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Interleukin 18 and neutrophil-gelatinase associated lipocalin in assessment of the risk of contrast-induced nephropathy in children

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Abstract

The aim of the study was to determine the usefulness of interleukin 18 (IL-18) and neutrophil-gelatinase associated lipocalin (NGAL) in the risk assessment of contrast nephropathy in children. The study included patients among whom radiological examinations were performed using intravascular contrast agent. The material consisted of 33 children (19 girls, 14 boys) aged 6.37 ±5.41 years. 20/33 (61%) of patients had hydronephrosis, 9/33 (27%) had other urinary tract defects referred as "no hydronephrosis" and 4/33 (12%) had urolithiasis. NGAL determination was performed with the use of Human Lipocalin-2 / NGAL Immunoassay. To determine the concentration of human IL-18 an ELISA Kit (MBL International Corporation) was used. There were no statistically significant differences in the concentrations of NGAL and IL-18 in serum determined before the procedure, and after the administration of contrast agent. Concentrations of NGAL and IL-18 were determined in urine three times: before the procedure, 2-4 hours after administration of the contrast agent, and 48 hours after the performed procedure. The analysis showed that the concentration of IL-18 and NGAL in urine did not differ significantly in three consecutive preformed measurements. The study has also found no statistically significant differences between serum creatinine before and 48 hours after injection of contrast. Implementation of new biomarkers such as NGAL and IL-18 expands the possibilities of renal function assessment in children undergoing radiological procedures using contrast agents. In examined children with normal or slightly impaired renal function they did not demonstrate the risk of contrast nephropathy.

Key words: *contrast-induced nephropathy, acute kidney injury, NGAL, IL-18, renal function assessment.*

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Introduction

It has been 60 years since the first description of acute kidney injury after intravenous administration of a radiocontrast agent [1]. Access to diagnostic tests including numerous radiological examinations using contrast media has been systematically growing in recent years. Iodine-based contrast media have become an important and common tool used both for diagnostic imaging and surgical procedures. Despite increased knowledge about the adverse effects of contrast agents and the introduction of the new so-called safe contrast agents, the incidence of contrast-induced nephropathy is not so greatly reduced. For this reason, more and more studies pay attention to risks associated with the use of intravenous contrast agents.

In the literature, there are many different definitions of kidney failure after administration of contrast agents. In 2005 Acute Kidney Injury Network (AKIN) proposed new diagnostic criteria for acute kidney injury (AKI) that occurred within 48 hours after exposure to nephrotoxic agent, including contrast agent. Two distinct diagnostic criteria have been proposed: the first based on the absolute increase of serum creatinine of at least 0.3 mg/dl (> 25 μmol/l) within 48 hours or increase in serum creatinine of at least 1.5 times from baseline, which is known or presumed to have occurred within the prior 7 days. The second criterion for diagnosis of AKI takes into account a reduction of urinary output below 0.5 ml/kg/h lasting at least 6 hours. A new acronym for contrast nephropathy – CI-AKI (contrast-media induced acute kidney injury) – has

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also been introduced. It is currently one of the most commonly used definition of contrast-induced nephropathy, used by both clinicians and scientists [2].

There are particular difficulties in recognition of contrast nephropathy among children. Criteria for diagnosis of acute renal insufficiency among adults – absolute or relative increase in creatinine level – are not sufficiently sensitive indicators of acute kidney injury in children. Currently, the classification of AKI in children is based on a modified pediatric scale (pRIFLE – risk, injury, failure, loss of function, end stage kidney disease), which divides the patients in terms of severity of the damage and allows to estimate the need for therapeutic intervention and prognosis [3, 4].

Unfortunately serum creatinine is a late marker of acute kidney injury. Creatinine increases in serum 48-72 hours after exposure to nephrotoxic agent, while the renal tubular damage occurs much earlier – at the time of increase in serum creatinine, worsening of renal function reaches 50% of the optimum [5]. Therefore, research has focused on identifying earlier biomarkers of AKI.

Most recent markers of renal function deterioration used in cases of contrast nephropathy are interleukin 18 (IL-18) and neutrophil-gelatinase associated lipocalin (NGAL). Mentioned markers are being considered useful in the rapid detection of AKI in the diagnostic process, as well as in predicting its occurrence or the conversion of acute kidney disorder into chronic disease of this organ.

