8–9.5 Fr cystoscopy was carried out with a 4–5 Fr working channel. The ureterovesical stenosis was bypassed with a flexible guidewire (0.021-in. Fixed Core Wire Guide, Cook Medical, Bloomington, IN, USA) introduced up to the renal pelvis and filled with radiologic contrast, confirming the diagnosis of megaureter and defining the anatomy. A 3–5 Fr dilating balloon catheter (the balloon length was 4 cm and the diameter was 6 mm) (STAR PTA balloon catheter, Optimed, Medizinische Instrumente GmbH, Ettlingen, Germany) was insufflated to 12 or 14 atm until disappearance of the stenotic ring (from 3 to 6 min waiting time). The dilation never had to be prolonged for more than 5 min to see that the stenotic ring had disappeared. The stenotic ring was always visible before dilation.

Finally, distal ureteroscopy was performed, confirming dilation of the stenotic segment, and a 4.8 × 16–26 cm double-J stent was placed through a ureteral bridge (safety wire guide introducer 4.8 Fr/16-26 cm Cook Medical, Bloomington, IN, USA) between the urethral and the ureteral meatuses. As the procedure is quite complicated owing to the pronounced bends in the ureter after a long-standing obstruction, this ureteral bridge is used to straighten the bends along the ureter and helps to position the double-J stent up to the renal pelvis. In cases of severe hydroureteronephrosis, long stents (4.8 × 26 cm) and great ureteric tortuosity are used, so it is important for the catheter to remain placed in the pelvic area to avoid catheter migration (Fig. 1). The bladder catheter was withdrawn 24 h after surgery, and the patient was discharged after 48 h. In all cases, the double-J stent was removed two months after surgery under general anesthesia, and the caliber was confirmed by distal ureteroscopy.

During the follow-up, patients underwent renal ultrasound at 1, 3, 9 and 12 months and annually thereafter until adulthood. Renography was performed to assess renal function, upper tract anatomy and drainage at six months, two and five years. During the follow-up, a VCUG was performed if a patient had a febrile UTI (Fig. 2).

For statistical analysis, a Chi-squared test or Fisher’s test was used for qualitative variables and Student’s t-test and Wilcoxon test for quantitative analysis. The analyses were done using SPSS 18 software.

Results

There were no perioperative complications (Clavien I). All 19 patients had a smooth postoperative course; there were no morbidities. There were no difficulties in ureter catheterization or any incidence of ureteral stent migration. The
mean follow-up was 6.9 years (range: 3.9–13.3 years). One patient was lost to follow-up after the procedure (Table 1).

Eighteen of the ureters showed a non-obstructive pattern on MAG-3 renogram after the first endoscopic dilation, and remained stable (T1/2 16.40 min). Statistical analysis revealed significant differences before and after surgery in the average time of elimination on the MAG-3 renogram (T1/2 69.56 min vs 16.40 min, \( P < 0.001 \)). The overall rate of success was 90\% after the first dilation. Patient 14 required a second balloon dilation owing to persistence of obstructive manifestations. This procedure was successful, increasing the success rate to 95\%. A cutting balloon was not required in any cases because the stenotic ring disappeared immediately after endoscopic balloon dilation. Patient 6 showed no improvement on MAG-3 renogram at six months; it was decided to adopt a wait-and-see approach because the differential renal function was quite disturbed.

There was significant improvement in hydronephrosis in all patients except the one who required a second dilation. Significant differences were observed in hydronephrosis grade before and after endoscopic dilation (\( P < 0.001 \)) (Table 2).

Renal function was preserved in 18 patients (95\%), without subsequent deterioration. No significant differences were observed in preoperative and postoperative renal function (DRF 41.26\% vs 41.50\%, \( P = 0.59 \)).

It is worth noting that 14 months after the endoscopic dilation, patient 10 had a febrile UTI, and a VUR (Grade II) was diagnosed by VCUG. Endoscopic injection of a dextranomer/hyaluronic acid copolymer (Deflux, Q-Med Scandinavia, Uppsala, Sweden) was necessary. At the last follow-up the patient was asymptomatic, with no further episodes of infection and without loss of renal function. Patient 15 also had a febrile UTI six months after the procedure and was tested by a VCUG, which proved negative for reflux.

Two patients who initially had lithiasis had a recurrence after one year (not obstructive renogram) (10.5\%). A mean of three stones was found in the distal ureter. Lithotripsy with holmium laser and ureterotomy were performed. Laser incision was performed along the 6 o’clock position within the ureter using a holmium: YAG laser set on 0.6 joules and 6 hertz. The stones that had been formed were calcium oxalate dihydrate.

