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Pediatric Urology an Antibiotic Prophylaxis on a Continuous Basis

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Abstract

The Greek word prophylaxis means "to guard or prevent beforehand." In Pediatric Urology, antibiotic prophylaxis is the attempt to prevent urinary tract infections (UTIs) in children who are predisposed to them, such as those with vesicoureteral reflux (VUR) and hydroureteronephrosis. Antibiotic prophylaxis for paediatric urologic conditions has both demonstrated benefit and demonstrated harm. Antibiotic prophylaxis for all children with VUR, as well as those with all grades of hydronephrosis (HN) and hydroureteronephrosis, is at best unnecessary and at worst harmful. The full impact of prophylactic antibiotics on the developing and ageing body, for better or worse is unknown. Over the last two decades, increased public and physician awareness of the truth of previous statements has resulted in a more selective approach to the use of prophylactic antibiotics. Although it was previously thought that most children with conditions such as VUR or hydronephrosis were at high risk of UTI and thus would benefit from continuous antibiotic prophylaxis (CAP), data from multiple studies has shown otherwise.

Keywords: Urinary tract infections • Vesicoureteral reflux

Introduction

Studies now allow for the better identification of children who are most likely to benefit from antibiotic prophylaxis, allowing for a more selective and individualised approach to health care. The benefits and risks of antibiotic prophylaxis in the context of several common paediatric urologic conditions, including VUR, prenatally detected HN, and hydroureter, are discussed in this article. Patient characteristics that place the child at increased risk of UTI and its sequelae are noted for each condition. Prophylactic antibiotics' impact on bacterial resistance, the microbiome, and potential long-term side effects are discussed. The article concludes with a discussion of the evolving field of antibiotic prophylaxis alternatives, including prebiotics and probiotics.

Vesicoureteral reflux

The most heated debate in paediatric urology revolves around the use of CAP in children with VUR. Antibiotics are unquestionably effective at killing bacteria and preventing UTIs. The Randomized Intervention for Vesicoureteral Reflux (RIVUR) and Swedish Reflux trials both found that children who received CAP had fewer UTIs. What is still being debated is the practise of putting every child with VUR on CAP [1-3]. Furthermore, there is still debate about whether children should have a voiding cystourethrogram and be diagnosed with VUR after their first febrile UTI. Over the last two decades, there has been a growing recognition that many children with VUR do not benefit from diagnosis or treatment. Many children's reflux is self-limited and innocuous; however, a subset of children with VUR benefit from both diagnosis and treatment with either CAP or surgical intervention.

Multiple risk factors for recurrent UTI, persistent VUR, pyelonephritis, and renal scars have now been identified, and when considered together, they help to better identify which children will benefit from antibiotic prophylaxis and which will not. The severity or grade of VUR has been used as a primary factor in predicting spontaneous reflux resolution and the risk of pyelonephritis and renal injury. Higher grades of reflux are linked to lower resolution rates and an increased prevalence of renal scars. Furthermore, VUR occurring earlier during bladder filling has been shown to be a risk factor for breakthrough UTIs regardless of grade. Other factors that predict reflux resolution, UTI, and/or the risk of renal injury, in addition to grade and bladder volume at the onset of reflux, include gender, age, race, laterality, bladder pressure at the onset of reflux, the presence of renal scars, the presence of bowel and bladder dysfunction, and a history of recurrent UTIs.

The most significant assessable risk factors for the development of UTI in children are bladder and bowel dysfunction (BBD). Even when they are on CAP, children with VUR and bowel and/or bladder dysfunction are especially predisposed to recurrent pyelonephritis. The cost of recurring UTIs is estimated to be occurring in approximately 45% to 56% of these children, compared to 15% to 25% of children who do not have BBD. Furthermore, children with BBD have a higher incidence of renal scarring, a lower rate of spontaneous resolution, and a higher failure rate after antireflux surgery [4].

The recurrence rate is highest in the first 3 to 6 months after a UTI and the more frequent and recurring a child's UTI, the more likely he or she is to have another UTI [1]. Neither the AAP nor the National Institute of Health and Care Excellence guidelines recommend routinely prescribing prophylactic antibiotics to infants and children following their first UTI. Prior to the RIVUR and Swedish reflux trials, several small randomised trials involving children with low grades of VUR called into question the efficacy of prophylaxis in children with VUR. Trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis was compared to placebo in 607 children with grade I-IV VUR following UTI in the RIVUR trial.

