CORRELATION OF ROUTINE URINE CULTURE, STONE CULTURE AND POST-OPERATIVE SIRS

[1]Taufik Indrawan, [1]Sunaryo Hardjowijoto, [1]Doddy M. Soebadi, [2]Juniastuti, [3]Budiono.

[1]Department of Urology, Faculty of Medicine/Airlangga University, Soetomo Hospital, Surabaya.
[2]Department of Microbiology, Faculty of Medicine/Airlangga University, Soetomo Hospital, Surabaya.
[3]Biostatistic of Public Health Department, Faculty of Medicine/Airlangga University, Surabaya.

ABSTRACT

Objective: *This study evaluated the correlation between preoperative urine culture and intraoperative stone culture and the impact of stone culture findings on post-operative systemic inflammatory response syndrome.* ***Material & Method:*** *Patients with kidney stones who underwent percutaneous nephrolithotomy (PCNL) from February to May 2012 were prospectively analyzed. A pre-operative urine culture was obtained in the morning before the operation, fragmented stone collected were cultured in Department of Microbiology. Patients were monitored closely in the postoperative period for signs of systemic inflammatory response syndrome (SIRS).* ***Results:*** *A total of 33 patients underwent PCNL and examined for urine cultures, stone culture and postoperative SIRS, 15 (45.45%) patients with positive urine culture, 18 patients (54.54%) with positive stone culture but only 1 patient (3.03%) had same pathogen (p = 0.629). Ten patients (55.6%) with positive stone cultures had evidence of systemic inflammatory respose syndrome postoperatively. The calculated stone culture value for sensitivity, specificity, positive predictive value and negative predictive value were 100%, 65.2%, 55.6%, and 100%. Preoperative hydronephrosis (p = 0.003) and operative time (p = 0.001) are identified as the key risk factors for SIRS after PCNL.* ***Conclusion:*** *Positive stone culture are better predictors for SIRS after PCNL. Stone culture examination is an essential in directing the proper antibiotic therapy in patients with SIRS after PCNL.*

Keywords: *Percutaneous nephrolithotomy (PCNL), urine culture, stone culture, systemic inflammatory response syndrome after PCNL.*

ABSTRAK

Tujuan : *Penelitian ini bertujuan untuk mengetahui korelasi antara kultur urin porsi tengah dan kultur pecahan (fragmen) batu dengan kejadian systemic inflammatory response syndrome (SIRS) pasca operasi percutaneous nephrolithotomy (PCNL).* ***Bahan & Cara:*** *Penelitian ini adalah penelitian observasional analitik prospektif. Sebanyak 33 pasien dengan batu ginjal dilakukan PCNL, kultur urine diperiksa pagi hari sebelum operasi, kultur batu diperiksa setelah operasi dilakukan, keduanya dikirim ke bagian Mikrobiologi. Tanda SIRS dievaluasi pada seluruh pasien pasca PCNL.* ***Hasil:*** *PCNL dilakukan pada 33 pasien, didapat pertumbuhan kuman pada 15 pasien (45.45%). Pada 18 pasien (54.54%) dengan pertumbuhan kuman pada kultur batu hanya 1 pasien (3.03%) yang memiliki jenis bakteri patogen yang sama dengan kultur urine (p = 0.629). Pasien dengan kultur batu positif 55.6% mengalami SIRS. Hasil uji regresi logistik didapatkan nilai signifikansi p = 0.001 (p < 0.005). Kultur batu memiliki sensitivitas sebesar 100%, spesifitas sebesar 65.2%, dan memiliki nilai prediksi positif 55.6% dan nilai prediksi negatif 100%. Hidronefrosis preoperatif (p = 0.003) dan lama waktu operasi (p = 0.001) juga berhubungan signifikan dengan kejadian SIRS pasca PCNL.* ***Simpulan:*** *Kultur fragmen batu yang positif dapat dijadikan sebagai prediktor yang lebih baik untuk kejadian SIRS pasca PCNL dibanding kultur urine.*

Kata Kunci: *Percutaneous nephrolithotomy (PCNL), kultur urine, kultur batu, systemic inflammatory response syndrome paska PCNL.*

Correspondence: Taufik Indrawan, c/o: Department of Urology, Faculty of Medicine/Airlangga University, Soetomo Hospital Surabaya. Jl. Mayjen. Prof. Dr. Moestopo 6-8 Surabaya 60286. Office phone: 031-5501318. Mobile phone: 08123263061. Email: tfkurologi@gmail.com.

