Antibiotic Prophylaxis and risk of post-operative Urinary tract Infections after cystoscopy in pediatric population. A prospective, observational, multicentric study

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1. Background/Introduction

Endoscopic approach to the bladder, both diagnostic and operative, represents a large proportion of the procedures performed in pediatric and adult urology. Development of a UTI following a cystoscopy is one of the most common and feared post-operative complication; to reduce their incidence, the use of antibiotic prophylaxis is universally accepted[1-3].
There is however, a growing body of literature addressing concerns associated with bacterial resistance[1]. In pediatric urology, the resistance pattern of uropathogens has been evolving and compared to the years 2002–2004, trimethoprim/sulfamethoxazole resistance rates for E. coli pediatric urinary tract infections (UTIs) increased in both boys (from 23% up to 31%) and girls (from 20% up to 23%) in 2009. There was also a 10-fold increase in E. coli resistance to ciprofloxacin in boys (from 1% in 2002–2004 to 10% in 2009) and girls (from 0.6% to 4%) in pediatric UTIs[7]. Interestingly, patients receiving prophylactic antibiotics had a high rate of resistance to third-generation cephalosporins, despite not receiving third-generation cephalosporins for prophylaxis. A mechanism to explain the above explains the selection of bacteria that have resistance to multiple antibiotics as consequence of the alteration of the patient's intestinal flora, caused by the antibiotic prophylaxis[8].

Considering the number of cystoscopy procedures performed every year a rationalized use of perioperative as well as postoperative antibiotic prophylaxis is paramount to reduce the potential risk of both UTI development and antimicrobial overuse[3]. In addition, the optimization of antibiotic treatments should minimize the likelihood of adverse events related to their use[4,5].

Our study aims to identify current practice in the use of antibiotic prophylaxis at the time of cystoscopy in the pediatric population across different Institutions/Countries. This could lead to further research questions and develop future research projects aimed at minimizing the use of antibiotics without jeopardizing patients' safety.

2. Research Question

What antibiotic prophylaxis protocols are currently in use among different Institutions/Countries?

What is rate of post-cystoscopy febrile UTI (fUTI)?

Is there any difference based upon geography/institution/center protocol?

3. Primary and Secondary Aims

Primary Aim: -To identify the current practice across different Countries

Secondary Aim: -To estimate rate of post-cystoscopy fUTI

-To identify possible risk factors for post-cystoscopy fUTI

4. **Outcome Definitions/Data Points Collected (see appendix 1)**

Preoperatively	Postoperatively
Demographic data	Evidence of febrile UTIs up to 7 days post op
Antibiotic data – if given, what is given, what dose	
Urine dipstick analysis (if done routinely)	
Urine microscopy and culture if dipstick is positive (if done routinely)	
Indications for cystoscopy And type of cystoscopy performed	

5. **Study Design**

Multi-center, international, non-interventional, observational study

6. **Target Population**

Pediatric population - all patients <16 years of age undergoing a diagnostic or therapeutic cystoscopy

7. **Inclusion/Exclusion Criteria**

Inclusion criteria:

- All patients <16 years of age undergoing a diagnostic or therapeutic cystoscopy at the participating centers

Exclusion criteria:

- incomplete outcome data
- withdrawal from study

8. **Data collection**

- Participating centers will be identified before the study period
- Participating centers will enter data concerning all cystoscopies performed in children <16 years of age during the study period
- ***No patient identifiable data will be collected.***
- Data will be collected and stored online through a secure server running the Research Electronic Data (clinsight)
- Hospital Leads will be provided with Clinsight server login details, allowing them to securely submit data
- The Clinsight server is managed by the Centre Hospitalier Universitaire de La Réunion

9. **Study Procedures**

All patients will receive their routine care as planned without any modification to each centers standard care. All data will be entered into an anonymized, secured database.

Each participating unit will only be able to access their data and no other participating unit. Only the PI/Co-PIs will be able to see all data.

A local investigator will be identified and invited to ensure maximum data collection from his/her center.