Neutrophil gelatinase-associated lipocalin is a 25 kDa protein composed of 179 amino acids, covalently attached to human neutrophil gelatinase, secreted by activated neutrophils. Lipocalins are proteins binding small lipophilic molecules and transporting them between the cells of the body. Among these molecules we can distinguish siderophores, which role is to transport an iron. NGAL is involved in processes of cell-mediated immunity, bacteriostatic effects, cell proliferation, differentiation and apoptosis processes. Bacteriostatic properties result from the inhibition of iron uptake by the bacteria which leads to inhibition of their proliferation [6]. NGAL is present in low levels in many human tissues. In the kidney, it is mainly expressed in the loop of Henle and distal convoluted tubules. NGAL is filtered by the renal glomeruli and reversibly reabsorbed in the proximal convoluted tubules.

The first study evaluating NGAL as a predictor of evolving AKI was conducted on children undergoing cardiac surgery. Serum level of NGAL raised 20-fold and in urine 100-fold up to 48 h before AKI was detected by creatinine [7]. NGAL is a sensitive marker of kidney damage that correlates with serum creatinine, but precede its growth. Probably NGAL expression after activation of damaging agent is linked to its effect on the proliferation of new cells [8]. An increase of NGAL concentration has been observed in many studies concerning acute kidney injury: in the states of hypoxia that occurs during cardiac surgery with extracorporeal circulation, after radiographic contrast and after exposure of the kidney on toxic effects of cytostatic drugs [9]. Reference range for NGAL in a healthy pediatric population is between 2.8-17 mg/dl (median values 6.6 mg/dl) [10].

Interleukin 18 is also a sensitive and specific marker that helps to assess the occurrence of acute kidney injury, it is measured in urine and serum as well. It is a pro-inflammatory cytokine with a molecular weight of 18 kDa activated via an inactive form of caspase-1. This cytokine is secreted by many cells in the human body, such as osteoblasts, keratinocytes, small intestine cells, dendritic cells, and epithelial cells of renal tubules [11].

The increase in IL-18 occurs during acute kidney injury caused by hypoxia, ischemia and exposure of proximal tubular cells to nephrotoxic agents [12]. Reference range for IL-18 in healthy pediatric population is 13.6-32.9 (median values 21.6 pg/ml) [10].

Aim of the study

The aim of this study was to determine the usefulness of IL-18 and NGAL in the risk assessment of contrast nephropathy in children.

Material and methods

Patient population

The study included patients treated in the Pediatric, Nephrology and Allergology Clinic of the Military Institute of Medicine in Warsaw, who underwent a radiological examination with intravenous contrast agent from September 1, 2011 to June 30, 2013. Exclusion criteria were acute or chronic infectious diseases. Patients care givers provided written informed consent for the child to participate in descriptive study. The study protocol and consent was approved by the Ethics Committee of Military Institute of Medicine in Warsaw.

Clinical data collection

The following clinical variables were evaluated: patient age, sex, height, weight, and admission diagnoses.

Laboratory data collection

Both blood and urine were collected as defined in the study protocol. Before radiological procedures with contrast agent, following laboratory tests were performed: serum creatinine and cystatin C, serum NGAL and IL-18; urine NGAL and IL-18; eGFR was calculated basing on obtained parameters. 2-4 hours after contrast agent administration urine NGAL and IL-18 concentrations were measured. Next, 48 hours after the use of intravenous contrast medium, analogous parameters as determined before radiological examination were assessed.

Preparation of material

Blood for determination of NGAL and IL-18 were collected in amount of 4 ml in a test-tube, followed by centrifugation for 10 minutes at the speed of 3000. After centrifugation, 1 ml of serum was collected in a special test-tube intended for deep-freezing and frozen at –70°C. Urine samples for determination of NGAL and IL-18 were taken in a test-tube with a volume of 4 ml, centrifuged for 10 minutes at 3000 rpm and then poured into the deep-freezing test-tubes and frozen at –70°C. On the day of tests collected material was defrosted at room temperature.

Methods

Serum concentrations of cystatin C and creatinine were determined by nephelometry and the kinetic Jaffe method respectively, using automated equipment. Established reference values in children for creatinine [13] and cystatin C [14] were used in this study. Estimated glomerular filtration rate (eGFR) was calculated using the Schwartz formula [15] and the Gao formula that is more accurate in children with normal renal function [16]. The two markers (NGAL, IL-18) were determined with ELISA method (Enzyme-linked immunosorbent assay) used for qualitative and quantitative determination of antigens contained in samples of biological materials. The study used an indirect test of a so-called double bond 'Sandwich' ELISA which uses two monoclonal antibodies recognizing different epitopes present on the same antigen molecule, in this case one of the markers determined. NGAL determination was performed using Human Lipocalin-2 / NGAL Immunoassay, Catalogue Number DLCN20 QUANTIKINE® R&D Systems. To determine the concentration of IL-18 Human, IL-18 ELISA Kit MBL International Corporation was used.