INTRODUCTION

The development of minimally invasive surgical techniques grows rapidly as it provides several advantages compared to classical surgical techniques. Percutaneous nephrolithotomy (PCNL), which is minimally invasive surgical technique, plays an important role in management of kidney stones with a stone-free rate of over 90% in optimal circumstances.[1,2] PCNL procedure in Dr. Soetomo Hospital is increasing from year to year. In 2009 from 295 patients with urinary tract stones treated, as many as 45.4% underwent PCNL procedure.[3]

The term sepsis is usually related to clinical response to infection. However, it may also occur in the absence of infection, so that it is more appropriately called as the Systemic Inflammatory Response Syndrome (SIRS). The clinical signs and symptoms of SIRS consists of pulse > 90 beats/min, body temperature > 38°C or < 36°C, respiratory rate > 20 times/min or hyper ventilation with PaCO2 levels < 32 mmHg, blood leukocyte count > 12.000/mm^3 or < 4.000/mm^3 or peripheral blood smear results reveal young neutrophils > 10% and at least 2 symptoms or signs are positive.[4] On the other hand, urosepsis and urinary tract infection (UTI) may occur at any time in patients undergoing operative procedure.[2] O'Keefe et al. have retrospectively reviewed 700 patients for the prevalence of post-operative urosepsis in patients with obstructive uropathy because of stones that have been operated with minimally invasive surgery 1.28% of which indicated SIRS signs 6 hours after surgery.[5]

Mariappan examined 54 patients who underwent PCNL concluded that positive stone culture and pelvic urine culture is a better predictor for urosepsis compared to urine culture ($p = 0.0009$).[6] The incidence of SIRS can be triggered by the release of endotoxins derived from micro-organisms present in urinary tract stones that can cause endotoxemia and bacteremia.[6] This study was performed because in Indonesia studies on the correlation between midstream urine culture and stones fractions (fragment) culture with the incidence of SIRS after PCNL operations had never been undertaken.

OBJECTIVE

This study evaluated the correlation between pre-operative urine culture and intra-operative stone culture and the impact of stone culture findings on post-operative systemic inflammatory response syndrome.

MATERIALS & METHODS

The study was conducted on 33 patients who came to Dr. Soetomo Hospital with kidney stones after PCNL at Dr. Soetomo Hospital between February to May 2012. The inclusion criteria were unilateral kidney stones with PCNL indication. Exclusion criteria included bilateral kidney stones, diseases of other organs that may cause of sepsis (eg. DM), and history of SIRS or the use of antibiotics 2 weeks prior to surgery.

Midstream urine culture was taken the morning before the surgery and then stone fragments culture was taken during PCNL. Both were sent to Microbiology Department for culture and sensitivity examination. The stone fragment was initially washed with 10 ml of saline fluid and then centrifuged for 10 minutes at 100 rpm. This procedure was repeated 3 times. Then the stone was crushed with a mortar until smooth and 10 ml of saline was added. Subsequently, stone fragments were incubated for 24 hours in 2 different media, the blood agar (BAP) and MacConkey's Agar (MAC).[7]

Patients with previous sterile urine culture were given 1 gr Cefotaxime prophylaxis, whereas patients with positive previous urine culture were given appropriate antimicrobials: 1.5 gr Ampicillin-Sulbactam for 5 patients, 1 gr Ceftriaxone in 4 patients, 500 mg Ciprofloxacin and 1 gr Meropenem respectively for 3 patients.

The first act was the placement of ureteral catheter on the site where the procedure would be taken. The patient was in general anesthesia. At this stage the patient was placed in lithotomy position, subjected to retrograde pyelography (RPG) and ureteral catheter was inserted. Foley catheter was fitted and fixed with ureteral catheter. Subsequently, the patient position was changed to prone on an X-ray-penetrabe operating table. The operating field was disinfected, and narrowed with sterile cloth. Then, percutaneous access was attempted with the help of the fluoroscopic contrast, followed by dilation up to 30 Fr., amplatz was inserted and stone was retrieved and broken with ultrasonic and pneumatic lithotripsy (Swiss Lithoclast, EMS). At procedure finish, 20 Fr. nefrostomy tube catheter was installed.

