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EDITORIAL

Childhood urinary tract infections: A Swedish perspective and comparison with other published guidelines

The optimal approach to the investigation and management of urinary tract infections (UTIs) in childhood has been a contentious issue. Concerns that the infections placed the immature kidney at significant risk of scarring and destruction, with the possibility of major long-term adverse sequelae, resulted in many years whereby invasive investigations and aggressive interventions were encouraged. With improved prenatal ultrasound, there was an increased recognition that much of the severe kidney damage responsible for the more severe morbidity was the consequence of congenital abnormalities of the kidney and urinary tract rather than acquired damage secondary to renal parenchymal infection.

Swedish investigators were and remain at the forefront of well-designed prospective studies and long-term follow-up that have improved our understanding of nature, appropriate interventions, and outcomes for childhood UTI. They were amongst the earliest to characterise asymptomatic bacteriuria and demonstrate that it did not warrant investigation and antibiotic treatment, even in the presence of previous kidney scarring.[1] Furthermore, when international investigators conducted prospective randomised controlled trials (RCTs) to assess the efficacy of antibiotic prophylaxis following a febrile UTI in children with absent or predominantly lesser grades of vesicoureteral reflux (VUR), they were the first to undertake RCTs on interventions, including surgery and antibiotic prophylaxis, exclusively in children with high grade dilating VUR.[2,3] Finally, while many studies have been cross-sectional at a point in time, or interventional RCTs restricted to 1–2 years follow-up, with recurrent UTI a surrogate marker for potential kidney damage, they were the first to report outcomes 16–26 years after a 1st fUTI in childhood.[4]

It is against this background, that in this issue of *Acta Paediatrica*, Brandström and Lindén briefly summarise our current understanding of childhood UTIs prior to presenting a resume of the Swedish guidelines on childhood UTIs, with clarification of the reasons for their approach, where controversy persists.[5] Secondly, they compare their recommendations with those of recently published guidelines by other bodies. The latter is of importance, as differences that occur signal where the evidence is of poor quality or lacking and highlights the direction in which future research should be focussed.

The paper summarises in considerable detail the 2013 Swedish national guidelines on UTI in children that were published locally in Swedish such that for the 1st time those outside Sweden can have some understanding of their approach to this controversial issue, and some insight as to the strategies they employed to formulate the document. The paper discusses aspects including UTI diagnosis, the level of infection, the importance of bladder and bowel dysfunction, treatment of the acute infection, asymptomatic bacteriuria and imaging follow-up. They take a 'top-down' approach with a DMSA scan within 1 month in children less than 2 years, if they have a defined risk factor or 2nd febrile UTI recurrence. The algorithm for investigation of a UTI is clearly suited to a developed country such as Sweden with ready access to advanced imaging, nuclear diagnostics, in particular, however, they do provide a second investigative algorithm for smaller and more remote hospitals that do not have immediate access to such facilities. An assessment of the findings and eventual outcomes for the children subject to the 2 different protocols would be of interest, the paper indicating that a nationwide multicentre study of adherence to the guidelines and quality of care for infants with UTI is underway. As the Swedish guidelines were only ever disseminated locally, the preamble describing them is essential for the purposes of comparison with published international guidelines. With any future revision, we would encourage their publication for the benefit of the wider international community such that the Swedish perspective may assist others in formulation and updating of their guidelines. As noted in this paper, the working group as well as conducting their own research relied on preparatory work of other groups including NICE and the AAP.

The Swedish childhood UTI guidelines were compared for differences and similarities to 5 medical and 1 surgical guideline. The diagnosis of what constitutes a UTI and the temperature that determines a febrile UTI, while appearing mundane to many, is immediately controversial. The original colony count of 10^5 organisms per ml of urine was set by Kass 60 years ago studying pregnant women with pyelonephritis.[6] At the time, he acknowledged the cut-off as arbitrary such that cases would be missed. In a recent publication, Swerkersson et al. demonstrated 19% of infants <1 year of age with asymptomatic UTI diagnosed by supra-pubic aspirate had a colony count of <105 organisms, 87% of whom had a count $<5 \times 10^4$.[7] The recent Diagnosis of Urinary Tract infection in Young children (DUTY) study attempted to validate an algorithm for the diagnosis of UTI in children presenting in a primary care setting only to find conflicting results between government and research laboratories.[8] It is no surprise that the acceptable bacterial counts for UTI diagnosis differ even when the same collection technique applies. The situation is no

clearer when the various guidelines recommend differences in collection technique, urinalysis for leukocyte esterase and the need or otherwise of blood tests including C-reactive protein, Procalcitonin, blood culture and full-blood count. In non-toilet trained children recommendations for collection in Sweden advocate a supra-pubic aspirate as 1st line with the need for 2 separate mid-stream urines should this option be considered. This contrasts with the NICE (UK) guidelines where a single mid-stream urine is the primary option with a supra-pubic aspirate a 3rd option after a pad collection. This likely reflects the majority of children with a UTI in Sweden appearing to present to a specialist paediatrician or paediatric nephrologist with the attendant collection skills while in the UK they present in most cases to general practitioners. This has important implications for the correct diagnosis of UTI that influences treatment and follow-up as well as the conduct of research in this field.

While prophylactic antibiotics are no longer routinely considered, the authors claim that the Swedish guidelines are more liberal in their use. With respect to the Italian guidelines[9] which took into consideration results of the Swedish reflux trial, we disagree as both are similar in their recommendations.

Follow-up imaging is an area where there is a contrast between the Swedish and other medical guidelines. The Swedish guidelines comprise a top-down model, with an initial ultrasound and an early DMSA scan for children with one or more risk factors, recurrent UTI or abnormal ultrasound with a repeat DMSA scan after 12 months, where the initial scan was abnormal. The purpose of this approach is detection of renal parenchymal infection, scarring or damage and reducing the number of distressful voiding cystourethrograms (VCUGs) now considered by all medical guidelines as unnecessary as a routine.[10] The only other guideline to proposing a top-down approach is by the EAU/ESPU urology group, where they consider it as an option to a bottom-up approach with a VCUG. At the time of formulation of the Swedish guidelines, we published a comparison of 5 diagnostic protocols were they applied to a cohort of children comprehensively investigated as part of an RCT.[11] Detection of scarring was closely linked to recommendations for DMSA scans and missed in all those where a DMSA scan was not recommended. However, this was associated with a concomitant higher cost and radiation burden. This trade-off is at the crux of the argument for investigation, the long-term risks of missed scarring are only now being evaluated as referenced by 3 papers cited by the authors.

Other differences that make the Swedish guidelines unique include their application to all UTIs, older children and long-term follow-up, rather than restriction to febrile infections, children up to 3 years of age and short-term follow-up.

Contrary to the authors claim that a VCUG is omitted in the primary workup for children without risk factors or signs of underlying uropathies, this is not the case for the one urological guideline included, where a focus remains on detecting VUR.

We welcome this paper clarifying the Swedish position on the investigation and management of UTIs in children. Their approach appears quite detailed and, in our opinion, maybe a little demanding from the diagnostic viewpoint. Some children find themselves subject to repeated blood tests, 2 mid-stream urine collections, and multiple imaging (ultrasound, VCUG and 2 DMSA scans), notwithstanding the paucity of adverse outcomes, as described by Swedish authors. Further research from this nephrology community will help to provide answers to many of the questions raised by this comparison of guidelines from different countries, each with a distinctive medical care system and different challenges dictated by referral patterns, cost constraints and access to facilities.

CONFLICT OF INTERESTS

There is no conflict of interest regarding this manuscript.

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