In 26/33 patient urography was performed, in 7/33 patient uroCT was made. Each patient was given a nonionic, low osmolality contrast agent (iodine concentration of 300 mg/ml) in dose 1-2 ml/kg of body weight. Contrast agent was intravenously administered. Johexol (trade name Omnipaque 300 mg I/ml) in all patients was given.

CIN was defined as more than 25% reduction in creatinine clearance according to pRIFLE criteria [3].

Statistical methods

Statistical analysis was performed by a professional statistics researcher. Continuous variables were tested for normal distribution with Kolmogorov-Smirnov statistics and were expressed as mean ± SD or as medians with interquartile ranges. Parametric (Student's *t*-test, ANOVA test) or non-parametric (Wilcoxon test, Friedman test) statistical analyses were used to compare continuous variables between groups. Categorical data were presented as absolute values and percentage. The χ^2 test with its modifications were used for the comparison of categorical variables. $P < 0.05$ was consider as statistically significant. The Statistic version 10.1 (StatSoft Co.) was used for all calculations.

Results

The study material consisted of 33 children aged from 1.5 months to 17 years (19 girls, 14 boys, age 6.37 ±5.41 years). 20/33 (61%) of patients had a diagnosis of hydronephrosis, in 9/33 (27%) patients other urinary tract defects referred to generally as "no hydronephrosis" were diagnosed (renal dysplasia, simple renal cyst, duplication of the ureter, posterior urethral valves, nephrocalcinosis). 4/33 (12%) patients were qualified to perform imaging studies because of urolithiasis. The distribution of the study group in terms of diagnosis is presented in Fig. 1.

Serum creatinine and cystatin C concentration before procedure in entire group were within normal limit for age. The median serum creatinine concentration was 0.3 mg/dl (0.2-0.5 mg/dl). In 10/33 patients serum creatinine slightly increase after procedure from 0.1 mg/dl to 0.2 mg/dl. The study found no statistically significant differences between serum creatinine before and 48 hours after contrast administration ($p > 0.05$, Table 1).

The study group consisted of pediatric patients with normal or mildly impaired renal function. Glomerular filtration rates (GFRs) estimated by Schwartz formula were over 90 ml/min/1.73 m^2 among 29/33 patient, in 4/33 patient eGFR were between 60-90 ml/min/1.73 m^2. Glomerular filtration rates (GFRs) estimated by Gao formula was evaluated in 31 patient: in 28/31 patient were over 90 ml/min/1.73 m^2 and in 3/31 patient were between 60-90 ml/min/1.73 m^2. eGFR estimation with Schwartz and Gao formula did not significantly differ before and after procedure (Table 1) so we did not categorize patients with decrease of eGFR as AKI.

Before procedure average NGAL serum value was 47806 pg/ml, the mean serum value of IL-18 was 253.13 pg/ml. There were no statistically significant differences

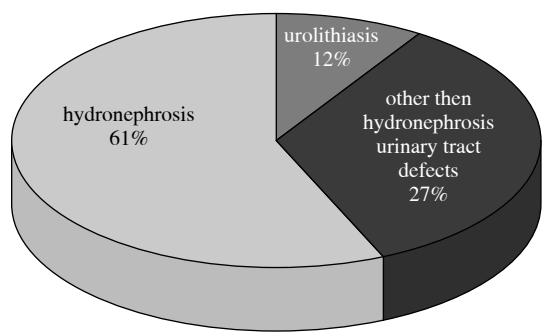

Fig. 1. Distribution of the group in terms of medical diagnosis

Table 1. Comparison of serum creatinine and eGFR evaluated according to Schwartz and Gao formula before and after contrast administration in the study group

	Before administration of contrast agent	48 h after administration of contrast agent	*p*
Cr_s (mg/dl) median and IQR	0.3 (0.2-0.5)	0.4 (0.3-0.4)	ns. (0.2)
eGFR (ml/min/1.73 m²) ac. to Schwartz formula medium ± SD	139.44 ±45.40	125.03 ±26.95	ns. (0.08)
eGFR (ml/min/1.73 m²) ac. to Gao formula, median and IQR	117.2 (108.7-121.5)	113.9 (107-119)	ns. (0.98)