Patient vital signs were observed during the first 2 x 24 hours post PCNL. SIRS was determined if two or more of the following conditions were met: pulse > 90 beats/min, body temperature > 38°C or < 36°C, respiratory rate > 20 times/min or hyperventilation with high levels of PaCO2 < 32 mmHg, blood leukocyte count > 12.000/mm^3 or < 4.000/mm^3 or peripheral blood smear revealed young neutrophils > 10%.

Data were analyzed using logistic regression because the independent variables had nominal and numerical scales, while dependent variable was nominal dichotomous. We examined significant correlation between stone culture and post-PCNL SIRS incidence.

RESULTS

From February to May 2012, there were 33 patients who underwent percutaneous nephrolithotomy (PCNL) at Dr. Soetomo Hospital, who met inclusion criteria. Sample distribution was divided by gender, age, stone size, number and position of stones, signs of obstruction, operating time and results of midstream urine culture with stone culture (Table 1).

Table 1. Sample distribution by gender, age, stone size, stone number and position, sign of obstruction.

Variables		Values
Age (year)	Age range	37 - 68
	Mean age	50.18 ± 10.44
Sex	Male	21 (63.6)
	Female	12 (36.4)
Number of stone	Single	24 (72.73)
	Multiple	9 (27.27)
Stone location	Calyx Inferior	6 (18.18)
	Pyelum	19 (57.58)
	Calyx inf + pyelum	9 (24.24)
Obstruction signs	Hydronephrosis (-)	1 (3.03)
	Hydronephrosis grade I-II	20 (60.6)
	Hydronephrosis grade III-IV	12 (36.37)
Length of operation (minutes)	Mean	81.96 ± 10.61

Table 2. Pre-PCNL middle portion urine culture and post-PCNL stone culture.

Bacteria growth	Urine culture (n = 33)		Stone culture (n = 33)	
	Frequency	%	Frequency	%
Sterile	18	54.5	15	40.5
Escherichia coli	4	12.1	4	10.8
Escherichia coli ESBL+	1	3.0	0	0.0
Klebsiella pnemonie	2	6.1	2	5.4
Staphylococcus hemolyticus	1	3.0	0	0
Streptococcus non hemolyticus	0	0.0	1	2.7
Staphylococcus coagulase (-)	2	6.1	7	18.9
Proteus mirabilis	1	3.0	0	0.0
Pantoea agglomerans	1	3.0	0	0.0
Enterobacter cloacae	1	3.0	0	0.0
Acinetobacter spp.	2	6.1	3	8.1
Pseudomonas aeroginosa	0	0.0	2	5.4
Providencia rettgeria	0	0.0	1	2.7
Enterobacter aerogenes	0	0.0	1	2.7
Acinetobacter wolfii	0	0.0	1	2.7

From 33 patients with kidney stones undergoing PCNL, mostly (63.6%) were men with a mean age of 50 ± 11 years and range 37-68 years from February to May 2012. Table 1 shows location and number of stones along with the presence of hydronephrosis. The location of kidney stones in those undergoing PCNL in this study was mostly in pyelum (57.58%), followed by pyelum and inferior calyx (24.24%), and finally in inferior calyx alone (18.18%). Stone subjected to operative action was single in 72.73% and multiple in 27.27%. Of the 33 patients who performed PCNL, 60.6% had hydronephrosis grade I-II, 36.37% had hydronephrosis grade II-IV, and only 3.03% without hydronephrosis. Mean operation length was 81.96 ± 10.61 minutes.

Pre-PCNL midstream urine culture showed that 18 of 33 patients (54.55%) were sterile and in 15 patients (45.45%) the urine culture contained bacterial growth. Most pathogenic bacteria were E. coli in 12.12% patients, and Klebsiella Pn. - Staphylococcus COAG - Acinetobacter spp. in respectively 6.1% patients, and E. coli - Enterobacter cloacae - Pantoea agglomerans - Proteus mirabillis - Staphylococcus haemolyticus in respectively 3.03% patients.

Table 3. Cross tabulation of urine culture and stone culture

Urine culture	Stone culture	Total	p value
Sterile	Sterile	8 (24.2)	0.629
Sterile	Bacteria (+)	10 (30.3)	
Bacteria (+)	Sterile	7 (21.2)	
Bacteria (+)	Bacteria (+)	8 (24.2)	
		1 (same bacterial type)	
		7 (different bacterial type)	

Table 4. Analysis of predictor variables on the incidence of SIRS after PCNL.

