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Case Report

D-Mannose Reduces the Risk of UTI in Complex Paediatric Urology Patients

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Abstract

Introduction: Urinary Tract Infections (UTIs) common in complex paediatriac urology patients, resulting in repeated admission, progressive renal impairment, renal transplant losses. Prophylactic antibiotics associated with colonisation with multi-resistant bacteria, eg. ESBL. D-mannose is a fruit extract, inhibiting bacterial adhesion to the urinary tract. We aimed to identify if D-mannose could reduce risk of recurrent UTI and ESBL colonisation in complex urology patients.

Materials and Methods: Tertiary paediatric urology centre. Identified complex paediatric urology patients changed from antibiotic prophylaxis to D-mannose. Demographics, diagnoses, UTI dates, cultures, pyuria recorded before and after starting D-mannose. Paired data compared: UTI/month pre- and post-starting D-mannose. Wilcoxon and Fisher exact test, $P<0.05$ taken as significant.

Results: 11 patients, median age 11 years (range 7-17). UTI rate reduced 53% from 0.55(0.44-0.79) to 0.26(0-0.38) UTIs/month, $P=0.0029$. 6 ESBL isolates in 3 patients pre- vs. 1 persisting ESBL isolate on D-mannose. D-mannose well tolerated: only 1 child developing loose stool.

Conclusion: D-mannose is effective prophylaxis, reducing risk of recurrent UTIs by 53% in complex urology patients. This will reduce need for long-term prophylactic antibiotics and may reduce risk of multi-resistant organism colonisation.

Keywords: Complex paediatric urology; D-Mannose; Prophylaxis; Urinary tract infection

Introduction

Urinary Tract Infection (UTI) is common in children, affecting approximately 2% of boys and 8% of girls up to 7 years of age and up to half of these children will suffer at least one recurrence of UTI [1,2]. In children with structurally and functionally complex urological systems the rate of infection can be higher. Morbidity of recurrent infection can include repeated hospital admissions, time missed from school, progressive renal impairment and renal scarring, and potential loss of renal transplants [3]. The most established method for prevention of UTI is the use of long-term prophylactic antibiotics at a low dose [4]. In children with Vesico-Ureteric Reflux (VUR) a meta-analysis has shown that antibiotic prophylaxis may be beneficial in all children [5], and the RIVUR study showed that in patients with VUR prophylactic antibiotics reduce the risk of UTI but not the risk of renal scarring [6]. Repeated use of antibiotics and prophylactic antibiotics are known to be associated with bacterial resistance [7], and the rise of multi-resistant organisms such as Extended Spectrum Beta Lactamase (ESBL) producing *E. coli* species is particularly concerning. Colonisation by such organisms is a potential problem for complex urology patients, who have a high risk of urinary tract infections and have often had multiple courses of antibiotics [8].

D-Mannose is a simple sugar found in many fruits. It has been shown that D-Mannose competitively binds with cell-surface receptors on uropathogenic bacteria, reducing their ability to bind to urothelium [9]. In an RCT regarding women with recurrent cystitis,

D-Mannose was shown to be effective in significantly reducing the incidence of UTI and in this group it was more effective than antibiotic prophylaxis [10]. Our aim was to investigate whether D-Mannose could reduce the incidence of recurrent UTIs and of ESBL colonisation in a cohort of complex paediatric urology patients.

Materials and Methods

Approval was granted by the trust audit committee for a service development project (CARM-00989) to use of D-mannose as UTI prophylaxis in complex patients with recurrent UTIs being followed up in a tertiary paediatric urology centre. D-Mannose was commenced during a six-month trial period, running between May – November 2017. Use of D-Mannose was at the discretion of the treating clinician and in discussion with the patient (where appropriate) and parents. Indications for starting D-Mannose were complex underlying urological conditions and recurrent UTIs. Antibiotic prophylaxis was stopped and D-Mannose commenced. Patients aged 12-16 years were given a dose of 500mg (half the adult dose) orally TDS for 3 days, then BD ongoing was prescribed. This dose was further halved for patients 6-12 years of age, and halved again for those under 6 years old (This equated to a dose of 15mg/Kg). Patients were followed up in the urology outpatient clinic and advised to present to our Urology Nurse Specialists for assessment and urine culture if demonstrating signs of UTIs.

Demographics, diagnoses, UTI dates, culture results and pyuria were recorded before and after starting D-mannose. Paired data were compared as UTIs per month pre- and post- starting D-Mannose.

Analysis was by Wilcoxon and Fisher exact test, $P<0.05$ taken as significant.