Cr_s – creatinine concentration in serum; IQR – interquartile range

Table 2. Comparison of NGAL and IL-18 in serum before and after the administration of contrast in the study group

	Before administration of contrast agent	48 h after administration of contrast agent	*p*
NGALs (pg/ml) (average ± SD)	47806 ±25999	51860 ±28677	ns. (0.54)
IL18s (pg/ml) (average ± SD)	253.13 ±242.73	322.95 ±304.83	ns. (0.13)

NGALs – NGAL concentration in serum; IL18s – the concentration of interleukin 18 in serum; ns – not significant; SD – standard deviation; p – level of significance

Table 3. Analysis of NGAL and IL-18 in the urine before the administration of contrast agent, 2-4 hours after contrast administration and 48 hours after injection of contrast agent in the study group

	Before administration of contrast agent	2-4 hours after administration of contrast agent	48 hours after administration of contrast agent	*p*
$NGAL_u$ (pg/ml) median and IQR	9150.90 (2002.50-15969.00)	4996.00 (2139.30-22613.00)	4945.20 (1738.00-13043.10)	ns. (0.43)
$IL\text{-}18_u$ (pg/ml) median and IQR	10.80 (1.50-24.75)	20.10 (7.40-38.40)	19.55 (5.95-29.40)	ns. (0.17)

$NGAL_u$ – NGAL concentration in urine; $IL\text{-}18_u$ – the concentration of interleukin 18 in urine; ns – not significant; p – level of significance; IQR – interquartile range

in the concentrations of NGAL and IL-18 in serum determined before the procedure, and after the administration of contrast agent (Table 2).

The analysis has shown that the concentration of IL-18 and NGAL in urine did not differ significantly in three consecutive preformed measurements (Table 3).

Discussion

Research results showed that contrast nephropathy is the third most common cause of acute kidney injury (after renal damage in the course of shock and dehydration, and surgery), and the first toxic cause of AKI in hospitalized patients. Moreover, contrast nephropathy accounts for about 10% of the cases of acute kidney injury acquired in a hospital [5]. Impact of various risk factors of CI-AKI has been proven. In healthy individuals, Cl – AKI occurs in approximately 1-2% of patients that underwent imaging studies with contrast. It may seem that the risk of contrast nephropathy is low, however, due to the development of diagnostic imaging, the incidence of acute renal insufficiency in developing countries may reach several million cases per year [17]. In the presence of other risk factors, mainly existing kidney damage and diabetes, contrast nephropathy risk increases by more than 50% [18, 19]. CI-AKI occurs also in children, however, the real incidence of this complication in this age group is not known.

Most cases of CIN are observed after intravascular administration of iodinated contrast agents, although it should be noted that the synthetic non-iodinated contrast agents (such as gadolinium contrast agents) may occasionally cause acute renal failure as well. The course of contrast nephropathy is usually mild, and serum creatinine returns to the baseline within 7-10 days. Oliguria is not usually observed; renal injury requiring dialysis, occurs very rarely, although this complication is also present [20]. In present study each patient was given a nonionic, low osmolality contrast agent (iodine concentration of 300 mg/ml) in dose 1-2 ml/kg of body weight. Contrast agent was administered intravenously. There is consensus that the risk of CIN is significantly lower following intravenous than intra-arterial administration [20]. An important question is whether there are significant differences in renal safety between contrast from the same group of osmolality and between the low-osmolar contrast media and iso-osmolar contrast media. Ajami *et al*. determined the incidence of CIN for two nonionic low-osmolar contrast media: iopromide and iohexol, among 80 patients younger

than 18 years who underwent cardiac angiography. Authors revealed that incidence of CIN depended on dosage but not on type of consumed nonionic contrast medium [21]. Zo'o *et al.* compared the incidence of CIN in children undergoing contrast -enhanced multidetector computer tomography with intravenous injection of low-osmolar (iobitridol) or an iso-osmolar (iodixanol) iodinated contrast medium. One hundred forty-six children with normal renal function were included in the trial. Authors revealed comparable satisfactory safety profiles for both contrast media with no significant difference in the incidence of CIN in children with normal renal function [22].

There have been many studies on the changes of concentration of enzymes excreted in urine and concentration of markers of function of renal tubules or glomeruli in serum after administration of contrast agents. In the 90s of twentieth century, much attention was paid to the influence of contrast agents on substances such as: urinary N-acetyl-β-D-glucosaminidase, γ-glutamyl transferase [23], alkaline phosphatase and excreted in the urine protein-β2-microglobulin or albuminuria [24, 25]. Nevertheless, none of these markers were found useful in assessment of risk of developing CI-AKI. The detectable in urine and serum IL-18 and NGAL are new potential markers of acute kidney injury that could be used in clinical practice.

