

Acute kidney injury biomarkers in patients with ureteric stones after retrograde ureterolithotripsy

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Abstract

The conventional diagnosis of acute kidney injury is based on serum creatinine measurement, but this marker is not appropriate for early recognition. During last decade there were a lot of studies evaluating biomarkers of kidney injury after minimally invasive treatment of kidney stones. However, there is no published data about biomarkers level after treatment of ureteric stones. The aim of our study was to evaluate impact of different treatment methods on kidney parenchyma in patients with proximal ureteric stones. From 1st January to 31st October 2017 a total of 75 patients with unilateral large proximal ureteric stones were prospectively included in our study. They were randomized in three groups. In group 1 patient's undergone to retrograde ureterolithotripsy, in group 2 ESWL was performed and in group 3 mini-percutaneous antegrade ureterolithotripsy was treatment method. In all groups some biomarkers level were measured, including KIM-1, NAG and cystatin C, preoperatively, 2 hours, 24 hours and 72 hours after procedure. Also, we evaluate stone-free rate (residual fragments < 4 mm) and complications rate. In all cases KUB and renal ultrasound were performed one month after intervention. The mean stone size was 12 mm (9-13), 11 (8-12) and 13 mm (8-14) ($p < 0.05$). The mean age was 56 years (64, 57 and 62 years respectively). Stone-free rate in group 1, 2 and 3 was 76%, 60% and 88%. In all groups there was no significant difference in baseline biomarker level, except slight elevation of cystatin C in group 2 ($p > 0.05$). In all groups the mean KIM1, cystatin C and NAG level increased two hours after intervention. However, after 1 and 7 days in group 1 the level of all biomarkers was not significantly different compared to baseline level. In group 2 and 3 KIM-1 and NAG level increased after 1 and 7 days after intervention, but in group 2 elevation at 7 days was not significant. Complication rate in group 1, 2 and 3 was 16%, 8% and 28%. There was greater grade 2 complication (according to Clavien-Dindo). Our study showed that retrograde ureterolithotripsy is safe treatment method, which cause minimal kidney parenchyma injury, according to biomarkers level change. Percutaneous antegrade ureterolithotripsy is the most invasive but the most efficient method; however, first day after intervention biomarker elevation is comparable with ESWL, despite on its minimally-invasive nature. These data must be confirmed in large study with strict laboratory and clinical follow-up.

Introduction:

Acute kidney injury is typically diagnosed by measuring serum creatinine but, serum creatinine does not allow for early detection of AKI due to its inability to identify early kidney damage, need for alternative biochemical markers. Recent report has investigated

multiple ways to determine AKI through the evaluation of various biomarkers of renal injury. The current literature suggests that the most effective biomarkers of AKI are kidney injury molecule-1, neutrophil gelatinase-associated lipocalin, N-acetyl- β -D-glucosaminidase and liver-type fatty acid binding protein, which are expressed after ischemic and nephrotoxic AKI. KIM-1 is a type 1 transmembrane glycoprotein containing a novel 6-cysteine immunoglobulin-like domain plus a threonine/serine and proline-rich domain characteristic of mucin-like O-glycosylated proteins. Recent reports suggest that human and animal kidney proximal tubule epithelial cells expressed high levels of KIM-1 after ischemic or toxic injury. NAG is a lysosomal enzyme that it is abundantly expressed in pTECs. Urinary NAG enzyme leakage from the proximal tubular cells into the tubular lumen. It was found that urinary NAG can be identified in patients with established AKI from a control group, including both normal individuals and patients with urinary tract infection. NGAL is AKI biomarker which the endogenous and molecular role in AKI remains unclear, however; it is believed to play a role in iron transportation. The NGAL has been used to identify AKI after pediatric cardiac surgery and after cardiopulmonary bypass. Liver fatty acid binding protein (LFABP) is a protein that is normally expressed in the proximal tubules of the kidney, which has been observed to be elevated in animal models of AKI. In a recent prospective study of children undergoing cardiac surgery, urine LFABP increased at 4 hours post-bypass. Various studies proposed that KIM-1, NGAL, NAG, LFABP are promising biomarkers for diagnosing AKI and evaluating clinical improvement about kidney.

Discussion:

RIRS has been used successfully to access and treat complex renal calculi smaller than 2 cm with high reported stone-free rates. It has fewer overall complications compared to PCNL, with a high absence of renal injury. However, the small working channels of RIRS had limited the usefulness of effective instrumentation that allows concurrent stone fragmentation and removal. RIRS for kidney stone treatment is known as a safe, minimally invasive method and does not directly damage the kidney because it is a retrograde process that is conducted using a flexible device that is able to move freely in the kidney. To what extent the kidney is affected during the process of renal parenchyma in studies based on subjective data is limited. The holmium laser that is used during the procedure is recognized as a mode urinary stones fragmentation. Lasers produce a cavitation vapor bubble at the water-stone interface due to direct absorption of the laser energy in the water. The pulse duration also results in acoustic effect that aids stone fragmentation

and destruction. Creatinine has been used a long time for kidney damage, but in showing early response has been inadequate. We thought kidney injury molecules could help us in this regard. During the operation the increase in pressure of the kidney depends on irrigation or holmium laser energy can have a damaging effect on the kidney. Recently, several biomarkers have been explored for the early diagnosis of AKI, as KIM-1, NGAL, NAG and LFABP. It has been reported that KIM-1 levels increase in multiple types of injury, including tubular, interstitial, and glomerular and were associated with the severity of kidney injury. It was found a positive correlation between the degree of scarring and KIM-1 levels in patients diagnosed with vesicoureteral reflux. In this study, it was observed significantly higher levels of the KIM-1/Cr 2 h after the surgery but 24 h after the surgery KIM-1/Cr levels returned to pre-operative levels. The results of the control group values and pre-operative values of patients with kidney stones were similar, not significantly different. It was found positive correlation between Kim/Cr and amount of irrigation 2 h after the surgery. NGAL protein is easily detected in the blood and urine soon after AKI in animal models. NGAL has also been evaluated as a biomarker of AKI in kidney transplantation. Several investigators have examined the role of NGAL as a predictive biomarker of nephrotoxicity following contrast administration, with promising results. In this study, patients NGAL/Cr levels were increased significantly 2 h after the surgery and returned initial level 24 h after surgery. It was

found positive correlation between NGAL/Cr with operation time and amount of irrigation. NAG is a lysosomal enzyme is located in proximal tubules. Therefore, increased activity of this enzyme in the urine may suggest injury to tubular cells and could serve as a specific urinary marker for tubular cell function.

Conclusion:

Among ureteric stone patients AKI is seen in 32% of patients. Factors associated with AKI in our study were weight, age, presence of bilateral stones, lower ureteric stones and other co-morbidities. Majority of patients developing AKI, recovered either partially or completely after surgical intervention for decompression. Ureteroscopy seems to be associated with more complications than currently reported. The present overview may help urologists to prevent, recognize and solve complications of ureteroscopy. It may also stimulate colleagues to perform prospective studies using standardized systems for classifying complications. These are warranted to compare results among different studies, to conduct meta-analyses, to inform health care workers and to counsel patients correctly about possible risks of ureteroscopy.