Variables	SIRS (n = 10)	Non-SIRS (n = 23)	p	RR	CI 95%
Age	51.4 ± 9.4	50.5 ± 12.5	0.838	1.0	0.9 – 1.1
Sex					
Female	4 (33.3)	8 (66.7)	0.775	1.3	0.3 – 5.8
Male	6 (28.6)	15 (71.4)	0.526		
Stone location					
Calyx inferior	3 (50.0)	3 (50.0)	-		
Pyelum	5 (26.3)	14 (73.7)	0.288	0.4	0.1 – 2.4
Calyx & Pyelum	2 (25.0)	6 (75.0)	0.341	0.3	0.04 – 3.2
Number of stones					
Multiple	2 (22.2)	7 (77.8)	0.539	0.6	0.1 – 3.4
Single	8 (33.3)	16 (66.7)			
Hydronephrosis					
Grade 3 – 4	8 (66.7)	4 (33.3)	0.003	18.0	2.7 – 119.2
Grade 1 – 2	2 (10.0)	18 (90.0)			
Negative	0 (0.0)	1 (100.0)	-	-	-
Length of operation					
≥ 90 minutes	10 (55.6)	8 (44.4)	0.001	NA	
< 90 minutes	0 (0.0)	15 (100.0)			
Urine culture					
Positive	4 (40.0)	11 (47.8)	0.679	0.7	0.2 – 3.3
Negative	6 (60.0)	12 (52.2)			
Stone culture					
Positive	10 (100.0)	8 (34.8)	0.001	NA	
Negative	0 (0.0)	15 (65.2)			

Table 5. Diagnostic test of urine and stone culture on the incidence of SIRS.

Results of diagnostic test	Urine culture	Stone culture
Sensitivity	40.0 (13.7 – 72.6)	100.0 (65.5 – 100.0)
Specificity	52.2 (31.1 – 72.6)	65.2 (42.8 – 82.8)
Positive prediction value	26.7 (8.9 – 55.2)	55.6 (31.3 – 77.6)
Negative prediction value	66.7 (41.2 – 85.6)	100.0 (74.7 – 100.0)

Post-PCNL stone culture in 33 patients showed that 15 patients (45.45%) had no bacterial growth, while 18 patients (54.54%) showed positive results. There were 4 patients or 4 pieces of stone culture with two types of pathogenic bacteria. Most of the pathogenic bacteria were Staphylococcus coagulase in 7 patients (18.9%), E. coli in 4 patients (10.8%), Acinetobacter spp. in 3 patients (8.1%), Klebsiella pn. and Pseudomonas aeroginsa in 2 patients (5.4%), Acinetobacter wolfii-Enterobacter aerogenes - Providencia retgerria - and Streptococcus non hemolyticus each in 1 patient (3.03%).

Table 3 shows that there were 18 patients (54.54%) whose stone culture contained bacterial growth, while urine culture with bacteria was found only in 15 patients (45.45%). In addition, the table also shows that patients with sterile urine and stone cultures were 8 (24.24%). Eight patients (24.24%) had urine and stone cultures with bacterial growth, but only 1 (3.03%) patients had the same type of pathogenic bacteria between urine and stone culture. Stone culture results also revealed 4 (12.12%) preparations with two different types of bacteria. No difference in positivity of the results of urine and stone cultures ($p > 0.05$).

We analyzed several other variables associated with the post-PCNL SIRS incidence, i.e. gender, location of stone, number of stones, the degree of hydronephrosis severity, length of surgery and the results of urine culture and stone culture. Three variables were found with $p < 0.05$, the incidence of preoperative hydronephrosis grade III-IV with $p = 0.003$, length of surgery > 90 minutes with $p = 0.001$ and stones culture containing bacterial growth with $p = 0.001$. Those variables showed a significant correlation to post-PCNL SIRS incidence.

Urine culture had a sensitivity of 40%, specificity of 52.17%, positive predictor value of 26.7 and a negative predictor value of 66.7 for the occurrence of SIRS post-PCNL. Stone culture has a sensitivity of 100%, specificity 65.2%, positive predictor value 55.6% and negative predictor value 100%.