At the last follow-up, all patients remain asymptomatic and showed no signs of UTI, lithiasis, or pyeloureteral dilation. No instances of obstruction were observed on MAG-3 renogram.

**Discussion**

Since the initial description using the term ‘megaureter’ by Caulk in 1923 [10], the concept of POM management has
changed radically from primary ureteral reimplantation with tapering, as described by Hendren [11], to one of initially conservative observation, as described by Williams and Hulme-Moir in 1970 [12]. Indications for surgery in POM include persistence of obstruction on the renogram with one or all of the following conditions: worsening of the differential renal function, increasing hydroureteronephrosis, or repeated febrile UTI in spite of antibiotic prophylaxis.

Historically, the surgical management of POM has been by ureteral reimplantation with or without ureteric remodeling, with reported success rates of 90–96%. However, complications and morbidity may occur, especially during the first year of life, since the procedure entails difficult bladder surgery that usually involves a significant dissection surface in the bladder and the ureter (within and outside the bladder) as well as ureteral tailoring. Furthermore, the reimplanted ureter almost always remains large, which requires a long submucous tunnel; this can cause vesical dysfunction in the long-term. Some authors therefore perform a temporary ureteral diversion, such as cutaneous ureterostomy, to preserve renal function and allow reduction of the megaureter diameter in an attempt to avoid ureter remodeling at definitive surgery.

The most frequently reported complications of open surgery are obstruction and induction of VUR [13]. In a group of 47 infants (aged less than 8 months) with POM who needed open surgery, Peters et al. reported a reoperation rate of 12%. Postoperative reflux was present in eight of the infants [14]. Perdzynski reported a VUR and restenosis rate of 3.57% [15]. Other described postoperative complications included hematuria, wound infection and urinary fistula.

In an era of minimally invasive techniques, the search for less-invasive procedures for treatment of POM has resulted in a variety of surgical options, including endourologic, laparoscopic, or robotic repair [16–19]. Definitive treatment by high-pressure balloon dilation seems to be a very interesting therapeutic solution. In 1998, Angulo et al. and, in 2007, Angerri et al. described the first POM treatment with endoscopic balloon dilation, which was believed to be a definitive, less invasive, and safe treatment for this disorder that avoids unnecessary open surgery [3,4]. This technique is easy to reproduce surgically because the learning curve is low. Furthermore, should an endoscopic approach fail, reimplant surgery can be performed. Few publications have reported short series with good results in the short-term and medium-term [5–9].

Torino et al. presented five cases in children aged less than one year – none of them showed evidence of obstruction at a mean follow-up of 23.8 months [7]. Garcia-Aparicio et al. presented a series of 13 patients treated by high-pressure balloon dilation [8]; the success rate was 84.6% and the need for ureteral reimplantation was avoided. Five of the patients had previously required a second dilation when the double-J stent was removed. Christman et al. added laser incision in patients with narrowed ureteral segments measuring 2–3 cm, and placed two ureteral stents within the ureter simultaneously. They presented good outcomes in 71% of patients at three months and among the five without significant improvement, magnetic resonance urography demonstrated resolution of the obstruction. After a follow-up of 3.2 years, two cases of recurrent lithiasis had occurred [6]. Romero et al. reported improvement of hydroureteronephrosis and drainage within the first 18 months after treatment in 69% of patients, and in two patients a further dilation was required with an excellent outcome.

The potential de novo onset of VUR in the dilated ureter may be the source of some controversy. There is concern that dilation and/or incision of the ureteral orifice could result in VUR. However, Bapat et al. performed incisions at 6 and 12 o’clock, and concluded that there was no possibility...
of inducing VUR [17]. Kajbafzadeh performed a ureteral incision at 6 o’clock and identified no VUR in 47 children [18]. It was considered that dilation does not significantly alter the antireflux mechanism. VCUG was not systematically performed because it is an invasive test [4]. This restricted the conclusions that could be drawn from the findings of the present study. In the single patient who developed VUR (5%) 14 months after dilation, it was diagnosed after a febrile UTI and managed successfully with endoscopic Deflux injection. Another patient presented with a febrile UTI, but the VCUG did not show reflux. It is not known whether the aforementioned 5% rate is the real rate of VUR, but the other patients have remained asymptomatic and continue to show normal renal function without hydronephrosis.

Christman et al. did not performed VCUG and none of their patients had febrile UTI [6]. Angulo et al. performed post-dilation VCUG in their first 11 cases and recorded two cases of reflux [3]. Nowadays, VCUG is only performed when the dilation persists or a UTI occurs; reflux appears in 17% of renal units [9]. Nevertheless, some groups continue to systematically perform VCUG [5,7,8].

