

Research Paper

Urine Metabolite Risk Factors of DJ Stent's Biofilm Formation in Patients with Urinary Tract Stones

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Abstract: Introduction: Since first introduced by Finney and Hepperlen in 1978, the Double-J "DJ" Stent has become a routine armament that every Urologist uses everyday. Over time, there have been developments and improvements in both designs and materials, in order to improve the efficacy of the stents themselves. The use of the DJ Stent can not be separated from the morbidity or complications that might occur, including discomfort arising from the insertion of stents, forgotten to remove, urinary tract infections, biofilm formation, even encrustation of the stent. This research aims to know the correlation between the urine metabolites condition and urinary tract infection in the formation of biofilm and encrustation in patients with urinary tract stones at Saiful Anwar General Hospital, Malang.

Method: This is a cohort study using chi-square analysis and relative risk calculation. The datas were obtained from patients at Saiful Anwar General Hospital from March 2016 until December 2017. The examination includes urine metabolites, urinalysis, and urine culture prior to the insertion of DJ Stent, at polyclinic, and before the removal of DJ Stent. After the DJ Stent was removed, we evaluate if there was an encrustation on the DJ Stent or not and biofilm using congo agar plate. The subjects in this research was patient with urinary tract stone and patient without urinary tract stone as control group.

Result: There were 60 patients with urinary track stones, as well as 60 patients without a urinary track stone as a control. We found that high level of uric acid prior to removal of DJ Stent and during polyclinic control, and also high level of magnesium urine before DJ Stent removal were five times higher to form biofilm in patients with urinary tract stones. The presence of urinary tract infections when the subject control at polyclinic and before DJ Stent removal, and the presence of bacteria in urine before the insertion of DJ Stent in patients with urinary tract stones is significantly have five times higher risk to form encrustation on the DJ stent. Patients without urinary tract stone have four times higher risk in the formation of encrustation with abnormal level of magnesium that found before the

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removal of DJ Stent. Delayed in DJ Stent removal in patients without urinary track stone were significantly have ten times higher risk in biofilm formation and six times higher risk in the formation of encrustation in patients with urinary tract stones.

Conclusions: There is a relationship between the condition of urine metabolites and urinary tract infections with biofilm formation and DJ Stent's encrustation in patients with urinary tract stones.

Keyword: Biofilm, DJ Stent, Encrustation, Urinary Tract Infection, Urinary Metabolite

1. INTRODUCTION

Since first introduced by Finney and Hepperlen in 1978, the Double-J "DJ" Stent has become a routine armament that every Urologist uses everyday. Over time, there have been developments and improvements in both designs and materials, in order to improve the efficacy of the stents themselves. (Al-Aown et al., 2010; Beiko, 2003). In clinical practice, DJ Stent mostly indicated for the treatment of ureteral obstruction, either because of intrinsic or extrinsic causes (Dakkak, 2012). Even though, the use of the DJ Stent can not be separated from the morbidity or complications that might occur, including discomfort arising from the insertion of stents, forgotten to remove, urinary tract infections, biofilm formation, even encrustation of the stent.

Urinary tract is a main source of nosocomial infections. About 80% of nosocomial infections arise from the instrumentation of it (Gabe, 2015). Bacterial colonization after DJ Stent insertion can occurs in less than 4 weeks in 2.2% patients, 4-6 weeks in 2.9% patients, and more than 25% in 6 weeks after the insertion (Ozgur, 2012). After the insertion, DJ Stent will coated with proteins, minerals, polysaccharides, and other matrix. This condition will promote further bacterial colonization (Donlan, 2001).

The biofilm formation begins with bacterial colonization at the surface of the stent. Overtime, this condition can promotes urinary obstruction, urinary tract infection that will lead to urosepsis, and stent

encrustation. The encrustation of DJ Stent can occurs in infected or sterile urine. In infected urine, the urea splitter bacteria play the important role. In the sterile urine, the encrustation occurs because of accumulation of urine electrolytes. Calcium oxalate is the most component found in encrusted DJ Stent (Keane, 1994; Wollin, 1998; Carlos, 2012). In patient with urinary tract stones, the risk of encrustation increase three times (Robert, 1997).