Neutrophil gelatinase-associated lipocalin is a protein, belonging to the family of lipocalin present in the granules of neutrophils [26]. In healthy individuals it is found in serum at low levels, and because of the low molecular weight and resistance to degradation it is secreted by cells of the ascending arm of the loop of Henle and collecting tubules and excreted in the urine.

As a result of toxic or ischemic kidney injury, NGAL concentration repeatedly and rapidly grows, what has been demonstrated in animal models [27]. This gave rise to numerous researches devoted to the use of NGAL in human populations including children, as a marker of the early phase of acute kidney injury [18].

In children such studies have been carried out for example after cardiac surgery. In a prospective study Mishra *et al.* showed that NGAL serum and urine concentration could be an early indicator of acute kidney injury [7]. In the group of 71 children who underwent cardiac surgery, AKI (defined as an increase in serum creatinine of at least 50% of baseline) occurred among 28% of patients, nevertheless the diagnosis of AKI based on serum creatinine increase was possible within 1-3 days after operation. Increased concentration of NGAL was observed in patients with AKI as early as 2-6 hours after surgery, and the area under the curve (ROC-AUC) was 0.998 for the urine NGAL concentration and 0.91 for the serum NGAL concentration.

In the study of Bennett *et al*., in 51% of 196 children who developed AKI after cardiac surgery, 2 hours after operation a 15-fold increase in urinary NGAL and 25-fold increase of NGAL after 4-6 hours has been observed (AUC 0.95; sensitivity 82%, specificity 90%) [39]. The referenced publications also showed the relationship between the concentration of NGAL in urine or plasma and the severity and course of AKI, duration of hospitalization, the need of dialysis and increased mortality [7, 28, 29]. The usefulness of urine NGAL concentration as a marker of AKI has also been shown in the study of Zappitelli *et al*., carried out on a group of 140 children treated in the intensive care unit with renal impairment of unknown time of kidney damage [30].

Toxic renal injury after administration of contrast agent is another example, where an increase in the synthesis and excretion of NGAL was observed. Bachórzewska-Gajewska *et al.* observed an increase in serum NGAL concentrations 2-4 hours, and in urine 4-8 hours after coronary surgery. A relationship between NGAL and other parameters of renal function as cystatin C, GFR and serum creatinine was also shown. On this basis, the authors came to conclusion that NGAL may be an useful marker for the early diagnosis of acute kidney injury in patients after coronary angiography [31].

Haase *et al*., conducted a meta-analysis of 19 studies from eight countries, including 2538 patients, 487 (19.2%) of them were diagnosed with AKI and have NGAL concentration evaluated as an early marker for acute renal dysfunction. One of the evaluated risk factors for AKI was the administration of intravascular contrast. Analysis has indicated a prognostic and diagnostic value of NGAL in the evaluation of acute kidney injury induced by contrast agent [32].

Neutrophil gelatinase-associated lipocalin as a potential marker of CI-AKI, was also subjected to analysis in children populations. Hirsh *et al*., in a prospective study evaluated NGAL concentration in urine and serum of 91 children aged between 0-18 years with congenital heart disease undergoing elective cardiac catheterization and angiography with contrast administered intravenously. Acute renal injury induced by contrast (defined by the authors as at least 50% increase in serum creatinine above baseline) were diagnosed in 11 patients within 6-24 hours after administration of contrast, while the increase in concentration of NGAL in urine was observed after 2 hours of surgery. The authors demonstrated that if established cut-off value equals 100 μg/l, the area under the ROC curve-AUC two hours after the administration of contrast medium are respectively: AUC = 0.92 in urine and AUC = 0.91 in plasma – that would indicate an excellent diagnostic output for NGAL. In the cited study, authors demonstrated, on the basis of multivariate analysis, that the urine and plasma NGAL concentration 2 hours after administration of contrast agent is an independent predictor of CI-AKI [33].

The usefulness of NGAL in the evaluation of renal function has unfortunately some limitations. Age, sex, inflammation, and diseases with accompanied liver dysfunc-

tion affect NGAL concentration [17]. Under physiological conditions NGAL is also present in low levels in other organs such as lungs, trachea, stomach, intestine, which may limit its specificity as a marker for kidney damage.