Despite the earlier findings from the RIVUR trial, a more thorough examination of the data revealed that 8 children would need to be treated with antibiotic prophylaxis for two years to prevent one case of febrile or symptomatic UTI. Furthermore, outcome renal scans (at the 2-year visit or 3-4 months after the child met treatment failure criteria) revealed no significant difference in the incidence of renal scarring between groups (11.9% in the prophylaxis group versus 10.2% in the placebo group). Children with BBD at baseline, a history of febrile UTI, or higher grades of VUR had the greatest risk reduction for recurrent UTI.

Following the publication of the AAP 2011 recommendations, de Bessa and colleagues conducted a meta-analysis. Following an initial review of the trials, it was determined that CAP was only beneficial in children with high-grade VUR (Grade III/ IV). However, with the addition of data from the 2014

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RIVUR study, the new pooled estimate supported the use of CAP in all children with VUR, regardless of reflux grade, to prevent recurrent UTI. The most recent systematic review and meta-analysis on the topic confirmed this benefit.

As with any systematic review, the applicability of these two meta-analyses is heavily dependent on the quality, validity, and heterogeneity of the data.of the studies included Furthermore, while randomised controlled trials provide the best available evidence, they do not always reflect our clinical patient population. As a result, these findings must be interpreted with caution. Although it is tempting to simply extrapolate the results of each RCT or systematic review to all children with VUR, this is risky. The patient cohorts in each of the eight RCTs were different, which likely reflected the differences in observed outcomes.

Renal scarring/reflux nephropathy

Although some studies have shown a small benefit in using antibiotic prophylaxis to prevent symptomatic and febrile UTIs, the prevention of renal scarring has not been established, owing to study underpowering [5]. Hewitt and colleagues examined the effect of antibiotic prophylaxis on UTI-mediated renal scarring in 1427 subjects aged 18 years or younger in a meta-analysis. Renal scarring increases with the number of febrile UTIs, so children at risk for renal injury include those at risk for recurrent or breakthrough UTIs. Furthermore, children with reflux and UTIs are more likely to develop renal scarring than children with UTIs but no reflux. Up to one-third of all VUR patients have renal scars, and 50% of children with grades III or IV reflux had scars when they entered the International Reflux Study.

Prompt antimicrobial treatment reduces the risk of permanent renal damage, as does the elimination of any subsequent episode of pyelonephritis. If a child's social situation makes it likely that he or she will not be promptly diagnosed and treated for a febrile UTI, this child may benefit more from prophylactic antibiotics because a delay in treatment is associated with an increased risk of renal injury and scarring. According to one study, every hour antimicrobial therapy was delayed in treating a febrile UTI increased the risk of new renal scarring by 0.8%.

In addition to limiting the situations in which CAP is prescribed, ensuring that only children with documented UTIs receive antibiotic treatment will limit antimicrobial use and reduce antibiotic resistance. According to a recent study, nearly one-third of children under the age of two did not have a urinalysis or a urine culture before being treated with antibiotics for suspected UTI symptoms [6]. This is in direct contrast to the most recent AAP guidelines for UTI management, which recommend obtaining a urine specimen for urinalysis and urine culture in a febrile infant with no obvious source of fever. Furthermore, even if only on an ad hoc basis, proper antibiotic treatment could aid in the reduction of antibiotic resistance.

The microbiota is a group of bacteria, archaea, fungi, protozoa, and viruses that live in different parts of the body. There are an enormous number of microbials that colonise the oral and nasal cavities, the skin surface, and the gastrointestinal tracts in humans. In fact, microbial cells outnumber human cells by a factor of ten, and the colon is the most heavily colonised site. Health care providers are finally realising that microbiota play an important role in normal body function and that a healthy microbiome plays an important role in host immunity, metabolism, and resistance to pathogens [7]. Furthermore, changes in the "normal" microbiota may result in disease states. Health-care-associated infections are examples of the consequences of antibiotic-induced changes in the human microbiota. Antimicrobial therapy is most likely the most significant risk factor for the development of Clostridium difficile-associated diarrhoea. 101 C difficile is naturally present in the gastrointestinal microbiota of some healthy Continuous Antibiotic Prophylaxis 7 people.

Conclusion

The common and widespread practise of using CAP for children with VUR, HN, and hydroureteronephrosis in a relatively nonselective manner is beginning to change. Individual risk factors for UTI and subsequent renal injury and its sequelae can now be identified more precisely, allowing for more selective and beneficial use of CAP. Because of the potential long-term side effects of antibiotics, health care providers must use CAP with caution. Reduced antibiotic use will help to reduce the development of bacterial resistance on an individual and community level. Furthermore, limiting antibiotic use will reduce the impact on a child's microbiota, which is increasingly being recognised to play an important role in normal body functions and development.

Current practise patterns influence and shape the future for each of our patients, as well as the treatment options that will be available to health care providers in the future. The known negative impact of our current practise patterns necessitates immediate change.

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Conflict of interest

None declared.

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