10. **Sample Size Justification**

The study will aim to recruit minimum 50 centers and each center will be required to collect data on 10 patients minimum. As the study is observational and descriptive only, a sample size has not been calculated.

11. **Feasibility, Accrual, and Expected Duration of Accrual**

Cystoscopy is a routine procedure carried out by all pediatric urologists. Approximately 5 (2-10) cystoscopy cases are performed in most pediatric urology units per week. The recruitment period is 10 weeks. We hope to recruit minimum 50 centers and between 20-100 patients per center. We expect the data collection to be performed during an 8-week period. We estimate 5% will have missing data. The total number of patients is estimated to be 1000-5000.

12. **Study Limitations**

As this is an observational study, we do not envisage limitations.

13. **Data Analysis**

The analysis will describe the primary and secondary outcomes in the cohort.

Descriptive data analysis. Qualitative data analysis with non-parametric tests

14. **Local study approvals**

The study will be conducted in accordance with national and international guidelines and legislation, as well as the basic principles of the protection of the rights and dignity of Human Beings, as set out in the Helsinki Declaration. It is an investigator-led, non-commercial, observational (no changes to normal patient care) study, which is extremely low risk. Only routinely available non-identifiable data will be collected. As such according to our legislation, no formal ethics committee approval is warranted and patient consent forms are not required.

Hospital Leads are responsible for obtaining necessary local approvals at each participating site in line with hospital and country regulations.

Administrative Organization/Roles and Responsibilities

The study is supported by the **European Society of Pediatric Urology** and is managed by the ESPU Research Committee. The official promotor is the University Hospital of La Réunion, France.

Use of Study Results

The results of the study will be used for presentations and publications.

Sponsoring

The study expenses for administratrive support and creation of the Clinsight database registry are covered by the European Society of Pediatric Urology.

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Appendix 1. Study questionnaire

DEMOGRAPHICS

Patient age at time of cystoscopy ** must provide value*	☐ ≤1 month ☐ >1 month to ≤1 year ☐ >1 year to ≤5 years ☐ >5 years - ≤12 years ☐ >12 years
Patient gender ** must provide value*	☐ Male ☐ Female ☐ Unassigned
If the patient was male, was he circumcised? ** must provide value*	☐ Yes ☐ No
Surgeon/Urologist's country of practice ** must provide value*	
Surgeon/Urologist's years in practice ** must provide value*	☐ < 5 years ☐ 5-10 years ☐ >10 years

HISTORY

Underlying Condition(s) [Check all that apply] ** must provide value*	☐ VUR ☐ UPJO ☐ PUV ☐ Neurogenic bladder ☐ Obstructive megaureter with ureterocele ☐ Obstructive megaureter without ureterocele ☐ Bladder exstrophy/epispadias ☐ Stone disease ☐ Hematuria ☐ Dysuria ☐ Cystoscopy + placement of supra-pubic catheter ☐ Other
Please Describe	
History of culture confirmed febrile UTI prior to cystoscopy? ** must provide value*	☐ Yes, ≤2 months before cystoscopy ☐ Yes, >2 months before cystoscopy ☐ No ☐ Unknown
Continuous antibiotic prophylaxis prior to cystoscopy? ** must provide value*	☐ Yes ☐ No
Clean intermittent catheterization (CIC)	☐ Yes

prior to cystoscopy? ☐ No

** must provide value*

PERIOPERATIVE DATA (1/2)

Indication for cystoscopy [Check all that apply] ** must provide value*	☐ Diagnostic cystoscopy ☐ Bulking agent *for VUR* ☐ Bulking agent *for incontinence* ☐ Balloon dilation ☐ Ureterocele incision ☐ PUV resection ☐ Botulinum toxin ☐ Stent removal ☐ Stent insertion ☐ Bladder dysfunction ☐ Bladder biopsy ☐ Stone disease ☐ Other
Describe	
Was preoperative urinalysis conducted? [Check all that apply] ** must provide value*	☐ >72 hours before surgery ☐ ≤72 hours before surgery ☐ At time of cystoscopy ☐ Not conducted
Was preoperative urine culture conducted? [Check all that apply] ** must provide value*	☐ >72 hours before surgery ☐ ≤72 hours before surgery ☐ At time of cystoscopy ☐ Not conducted

