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Urinary EGF level changes in hydronephrotic infant patients before and after surgery

Faramarz Fazeli[1], Seyed Hosein Soleimanzadeh Mousavi[2], *Simin Sadeghi-Bojd[3]

[1] Assistant Professor of Urology, Department of Urology, School of Medicine, Ali IbneAbitaleb Hospital, Zahedan University of Medical Sciences, Zahedan, Iran.

[2] Pediatric Nephrologist, Children & Adolescent Health Research Center, Resistant Tuberculosis Institute, Zahedan University of Medical Sciences, Zahedan, Iran.

[3] Pediatric Nephrologist, Children & Adolescent Health Research Center, Resistant Tuberculosis Institute, Zahedan University of Medical Sciences, Zahedan, Iran.

Abstract

Background: Urinary tract obstruction is defined as any disorder in the normal urinary flow tract in the pediatric group. In the field of urology, urine stasis and urinary obstructions play an important role in renal complications. Every obstruction in the urinary tract can lead to hydronephrosis, atrophy and even full destruction of renal function. In addition, tract obstruction can result in a urinary infection which exacerbates the destruction per se.

Methods: The present study was a descriptive-analytical study of 25 one-month-old to one-year-old children. In this study, one urine sample was collected the day before surgery, another urinary sample was taken from the affected pelvis during surgery, and the other urine sample was collected at the time of double J exertion and stored at a suitable temperature (minus 70. C). The EGF factor was measured in the collected samples, by the use of ELISA method.

Results: The findings revealed that the urinary level of EGF was significantly reduced after surgery, so that the average level of this marker before surgery for the study population was 40.12±12.55, while this amount after surgery equaled 37.32±11.51 mg/dL. The analysis of the data by the T test showed a significant relationship between EGF level and the time of measurement (P=0.0001).

Conclusion: The results of the above study show that obstruction of the urinary tract can increase the urinary level of EGF; and with increasing age, the amount of this marker increases in children who have obstruction of the urinary tract.

Key Words: EGF, Hydronephrosis, Urinary tract obstruction.

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**** Corresponding Author:***

Simin Sadeghi-Bojd, Pediatric Nephrologist, Children & Adolescent Health Research Center, Resistant Tuberculosis Institute, Zahedan University of Medical Sciences, Zahedan, Iran. Email: sisadegh@yahoo.com

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1- INTRODUCTION

Hydronephrosis is defined by an increase in the size of the pelvis and calyces and a progressive atrophy in the renal parenchyma that leads to obstruction of urinary flow (1). Neonatal hydrocephalus can be detected by increasing prenatal ultrasound, but in most cases there is no consensus on diagnostic and therapeutic follow-up of patients after birth, especially in connection with surgical interventions.

Many infants are diagnosed with prenatal nephritis as they increase in size, most of which do not have any specific clinical problems at the time of diagnosis, and their growth and development are normal. Although we know that some of these children develop kidney dysfunction over time, and the exact nature of these disorders is not clear; and despite the conducted research, there are still fundamental questions about the evaluation of fetuses, infants, and children with obstructive nephropathy. We now need to improve the evaluation methods for evaluating the patients with obstructive nephropathy until the time of treatment and also review the progress of responses to treatment in these patients, because creatinine plasma concentrations and nucleotide scans are not very effective for these purposes and new biomarkers are needed. However, the ultimate goal is to achieve new treatments to reduce the rate of damage to the kidneys, but medical experts are more interested in the potential role of plasma and urinary markers such as MCP-1(monocyte chemotactic protein1) and EGF (Epidermal Growth Factor) in this process (2).

EGF is a protein cytokine produced by cells in the ascending part of the Henle tube and the distal part of the urethra, regulating the growth and metabolism of epithelial cells (3, 4). EGF is known as a mediator for the normal growth of renal tubules and the reconstruction of tubules after injury. Decreased renal EGF expression or increased urinary excretion has been reported in acute and chronic tubular lesions in experimental models (5, 6, 7).

Any disturbance in the normal flow of urine and its consequences in children is called urinary obstruction. Urinary obstruction in the urinary tract is of great importance in impairing renal function from a urological point of view. Any obstruction in the urinary tract can eventually lead to atrophy, hydronephrosis and even complete destruction of kidney function. Furthermore, duct obstruction can cause infection and double the damage caused by obstruction. Numerous diseases cause obstruction of the urinary tract which the prognosis of them is variable, and depends on the location and severity of the obstruction and the body's reaction to this phenomenon that can cause more severe diseases (8).