DISCUSSION

Preoperative urine culture examination is a routine procedure performed prior to surgery in order to provide appropriate prophylactic antibiotics. Several studies have shown that midstream urine culture is no longer representative to describe infection of the urinary renal pelvis and kidney stones.[6,8] The incidence of SIRS can be triggered by the release of endotoxins derived from microorganisms residing in urinary tract stones that can cause endotoxemia and bacteremia.[9] Mariappan et al. in 73 patients with unilateral ureteral stones who underwent ureterorenoscopy (URS) and lithotripsy showed that preoperative culture examination of midstream urine, renal pelvic urine culture and stone fragments culture found that 25 patients (34.3%) had a positive stone culture, 43 patients (58.9%) had positive pelvic urine culture and 21 patients (28.8%) had positive midstream urine culture. There were 12 patients (19%) who showed symptoms of SIRS within 24 hours after surgery.[8] Another study by Mariappan in 54 patients with kidney stones undergoing percutaneous nephrolithotomy (PCNL) showed that preoperative examination of midstream urine culture, renal pelvic urine culture and stone fragments culture were found in 11.1% of the patients, positive stone culture in 35.2%, and positive renal pelvis urine culture was found in 20.4% of the patients. In these patients 37% had post-operative SIRS.[6] Margel et al. examined the relationship between urine culture and stone culture in patients who underwent PCNL. There are 75 patients studied, 36 patients (48%) had a positive

Table 6. Comparison of studies.

	Positive stone culture	SIRS Incidence
Mariappan[10]	34.3%	19%
Mariappan[8]	35.2%	37%
Margel[12]	48%	22%
This study	54.54%	30.3%

culture stones results, and 17 (22%) had SIRS symptoms.[10]

This study showed that in 18 patients (54.54%) the stone cultured contained bacterial growth, 10 patients (55.56%) had sterile urine culture, while there was only 1 patient (5.56%) who had the same type of pathogenic bacteria between urine and stone culture. Urinary tract stones can be infected in two ways. First, by bacterial ascending mechanism. When urinary tract stones are formed, ascending bacteria will reach the surface and become part of the stones. The second way is that the presence of living bacteria causes chronic UTI and can produce stone. These bacteria are called urea-splitting bacteria, for example, Proteus, Pseudomonas, Klebsiella, Staphylococcus, and Mycoplasma, with the most organism Proteus mirabilis. Urea-splitting bacteria will change the pH of the urine to be alkaline and will facilitate the process of phosphate precipitation with various components, especially ammonium and magnesium. This process will produce phosphate component called struvite (magnesium-ammonium-phosphate [MAP] stone and or triple phosphate stones).[11]

In this study, the incidence of SIRS (at least meeting 2 criteria) in 10 patients had a characteristic emergence after 6 hours of operation, and only lasted for a maximum 12 hours post procedure. There were two likely factors as cause of bacteremia after PCNL. The first is the colonization of bacteria or endotoxin lipopolysaccharide (LPS) contained in the urinary tract stones which are fragmented and exposed to continuous irrigation fluid. The second is the opening of the channel to blood circulation through small veins and lymphatic channels that are open during operation, combined with the pressure of irrigation fluid. This will stimulate the release endogenous mediators from monocytes or macrophages, endothelial cells, neutrophils, and others. Peptidoglycan and lipotechoic acid, gram-positive bacteria, certain polysaccharides materials, as well as certain extracellular enzymes and toxins can also trigger the same response as LPS.[12,13]

In this study, 55.6% of the patients with operation time more than 90 minutes had SIRS. Logistic regression results obtained significance level $p = 0.001$ ($p < 0.005$). One possible cause of postoperative SIRS is the release of cytokines, including IL-1, IL-6, tumor necrosis factor (TNF)-alpha and interferon (INF) which can be produced by a variety of tissues and cells in the body. Post-operative SIRS usually only lasts for 2-3 days, depending on the severity of the surgical procedure.[13] In addition, in patients who had hydronephrosis grade III-IV, 66.7% of them had SIRS. Logistic regression results obtained p value = 0.003 ($p < 0.005$) which means that the incidence of hydronephrosis had a significant correlation with SIRS incidence. Consistent with previous studies, the results of midstream urine culture could not describe infection in obstructed urinary tract so that during the operative procedure bacteria in pelvic urine or kidney stones enter into opening small veins and lymph channels due to PCNL procedure with the help of irrigant liquid.[13]

CONCLUSION

Culture of stone fragments can be used as a predictor of post-PCNL SIRS incidence. It should be further investigated whether SIRS signs are actually an infection process or a response to post-operative trauma.

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