Investigating the Effect of Montelukast on the Pyelonephritis Symptoms in Children

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Introduction:

Urinary tract infections as one of the most important infections in ۲ children, may be induce several complications. Three major forms of urinary tract infections include pyelonephritis, cystitis and asymptomatic bacteriuria. Acute pyelonephritis is one of the most common diseases of bacterial infections in children, and scarring in the kidney is one of the long-term complications in these patients.

In addition to antibiotic therapy, other therapies can be used to • control the clinical manifestations of the patients and the complications of urinary tract infections, which has been studied in a limited number of studies. Based on mentioned data and importance of complications of pyelonephritis, aim of this study was to investigating the effect of Montelukast on the pyelonephritis symptoms in children.

This review will critically highlight the role of leukotriene's as mediators of renal diseases and drug nephrotoxicity. Leukotriene's were shown to mediate drug-associated nephrotoxicity, transplant rejection and morbidity in several models of renal diseases. Although leukotriene's may be released by various infiltrating leukocytes, a recent study demonstrated that cytotoxic agents trigger production of leukotriene C4 in kidney cells.

However, it is believed that inflammation plays a central role in • the pathogenesis of UTI. One of the proposed mechanisms is the presence of leukotriene receptors in the detrusor muscle cells, increased urinary levels of leukotriene E4 in patients with UTI mastocytosis, suggesting a role of these and detrusor proinflammatory mediators in UTI. Leukotriene E4 plays a role in the activation of mast cells and eosinophils.

• Once the mast cells are activated, they release vasoactive, inflammatory mediators, including kinin, leukotrienes, protease, prostaglandins, and nitric oxide, which are of most importance in chronic inflammatory disorders. Many symptoms and findings of UTI such as pain, urinary frequency, edema, and fibrosis can be explained by mast cell-derived mediators. Montelukast, a cysteinyl leukotriene receptor-1 antagonist, has an antiinflammatory role by inhibiting leukotriene receptors present in the bladder, thus, preventing the activation of mast cells.



Leukotriene metabolites and their actions.

Patients and Methods:

In this study, 100 children with pyelonephritis were divided into ٠ two groups of intervention (n = 50) and control (n = 50). Patients in both groups received routine antibiotic therapy and in the case group, montelukast (5 mg / day, oral) was also prescribed (duration of treatment was 14 days). Finally, the clinical manifestations of patients were evaluated and compared in two groups.

Results:

- The mean age (±SD) in case and control group was 7.2 (± 0.43) and 7.18 (± 0.43) years, respectively. In addition minimal and maximal age of patients was 3 and 14 years, respectively.
- Also about gender of patients n intervention group 38 cases were female, and 12 cases were male, and in control group 34 cases were female and 16 cases were male (Table 1).

 Table 1 : Comparison of age and gender in intervention and control groups

Variables	Groups		P Value
	Control	Intervention	
Age			0.9
Mean	7.18	7.2	
SD	0.43	0.43	
Gender			0.07
Male	12) 24(38) 76(
Female	16) 32(34) 68(

In addition analysis of the results showed that the mean and standard deviation of duration (day) of clinical manifestations of pyelonephritis were significantly lower in intervention group rather than control group. These clinical manifestation included as duration of fever (P <0.0001), dysuria (P <0.0001), abdominal pain (P <0.0001), and urgency (P = 0.003), were significantly lower in intervention group rather than control group (Table 2).

Table 2: Comparison of the duration of clinical manifestations in the intervention and control

Clinical Manifestations	Groups		P Value
	Control	Intervention	
Fever			>0.0001
Mean ± SD	1.62 ± 0.07	1.06 ± 0.03	
Dysuria			>0.0001
Mean ± SD	$1.4{\pm}0.09$	0.8 ± 0.08	
Abdominal Pain			>0.0001
Mean ± SD	2.8 ± 0.08	1.6 ± 0.06	
Urgency			0.032
Mean ± SD	1.12 ± 0.1	0.72±0.7	

Discussion :

- In this study we observed that time of clinical manifestations of pyelonephritis in interventional group were lower than control group. However in other studies there are some other results that be discussed in following.
- Abdel-Raheem et al. in a study, evaluated the montelukast influence in supporting the kidneys in the patients that consumes methotrexate and concluded that montelukast reduced the effects of methotrexate on the kidney.

These results are consistent with results that observed in the study, which indicates the beneficial effects of this drug in treating patients. Otunctemur et al. also evaluated the effect of montelukast on the reduction of renal complications from gentamicin and stress, and they compared the interactions between these two drugs in experimental mice, based on these, they concluded that montelukast acts as an agent for the prevention of complications. These results are also consistent with the results of this evaluation. On the other hand, Bisgaard et al.

Conclusion:

• Cysteinyl leukotriene's released by mast cells trigger the symptoms and complications of UTI such as acute kidney disease, scar nephropathy, fever, frequency, urgency and etc. Therefore, effective leukotriene inhibitors were approved as orally in addition to administered anti-bacterial drugs in UTI. The findings that leukotrienes mediate the cytotoxicity of nephrotoxic drugs, and are involved in numerous renal diseases, suggest that such Montelukast may ameliorate drug-induced nephrotoxicity, as well as some renal diseases.

 Based on this study, other studies that conducted in this field, montelukast lead to rapid improvement of clinical manifestations in children with pyelonephritis and it can be used as an effective auxiliary treatment in these patients.