Results

11 patients were recruited to the service development project within the reference period. These patients had a median age of 11 years (range 6-17 years). Underlying urological conditions included: Posterior Urethral Valves; Renal Transplantation; Bladder Augmentation; Mitrofanoff; Cloaca; (see Table 1).

Underlying Diagnosis	Frequency
Renal Transplantation	7
Mitrofanoff	6
Posterior Urethral Valves	4
Bladder Augmentation	4
Cloaca	2
Megaureter	1
Long-term ureteric stent	1

Table 1: Underlying urological conditions. (There was more than one diagnosis per patient).

Data was collected for a mean of 5.3 months before commencing D-mannose and 5.4 months after starting D-mannose. UTI rate reduced from a median of 0.55 (IQR 0.44-0.79) to 0.26 (IQR 0-0.38) UTIs per month. This equates to a 53% reduction in UTI rate, P=0.0029. In 3 patients, nephrologists restarted prophylactic antibiotics. Doing sub-group analysis on the 8 patients who remained solely on D-Mannose, there was still a significant reduction in rate of UTIs/month, from a median of 0.55(0.35-0.85) to 0.24(0.05-0.32), P=0.0056.

There were 6 ESBL isolates in 3 patients prior to starting D-mannose prophylaxis but only 1 persisting ESBL isolate in 1 patient whilst on D-mannose. This was not significant, P=0.66. D-mannose was well tolerated with only 1 child developing slightly loose stools (Figures 1 and 2).

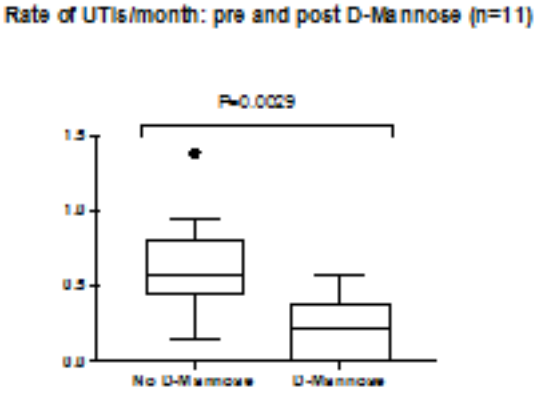

Figure 1: Rate of UTI's per month: pre and post D-Mannose.

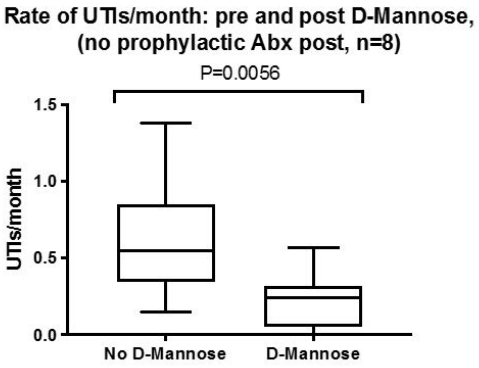

Figure 2: Rate of UTI's per month: pre and post D-Mannose (no prophylactic antibiotics).

Discussion

This study is the first to assess use of D-Mannose for prophylaxis of UTIs in children and has shown it to significantly

reduce the rate of UTIs in complex paediatric urology patients who have had recurrent UTIs on conventional prophylactic antiobiotics. There are three papers showing reduced rates of UTIs in women but this is the first in a paediatric population [10-12].

Until now, the "search … to find a safer, effective and acceptable alternative" to antibiotics for prophylaxis of UTIs in children has shown "some promise", but nothing has "provided so far a definitive effective answer" [13]. This paper has shown D-Mannose to be an effective answer: it is safe – a simple sugar found in fruits; effective – significantly reducing the rate of UTIs in this cohort of complex paediatric urology patients; and acceptable – very well tolerated by patients, with the only side effect being slightly loose stools, which was only experienced by one patient in this group.

We also tested acceptability on ourselves and our colleagues – 11 paediatric surgeons and urologists sampled D-mannose – none reported side-effects and all found the taste to be acceptable. Small sample size is a potential limitation of this study. A significant reduction in overall number of UTIs was shown, but the reduction in number of ESBL isolates did not reach significance – with a larger sample size this may have been achieved. We chose to start using D-Mannose in a relatively small group of complex paediatric urology patients in whom conventional antibiotic prophylaxis was not preventing UTIs. Our next step will be to carry out a blinded crossover trial comparing D-Mannose and Trimethoprim in a much larger cohort of less complex patients.

Conclusion

D-mannose is effective prophylaxis, reducing risk of recurrent UTIs by 53% in complex paediatric urology patients. This will reduce the need for long-term prophylactic antibiotics in these patients and may help reduce the risk of multi-resistant organism colonisation.

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