A promising marker for early detection of impaired renal function is also IL-18. It is a mediator of inflammation and tissue damage caused by ischemia in many organs. Studies of ischemic acute renal injury in animal models have shown that activated by caspase-1, IL-18 is secreted by the damaged cells of the proximal tubule and consequently an increase in its concentration in urine is observed [16].

The cross-sectional study of Parikh *et al.* showed that in patients with recognized AKI, IL-18 concentration in urine were significantly increased not only in comparison with a population of healthy individuals, but also compared to patients with urinary tract infections, chronic kidney disease, prerenal acute kidney injury or patients with nephritic syndrome [34].

The usefulness of IL-18 in the urine, as a predictor of AKI, has also been demonstrated in children population. Washburn *et al*., conducted a study of 137 children hospitalized in the intensive care unit requiring mechanical ventilation. The maximum concentration of IL-18 correlated with the severity of AKI evaluated using pRIFLE criteria and was an independent predictor of mortality in the study group. In the subgroup of patients diagnosed with AKI but without sepsis, the increase of urine IL-18 concentration preceded, even ahead of two days, an increase in serum creatinine [35]. Parikh *et al.* evaluated the concentration of IL-18 in pediatric patients undergoing cardiac surgery. Increased concentration of IL-18 has been observed as soon as 6 hours after surgery and maximum concentration (exceeding 25-fold above baseline) occurred after 12 hours and it has continued for 48 hours after surgery. In the cited study, IL-18 has been considered as a good predictor of AKI (AUC 0.75) [36].

The study of He *et al.* verified that urinary IL-18 may be an early diagnostic marker for contrast induced AKI. A total of 180 patients undergoing coronary interventional procedure were selected. CIN occurred in 16 of 180 (8.9%) patients. The urinary IL-18 levels in CIN group increased significantly at 6 and 12 h after the procedure compared with those in the non-CIN group ($p < 0.01$) and began to decline 24 h after the procedure. Study have also shown that urinary IL-18 is at its peak 12-24 h after administration of contrast agent. Authors concluded that urinary IL-18 level increases earlier than serum creatinine and may be a promising indicator for early prediction of CIN [37]. Opposite results received Bulent Gul *et al*. who compared 15 cases of CIN with 36 controls patients admitted for elective percutaneous coronary intervention. No statistically differences in urinary IL-18 were detected between CIN cases and controls or between the patients samples obtained before PCI and after the invasive procedure in both study groups. Authors suggested that urinary IL-18 is nor useful as a CIN biomarker or that any effect is too small for it to be detected using this cohort size [38].

The influence of certain clinical situations on IL-18 concentration in urine, limiting its clinical usefulness in the diagnosis of AKI, was proved for immune disorders, nephrotoxic drugs such as cisplatin or endotoxemia [9]. The current opinion of CIN Consensus Working Panel indicates that potential AKI markers currently have limited clinical utility, but they are still an important research tool and may in future lead to redefinition of CI-AKI [20].

In literature we did not find results concerning possibility of CI-AKI in children with normal renal function examined with the use of radiocontrast media.

Accordingly in the present study changes in concentration of NGAL and IL-18 in serum and urine were analyzed in children with urinary tract abnormalities but with normal or mildly impaired renal function. Concentrations of NGAL and IL-18 were measured three times in the urine (pre-contrast, after 2 hours and 48 hours after administration of contrast agent) and twice in serum (before dosing and 48 hours after administration of contrast agent). In the whole group of 33 patients, there was no statistically significant difference in the concentration of NGAL and IL-18 both within serum and urine before and after administration of contrast medium, even though there are considered "more sensitive" indicators of acute kidney injury.

Further analysis with the use of much bigger group of pediatric patients are needed to show if contrast agents administration is safe in children with normal or slightly impaired renal function or if NGAL and IL-18 are proper markers to show CI-AKI incidence in such cases.

Conclusions

Implementation of new biomarkers such as NGAL and IL-18 potentially expands the possibilities of renal function assessment among children undergoing radiological procedures using contrast agents.

The concentration of IL-18 and NGAL in serum and urine as well as serum creatinine in the blood of examined children who underwent examination with the use of intravascular radiographic contrast agent did not show the risk of CI-AKI.

In children with normal or mildly impaired renal function the use of low-osmolality contrast media appears to be safe but should not exempt physicians from careful qualification of patients for imaging with contrast agent and monitoring of renal function after the procedure.

The authors declare no conflict of interest.

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