This research aims to know the correlation between the urine metabolites condition and urinary tract infection in the formation of biofilm and encrustation in patients with urinary tract stones at Saiful Anwar General Hospital, Malang.

2. MATERIAL AND METHOD

Asdaasd This is a cohort study using chi-square analysis and relative risk calculation. The datas were obtained from patients at Saiful Anwar General Hospital from March 2016 until December 2017. The examination includes urine metabolites, urinalysis, and urine culture prior to the insertion of DJ Stent, at polyclinic, and before the removal of DJ Stent. After the DJ Stent was removed, we evaluate if there was an encrustation on the DJ Stent or not and biofilm using congo agar plate. The subjects in this research was patient with urinary tract stone and patient without urinary tract stone as control group.

3. RESULT

There were 60 patients with urinary track stones, as well as 60 patients without a

urinary track stone as a control. We found that high level of uric acid prior to removal of DJ Stent and during polyclinic control, and also high level of magnesium urine before DJ Stent removal were five times higher to form biofilm in patients with urinary tract stones. The presence of urinary tract infections when the subject control at polyclinic and before DJ Stent removal, and the presence of bacteria in urine before the insertion of DJ Stent in patients with urinary tract stones is significantly have five times higher risk to form encrustation on the DJ stent. Patients without urinary tract stone have four times higher risk in the formation of encrustation with abnormal level of magnesium that found before the removal of DJ Stent. Delayed in DJ Stent removal in patients without urinary track stone were significantly have ten times higher risk in biofilm formation and six times higher risk in the formation of encrustation in patients with urinary tract stones.

4. DISCUSSION

In this study we found a significant relationship between the level of uric acid patients before DJ stent insertion ($p = 0.017$, $RR = 5.25$) and in the polyclinic ($p = 0.048$, $RR = 4.929$) with biofilm formation in the patients with stones. The high level of uric acid in the urine accompanied by low urinary pH will trigger the formation of uric acid stones. At normal pH level, high level of uric acid will trigger the formation of calcium stone (Margaret, 2012). The presence of stent will be encased by proteins, minerals, polysaccharides, and other urine-forming compositions which in the appropriate urine conditions can trigger attachment and proliferation on the surface of the stent to form biofilm. The presence of bacteria in the urine, can also trigger biofilm formation in the ureteral stent (Donlan, 2001).

In this study also found a significant relationship ($p = 0.009$ and $RR = 6.143$) between the level of magnesium urine before DJ stent removal with biofilm formation in the urinary tract stones group, as well as in the control group with the DJ Stent encrustation formation ($p = 0.049$, and $RR = 3.7$). In a study conducted by Takashi in 2012 it was stated that the mechanism of biofilm formation is the result of the union of organic components of urine with the surface of the biomaterial on the ureteric stent. In a longer time can trigger further bacterial growth, thus causing an increase in urease production which can increase urine pH level. The increase in urinary pH will attract calcium and magnesium ions in the biofilm matrix which can eventually cause crystallization (Takashi, 2012). Wollin's research in 1998 found that magnesium is one of the component that can cause encrustation, and the presence of this component on the surface of the stent indicates the presence of an encrustation process (Wollin, 1998). Encrustation of calcium and magnesium salts is enhanced by crystalline biofilms from the *Proteus mirabilis* bacteria, where this bacteria help crystallization through increased urine alkalinity. The condition of urine with high pH level will create optimal conditions for the formation of calcium crystalline and struvite stones nuclei (Stickler, 1993; Keane, 1994; Venkatesan et al., 2010). This was in accordance with this study, which found a significant relationship between the presence of bacteria in urine before the insertion of DJ Stent ($p = 0.001$, $RR = 7$), in the polyclinic ($p = 0.004$, $RR = 5.167$) and before the removal ($p = 0.006$, $RR = 4,889$) with the formation of encrustation in urinary tract stone patients. In addition, the presence of bacteria was also shown to have a significant number of encrustation formation ($p = 0.011$, $RR = 4.5$) in the group with urinary tract stones. Another study stated that the presence of

urinary tract stones and urinary tract infections are factors that can increase the incidence of encrustation formation (Cao et al., 2015).