Urinary tract obstruction causes hemodynamic changes and intracellular pressure disturbances that damage kidney tissue, and this damage leads to atrophic tubules, damage cell proliferation, apoptosis, fibrosis, and scarring, where the fibrosis expansion motivates involution of other sites of renal tissue like kidney interstitium and tubules, glomerulus and renal arteries (8).

Because urinary tract obstruction, if it occurs in the early stages of kidney development, may affect the functional level of the kidney in the future (9), understanding these findings in children requires long years of follow-up, including repeated and continuous monitoring of renal function. To identify obstruction in the urinary tract or to perform kidney surgery, which is likely to result in loss of renal function (10), the diagnosis of developing urinary obstruction in the developing kidney is complex and can only be partially evaluated.

Pathological changes can include interstitial inflammation, apoptosis of tubular cells and associated fibrosis (11, 12). Various cytokines such as EGF and IGF-1 inhibit tubular cell apoptosis (13) and several studies have shown a significant reduction in the expression of renal EGF gene in children with UPJO (13, 14, 15).

Therefore, due to the undeniable importance of early detection of renal obstruction to prevent possible damages to all children and increase the quality of life, this study aimed to investigate the average changes in urinary EGF in children with hydronephrosis before and after surgery to create a safe way for early detection of the obstructive kidney disease.

2- METHODS

This study was a descriptive-analytical one conducted over a period of 15 months, on 25 children referred to a pediatric nephrology clinic with hydronephrosis diagnosed by ultrasound evaluate with the help of radiological studies such as VCUG for vesico urethral reflux (VUR) and posterior urethral valve (PUV) obstruction. In the absence of PUV and VUR, DTPA scan was requested for the patients. Due to the rate of evacuation of the renal system from the isotope material and the calculation of T1/2 (time interval from the moment of diuretic injection to the exit of 50% of the accumulated isotope material in the collector system), the presence or absence of obstruction in hydronephrotic systems was assessed and if T1/2 was more than 20 minutes, it was propounded for obstruction and the patient was entered to the study.

Patient information was recorded demographically in the information form. Then a urine sample was taken from the patient the day before surgery, another sample from pelvis during the operation, and the other urine sample was taken three to four weeks after the operation. The collected samples were temporarily stored at -20^{o} C and then transferred to 70^{o} C. In order to evaluate the amount of EGF in the collected samples, the amount of this factor was evaluated using the ELISA method in immunology and hematology laboratories.

In this study, according to the presented definitions, entry and exit criteria were defined and applied. Study entry criteria included children from one month to one year of age whose sonography showed evidence of hydronephrosis (Anterior posterior diameter of renal pelvis(APD) ≥ 15 mm), and exclusion criteria included children with other anomalies such as VUR and PUV based on imaging findings or other post bladder obstructions and urinary stones, children with a diagnosis of UTI and hematuria, bilateral hydronephrosis, children with a history of previous surgery in the urinary system, deformity of the lower bladder and ureter, and patients with neurogenic bladder.

The limitations of the study were the unavailability of laboratory kits and the difficulty in purchasing and supplying them and the lack of proper cooperation of patients during the study.

Finally, Pearson correlation and T test were used to analyze statistical information in SPSS version 20.

This study has been registered in the ethics committee of Zahedan University of Medical Sciences with the code number 1600 before being conducted.

3- RESULTS

This study was a descriptive-analytical one conducted over a period of 15 months on 25 children between the ages of one month to 12 months who had been referred to a pediatric nephrology clinic, had ultrasound evidence of hydronephrosis and their obstruction was confirmed by DTPA scan (Anterior posterior diameter of renal pelvis (APD) ≥ 15 mm).

The EGF rate in these children was measured once before surgery and, if hydronephrosis was proven, and other criteria as described above based on a urine sample, it was again measured during the operation and from the pelvis and once at the time of double J exertion.

According to the information obtained from this study, the mean urinary level before and during the operation was 40.12±12.55 and its mean after the operation was 37.32±11.51. Also, EGF values before and after the operation, had a normal distribution based on the Kolmogrov-smirnov test. More information is given in **Table 1**.