Was peroperative antibiotic prophylaxis administered? ** must provide value*	☐ Yes ☐ No
Route ** must provide value*	☐ Intravenous ☐ Oral

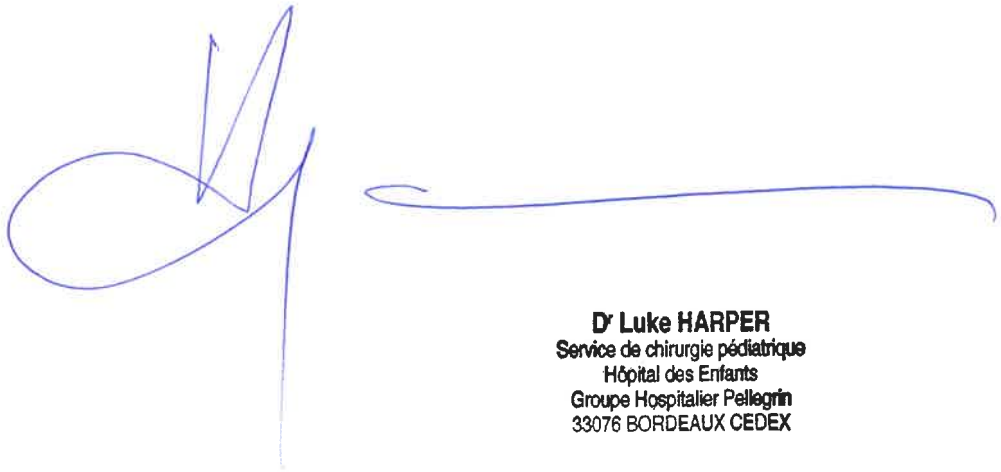
PERIOPERATIVE DATA (2/2)

Class ** must provide value*	☐ Penicillins ☐ Macrolides ☐ Cephalosporins ☐ Fluoroquinolones ☐ Beta-lactams with increased activity ☐ Tetracyclines ☐ Trimethoprimsulfamethoxazole ☐ Urinary anti-infectives ☐ Lincosamides
Duration ** must provide value*	☐ 1 dose ☐ ≤48 hours ☐ ≤48 hours
What was the basis for the decision to use/not use perioperative antibiotic prophylaxis? [Check all that apply] ** must provide value*	☐ Your local/regional or national protocol ☐ Atypical patient presentation ☐ Preoperative urinalysis ☐ Surgeon/Urologist preference ☐ No indication
Who made the decision about perioperative antibiotic prophylaxis? ** must provide value*	☐ Surgeon/Urologist ☐ Anesthesiologist ☐ Both

How long was the procedure (duration of cystoscopy) ** must provide value*	☐ ≤30 minutes ☐ 30 to ≤60 minutes ☐ 60 to ≤90 minutes ☐ 90 minutes or more

POSTOPERATIVE DATA

Was the patient treated for UTI within 7-days of cystoscopy? ***Only applies to illness/diagnosis AFTER the procedure (not intra-op urine collection/testing)***	☐ Yes ☐ No ☐ Unknown
Did the patient have fever ≥38.5 centigrade associated with UTI?	☐ Yes ☐ No ☐ Unknown
Did the patient have pyuria on urinalysis associated with UTI diagnosis? [Note: pyuria = any level of leukocyte esterase or >5wbc/hpf]	☐ Yes ☐ No ☐ Urinalysis not performed ☐ Unknown
Did the patient have a culture with a single organism >50.000 CFU?	☐ Yes ☐ No ☐ Culture not performed ☐ Unknown
How was urine specimen collected?	☐ Bagged ☐ Clean catch voided ☐ Catheterized ☐ Suprapubic puncture



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