Urea splitter bacteria plays a major role in the encrustation formation (Carlos, 2012). The commonest urea splitter bacteria are *Proteus*, *Klebsiella*, *Pseudomonas*, and *Staphylococcus* (Mellman, 2007). This is consistent with the results of the urine culture obtained in this study, where *Staphylococcus aureus* was found in the stone group before the insertion of DJ stent (12%), during control at the Polyclinic (12%) and before DJ Stent removal (17%). *Klebsiella* (7%) in the stone group before the removal of DJ stent and *Pseudomonas aeruginosa* in the stone group before DJ stent removal (7%) and control group in the Polyclinic (7%) and before DJ stent removal (12%).

In this study found that there was a significant relationship between the time of DJ Stent removal (more than 12 weeks after installation or forgotten) with biofilm formation ($p = 0.002$ and $RR = 10$) as well as with the encrustation formation ($p = 0.003$ and $RR = 5.571$). This is consistent with the results from several previous studies. In a study conducted by El-Faqih in 1991 in patients with urinary tract stones, the rate of formation of encrustation increased from 9.2% in less than 6 weeks to 47.5% in 6 - 12 weeks after the insertion of DJ Stent. This number increases to 76.3% if the stent is not removed for more than 12 weeks (El Faqih, 1991). There is a threefold risk of encrustation in patients with urinary tract stones compared to patients diagnosed without urinary tract stones (Robert, 1997). Also mentioned in another study that forgotten stents can cause various complications such as encrustation, incrustation, stone formation, and fragmentation (Takashi, 2012; Carlos, 2012).

Another study states that on stents for more than 1 year, the risk of forming an encrustation increases by 33% (Carlos, 2012). Several risk factors reported affect the incidence of encrustation, namely the presence of urinary tract infections (especially infections involving urea splitter bacteria) and pregnancy (Carlos, 2012). This is also in accordance with the research conducted by Takashi in 2012, that the rate of encrustation in stents less than 6 weeks was 26.8%, 56.9% in stents that were left in 6-12 weeks, and 75.9% in stents that were forgotten to be removed in more than 12 weeks (Takashi, 2012).

A study by Ozgu at 2013 stated that bacterial colonization increased significantly with the duration stent usage, and sterile urine culture did not exclude the possibility of colonization of the stent. The rate of colonization at stents ranged from 2.2%, 2.9%, up to 25% respectively in less than 4 weeks, 4-6 weeks, and more than 6 weeks after the insertion (Ozgu et al., 2013). The risk of bacteriuria and colonization on DJ stents increased significantly with the duration of stent usage, the risk was increased in those who were accompanied by systemic diseases such as diabetes mellitus, chronic renal failure, and diabetic nephropathy, so these patients tends to be shorter in usage of stents, adequate administration of antimicrobial prophylaxis, and strict follow-up to minimize the chance of infection (Takashi, 2012).

In a study by Gabi in 2011 it was found that a few minutes after inserting urethral catheter, deposition of urine components on the catheter surface can form a film that supports bacteria to be able to actively adhere to it (Gabi et al., 2011). It was also stated that *Enterococcus faecalis* is a pathogen associated with that biofilm formation (Venkatesan et al., 2010). In this

research was found that *Enterococcus faecalis* in stone group urine culture by 7% and in the non-stone group 8% at the time before the DJ stent was inserted, and it was also found at the polyclinic with 5% in subjects with stones and 10% in the control group, and in the stone group (7%) and non-stone (12%) before the removal of DJ stents.

5. CONCLUSION

There is a relationship between the condition of urine metabolites and urinary tract infections with biofilm formation and DJ Stent's encrustation in patients with urinary tract stones.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethic number approve
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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

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