Garcı´a-Aparicio compared outcomes between 13 high-pressure balloon dilations of the ureterovesical junction and 12 ureteral reimplantations. Postoperative VUR was observed in two patients from the endoscopic group and one from the reimplantation group. Secondary ureteral reimplantation was required in three patients from the endoscopic group and two from the reimplantation group. They concluded that the two techniques are equally effective [20].

Severely dilated and tortuous ureters may make proper stent placement within the renal pelvis difficult. As described previously, a 6-Fr ureteric bridge was used, which

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<th>Table 1</th>
<th>Clinical outcomes of POM patients managed with endoscopic balloon dilation.</th>
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<tr>
<td>Patient</td>
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8  M  R  Yes 4 UTI 47% (90 min) 1 45% (10 min) No 6.58
9  M  L  Yes 4 Increasing HUN 46% (37 min) 17 46% (4 min) No 6.58
10 F  L  +  R  No 3/3 ↓ DRF, UTI 35% (65 min) 5 50% (9 min) Yes (Deflux injection) 6.58
11 M  R  Yes 4 Increasing HUN 43% (71 min) 37 51% (13 min) No 5.41
12 M  L  No 4 ↓ DRF, Lumbar pain 22% (65 min) 63 17% (8 min) No 5.08
13 M  R  Yes 3 UTI 52% (68 min) 44 50% (12 min) No 4.50
14 M  R  Yes 4 ↓ DRF, Increasing HUN 25% (50 min) 8 24% (46 min) Yes (1 dilation) 4.25
15 M  R  No 4 UTI 51% (89 min) 11 52% (13 min) No 6.66
16 M  R  No 4 Lithiasis Ns 12 30% (19 min) Yes (laser lithotripsy + ureterotomy) 4.16
17 M  L  Yes 4 ↓ DRF 38% (95 min) 33 39% (10 min) No 4.66
18 M  L  No 4 UTI 57% (73 min) 25 55% (9 min) No 3.92
19 F  R  No 4 ↓ DRF 33% (85 min) 10 40% (12 min) No 22

Ns: non specified. POM: Primary Obstructive Megaureter, DRF: differential renal function, HUN: hydronephrosis.

a Lost patients in follow-up.

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<th>Table 2</th>
<th>Renal ultrasound findings after successful endoscopic dilation.</th>
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<td>Preoperative 12 months postoperative P-value (Wilcoxon test)</td>
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<td>Median distal ureter diameter (mm)</td>
<td>19.32 (range: 10–24) 3 (range: 0–11) P&lt;0.001</td>
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<tr>
<td>Median pelvis diameter (mm)</td>
<td>21 (range: 12–30) 3 (range: 0–12) P&lt;0.001</td>
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was placed after dilation, allowing straightening of the ureter throughout its length. This improves placement of the double-J stent enormously and allows use of a long catheter that stays anchored to the pelvis.

In the study by Angulo, 2 out of 29 patients could not be treated with endoscopic balloon dilation because it was impossible for the guidewire to pass through the VUJ. These authors reported another case in which the double-J stent could not be inserted because the guidewire moved externally. Additionally, the double-J stent had migrated into the renal pelvis and open ureteral reimplantation was required [9].

Other endourologic procedures proposed for POM have included double-J stenting and posterior ureterotomy, which are associated with some comorbidity. Ransley suggested the temporary insertion of a double-J stent in the megaureter to bypass the obstruction [21]. In 1999, Shenoy and Rance published the first report of the use of double-J stents in symptomatic infants with POM (n = 2) [22]. Castagnetti et al. needed open insertion of the double-J stent in 30% of their patients and more than half of the patients required surgery after stent removal [23]. Carroll et al. suggested that ureteric stenting is a useful option, but 50% of their patients suffered renal dysfunction and 35% finally required ureteral reimplantation. Since long-term stenting was required, complications such as UTIs, knotting of the stent, stent encrustation, stent migration, and ureteric perforation were described [16].

Conclusion

Endoscopic balloon dilation has been shown to be a safe, feasible, and less-invasive procedure that has good outcomes. It is an effective treatment with few postoperative complications at long-term follow-up and it may be considered first-line treatment in the management of POM in children. It also avoids unnecessary bladder surgery and the associated complications. However, it is acknowledged that a definitive judgment will require further multicenter studies or prospective trials studies to demonstrate definitively the real benefits of this approach.

Conflict of interest/Funding

None declared.

References