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Original Research Article

Reflux-Related Renal Injury (Reflux Nephropathy): Do Nonsteroidal Anti-Inflammatory Drugs (Ibuprofen) Increases' the Risks?

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Abstract: Reflux predisposes to facilitating the transport of bacteria from the bladder to the upper urinary tract and infection of the kidney by it. So the objectives of this study were to examine the influence of nonsteroidal anti-inflammatory drugs (Ibuprofen) in risk of reflux nephropathy. In this study we conducted a description of a case series (Children who had febrile UTI and treatment with ibuprofen 193(case group), and acetaminophen180 (control group)) in the pediatric clinic of Amirkabir hospital to characterize risk of Ibuprofen in a cohort study of patients with reflux nephropathy. The prevalence of reflux nephropathy was 4% in control group and 26% in case group. Based on chi-square test, the distribution of reflux nephropathy is difference in the two groups (p=0.0003). We concluded that there is apparent correlation between ibuprofen and reflux nephropathy.
Keywords: Reflux Nephropathy, Ibuprofen, NSAID.

INTRODUCTION:

Reflux predisposes to infection of the kidney by facilitating the transport of bacteria from the bladder to the upper urinary tract [1]. The inflammatory reaction caused by a pyelonephritic infection can result in renal injury or scarring, also termed reflux-related renal injury or reflux nephropathy. In children with a febrile urinary tract infection, those with reflux are 3 times more likely to develop renal injury compared to those without reflux [2, 3]. Extensive renal scarring impairs renal function and can result in rennin-mediated hypertension, renal insufficiency or end-stage renal disease, impaired somatic growth, and morbidity during pregnancy [4]. Reflux nephropathy once accounted for as much as 15-20% of end-stage renal disease in children and young adults. With greater attention to the management of UTIs and a better understanding of reflux, end-stage renal disease secondary to reflux nephropathy is uncommon. Reflux nephropathy remains one of the most common causes of hypertension in children. Reflux in the absence of infection or elevated bladder pressure does not cause renal injury [5, 6]. Analgesic nephropathy is injury to the kidney caused by analgesic medications such as ibuprofen. The specific kidney injuries induced by analgesics are renal papillary necrosis and chronic interstitial nephritis [7, 8]. They appear to result from decreased blood flow to the kidney, rapid consumption of antioxidants, and subsequent oxidative damage to the kidney. This kidney damage may lead to progressive chronic kidney failure, abnormal urinalysis results, high blood pressure, and anemia [9-11]. A small proportion of individuals with analgesic nephropathy may develop end-stage kidney disease [12, 13]. The aim of the study was to measure ibuprofen nephropathy in children with VUR and evaluates its relationship with reflux nephropathy.

MATERIAL AND METHOD:

This case-control study was conducted on the outpatients in the pediatric nephrology clinic of Amir

Kabir hospitals in Arak. Participants included 2-10 year-old girls who had developed a form of acute pyelonephritis, UTI, for the first time and had not indications of hospitalization due to UTI. Children who had febrile UTI and treatment with ibuprofen 193(case group), and acetaminophen180 (control group). Girls and their parents were interviewed and underwent laboratory examinations in order to analyze the inclusion criteria. These examinations included medical history of UTI symptoms, urinalysis and culture, ultrasonography of the Kidney, voiding cystourethrograms (VCUG) and Technetium (Tc)-99m dimercaptosuccinic acid scintigraphy (DMSA scan). Since E. Coli is the most common cause of urinary tract infection (UTI) and for easier cloning of the subjects for UTI factor organism, only the patients with UTI resulted by E. Coli were included in the study. Since this study aimed at analyzing urine samples with E. coli sensitive to Cefixime, E. coli isolated from urine cultures underwent sensitivity test for evaluating their resistance or sensitivity to Cefixime antibiotics. Since Technetium (Tc)-99m dimercaptosuccinic acid scintigraphy is the gold standard method for the diagnosis and localization of acute pediatric pyelonephritis; all Girls qualified for the study's initial conditions underwent this scan for the evaluation of acute pyelonephritis. Girls with diagnosed renal scarring after DMSA scan were not included in the study. Acute scintigraphy pyelonephritis was defined as focal or diffuse areas of decreased DMSA uptake without evidence of cortical loss and renal scar was defined as areas of negative DMSA uptake. Inclusion criteria included: 1) 1-5 year-old girls, 2)Girls with medical history and symptoms of UTI and girls diagnosed with acute pyelonephritis based on fever (without any source other than UTI) and evidence of renal inflammation in DMSA scan and VUR in VCUG ,3) Positive urinalysis and culture results for only one type of UTI-causing organism, i.e. E. coli, 4) Isolated E. coli sensitive to Cefixime antibiotics based on the disk diffusion method, 5)Receipt of informed consent from Girls' parents for participating in the study and their proper compliance for cooperation . Exclusion criteria included: 1) Diagnosis of renal scarring based on the results of DMSA scan 2) History of any form of UTI with any count, 3) Neurogenic bladder4) History of voiding dysfunctions5) Severe sepsis and bacteremia. After assessment of girls and their parents, they were included in two groups (treatment of fever with acetaminophen and ibuprofen) and matched in terms of age, sex, urinalysis and culture results, DMSA scan results. Medications were administered for 14 days in a way that all girls underwent routine UTI treatment. The treatment included 8 mg / kg / day of oral Cefixime in 2 divided doses. Considering the prevalence of UTI, sample size was determined 373 patients. Parents were provided with the necessary training for administering medicine to girls. They were also told to refer 7-10 days and 4-6 months after the treatment for repeated urine culture and DMSA scan, respectively. The forms included their demographic information, the results VCUG, and the results of DMSA scan 4-6 months after the treatment. The results of urine culture and DMSA were recorded in patients' clinical information forma at specific times and 4-6 months after the treatment, respectively. The collected data were analyzed using the SPSS software.

RESULTS:

The prevalence of reflux nephropathy was 4% in control group and 26% in case group. Based on chi-square test, the distribution of reflux nephropathy is difference in the two groups (p=0.0003).Mean grade of VUR were 1±3 and 2±3 for control and case groups respectively and no significant difference is observed between two group.

DISCUSSION:

In study of Yousefichaijan P, Mean Platelet Count was higher in patients with reflux nephropathy than non-reflux nephropathy patients and Mean Platelet Volume was lower in the patients with reflux nephropathy than patients without reflux nephropathy. MPV can be used as an indicator in diagnosis of reflux nephropathy in patients with VUR [14]. Yousefichaijan P found that, sacral ratio abnormality was more common in children with vesicoureteral reflux and reflux nephropathy than children with VUR without reflux nephropathy [7]. In study of Yousefichaijan P, Hyponatremia in children with reflux nephropathy was significantly more common than children without reflux nephropathy. The observed correlation between reflux-related injury and hyponatremia necessitates evaluation of electrolytes in children with pyelonephritis [15]. Yousefichaijan P found that, the data suggests that prenatal factors may affect the risk of IRN. Adequate prenatal care and good maternal support can be effective in the prevention of reflux-related renal injury [12]. In study of Yousefichaijan P, Results of our study showed that the prevalence of anemia in the Reflux Nephropathy group was not considerably different than that of the control group. We concluded that there isn't a direct correlation between anemia and reflux nephropathy in patients with vesicoureteral reflux [5].

CONCLUSION:

This study showed an apparent correlation between ibuprofen and reflux nephropathy. A multicenter study with a larger sample size is suggested to investigate the correlation between ibuprofen and reflux nephropathy.

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