Table-1: The mean levels of EGF

	Number	Mean + SD	Kolmogrov-smirnov P. Value
EGF before operation	25	40.12±12.55	0.219
EGF during operation	25	40.12±12.55	0.219
EGF after operation	25	37.32±11.51	0.572

The first goal of this study was to determine the relationship between the age of the children in the study and the urinary level of EGF. The age of the children who entered the study based on the information obtained was from minimum 2 months to the maximum 12 months old. Pearson correlation test was used to determine the relationship between age and urinary level in children. The results revealed a significant relationship between EGF urinary level and children's age. (R=0.696 / P=0.0001)

The next goal of this study was to compare the mean urinary level of cytokine EGF in children with previous urinary obstruction before, during and after the surgery. The findings demonstrated that there was no significant difference between urinary EGF levels before and during surgery and the values obtained were quite similar. However, data analysis based on the T test showed a significant difference between preoperative EGF values and postoperative EGF values (**Table 2**).

Table-2: Urinary EGF before and after operation compression

	Number	Mean	SD	P.Value
EGF before operation	25	40.12	12.55	0.0001
EGF after operation	25	37.32	12.55	

4- DISCUSSION

Infant hydronephrosis, which can be detected by pregnancy ultrasounds, is still a challenge. However, we know that many of these patients suffer from kidney dysfunction and there are still fundamental questions about the evaluation of fetuses, infants and children with obstructive nephropathy. Although the ultimate goal is to achieve new treatments to reduce kidney damage, medical scientists are increasingly interested in the possible role of plasma and urinary markers such as MCP-1 and EGF in this process (2). In a recent study, our goal was to determine the level of EGF to predict possible obstruction of the ducts.

The present study indicated that in 25 children, aged from 1 month to 1 year, who underwent unilateral UPJO surgery, the urinary level of EGF was significantly

reduced after surgery, so that the average level of this marker was 40.12±12.55 and this value after surgery was 37.32±11.51 mg/dL prior to surgery. The T-tests showed that the urinary level marker before removing the blockage was much higher than the time when it was removed. It indicates that this marker can be used for early diagnosis of blockage in the urethra in the pediatric group. This finding is consistent with the results of other studies such as those by Madson MG and Mohammad Jafari. In Madson MG study, 41 children were evaluated for EGF levels before and after UPJO blockage, among whom 28 children had obstruction and 13 were in the control group. The researcher had found evidence of a decrease in EGF levels in postoperative children (16). In the other study by Mohammad Jafari et al., On 50 preterm infants, it was also found that obstruction increased EGF levels in infants (17).

A 2012 study by Li Z et al. on 45 infants with before-birth unilateral hydronephrosis found that changes in urinary EGF levels were inversely proportional to hydronephrosis grade, which could suggest a protective role for urinary EGF in worsening hydronephrosis in infants (18). Based on these results, it seems that this evidence is inconsistent and contrary to the findings of our study, in which the level of EGF blockade increased with increasing severity and with its improvement after the operation, a significant decrease was observed.

Grandaliano's study also evaluated the EGF level in 24 children with UPJO and 15 healthy children. It was shown that the expression of the gene and urinary level of cytokine EGF in children with UPJO was lower than in the control group (19), which was in line with the study of Li and non-aligned with our study which showed the EGF levels were significantly reduced after removal of the obstruction.

This clinical study provides a new insight into serum and urinary EGF in children, with age being significantly associated with urinary EGF. Another prospect clarified in this study was a link between children's age and EGF urinary levels. This appears that age is impressive in changes in urinary levels and EGF gene expression.

Therefore, it is not always possible to consider an independent and constant amount of this variable as a criterion for all age groups in children. If we want to use this criterion to measure the rate of obstruction and response to treatment in UPJO patients, there is a vacancy for a reasonable average for each age group.

Therefore, based on the results of this study and data analysis based on Pearson correlation test according to R=0.696 and P. Value=0.001, it seems that these two variables are related to each other and have a significant relationship suggesting that with increasing age in children with urinary tract obstruction, the urinary level of the EGF marker also increases; this finding is consistent with studies such as those by Anna and NJ Evans, both of which have emphasized the effect of age on EGF levels (20, 21).

5- CONCLUSION

The results of this study revealed that urinary tract obstruction can increase the urinary level of EGF, and also with increasing age, the rate of this marker increases in children who have urinary tract obstruction.

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7- CONICT OF INTEREST: None.

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