นิพนธ์ต้นฉบับ

การศึกษาการเกาะตัวของนิ่วบนสายระบายท่อไตในผู้ป่วยกลุ่มที่ไม่เป็นนิ่ว

พญ.มัชฌิมา ฮวบกอง*, นพ.ชนธีร์ บุณยะรัตเวช*,
นพ.วัฒนชัย อึ้งเจริญวัฒนา**, สุประวีณ์ ป่าจิก**, รัชนี สิทธิมาก**

บทคัดย่อ

วัตถุประสงค์ : เพื่อศึกษาองค์ประกอบของนิ่วที่ก่อตัวบนสายระบายท่อไต ชนิด polyurethane ในผู้ป่วยกลุ่มที่ไม่เป็นนิ่ว

ผู้ป่วยและวิธีการศึกษา : ทำการศึกษาผู้ป่วยจำนวน 48 ราย ที่ได้รับการถอดสายระบายท่อไตออก โดยวิธีส่องกล้องกระเพาะปัสสาวะ ระหว่างเดือนกันยายน พ.ศ.2555 ถึงเดือนมกราคม พ.ศ.2556 ผู้ป่วยมีอายุเฉลี่ย 60 ปี โรคพื้นฐานของผู้ป่วย ได้แก่ มะเร็งในอุ้งเชิงกราน ท่อไตตีบ และ endometriosis ที่ทำให้เกิดการอุดกั้นท่อไต ตัวอย่างที่นำไปศึกษาได้จากการขูดผิวด้านนอก และด้านในของสายระบายท่อไต แล้วนำไปวิเคราะห์องค์ประกอบด้วย อินฟราเรดสเปกโตรสโคปี

ผลการศึกษา : องค์ประกอบของสารที่เกิดบนสายระบายท่อไตในกลุ่มผู้ป่วยที่ไม่เป็นนิ่ว เป็นนิ่วชนิดผสม (mixed stone) โดยพบว่า เป็นนิ่วชนิด Carbonate apatite (Dahllite) และชนิด Weddellite ผสมกันอยู่เป็นนิ่วผสมชนิดที่พบบ่อยที่สุด6 ตัวอย่างจาก 48 ตัวอย่าง โดยองค์ประกอบหลัก คือ Dahllite และ cystine ร้อยละ 33 และ 16 ตามลำดับ และองค์ประกอบที่พบมากที่สุด คือ Dahllite พบมากถึงร้อยละ 60

สรุป : Dahllite เป็นองค์ประกอบที่พบบ่อย ในคราบที่เกิดบนสายระบายท่อไตในผู้ป่วยกลุ่มไม่เป็นนิ่ว การศึกษาต่อไป ควรทำการศึกษาเพื่อป้องกันการเกิดคราบบนสายระบายท่อไต

คำสำคัญ : คราบบนสายระบายท่อไต คราบบนสาย double J ผู้ป่วยที่ไม่เป็นนิ่ว คราบ

** หน่วยศัลยศาสตร์ยูโรวิทยา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย*
*** หน่วยศัลยศาสตร์ระบบปัสสาวะ โรงพยาบาลสรรพสิทธิประสงค์*

Original article

Characteristics of ureteral stent encrustation in non-stone forming patients

Huabkong M[a], Bunyaratavej C[a], Ungchareonwattana W[b], Phajik S[b], Sittimak R[b]

Abstract

Objective: To determine the composition of crystalline encrustations on polyurethane ureteral stents inserted in non-stone formers.

Material and Method: Forty-eight self-retained polyurethane ureteral stents from non-stone formers removed by cystoscope between September 2012 and January 2013 were studied. Mean age of the patients was 60 years old. The primary diseases of the patients were pelvic malignancy, ureteric stricture and endometriosis, which caused ureteric obstruction. The specimens were collected by scraping all of the encrusted contents from the outer and inner surfaces, then analyzing them with Fourier-transform infrared spectroscopy.

Results: All the encrustations in non-stone formers were mixed stones. Carbonate Apatite (dahllite) mixed with weddellite was found in 6 of 48. The major mineral constituents of stones were dahllite and cystine accounting for 33% (16/48) and 16% (8/48). The highest prevalence was dahllite at 60% (29/48).

Conclusion: Dahllite was the most frequent composition found in non-stone forming ureteral stent encrustation. Prevention of encrustations should be studied further.

Keywords: ureteral stent encrustation, double-J stent encrustation, non-stone forming, encrustation

[a] *Division of Urology, Department of Surgery, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*

[b] *Department of Surgery, Sappasittiprasong Hospital, Ubon Ratchathani, Thailand.*

Introduction

Ureteral stent insertion is an effective treatment, both temporary and long term, preventing ureteric obstruction, which occurs from various causes, including stones, strictures, or insertion after surgery. Causes from outside of the ureteral tract include compression from other organs nearby, such as lymph nodes or tumors. However, ureteral stent insertion also has some side effects. The initial side effects can be pain or urinary bladder irritation; later side effects include ureteral stent encrustation, obstruction, shifting in position, and breakage. Ureteral stent encrustation is a side effect that occurs after insertion of the ureteral stent, which frequently occurs, and therefore require further treatment costing even more time and money. Previous studies found that in stone formers, encrustation of stones on the ureteral stents occurred 9.2% in 6 weeks, 47.5% in 6-12 weeks and 76.3% in 12 weeks and up[1]. Stone compositions found are calcium oxalate, calcium phosphate, and ammonium magnesium phosphate[2,3], which might also cause other problems, such as difficulties in stent removal, injuries to the ureteral tract, or in some cases ureteral stents that cannot be removed, require further treatment by endoscopic or other methods of surgery[4]. In case of obstruction, the obstruction typically occurs slowly with no apparent symptoms, resulting in a late diagnosis and treatment. Therefore, there is a risk of damaging the kidney[1]. A study conducted by Bithelis G. found that in non-stone formers, organic compounds are most frequently found encrusting the ureteral stent. However the non-stone formation cases in his study were few[1,3], comprise of patients diagnosed with cancer and obstructive uropathy. Some of whom could not undergo major surgery, while others required a longer duration of ureteral stent insertion.

There were efforts using technology to improve material qualities used for manufacturing ureteral stents such as Heparin-coated, Triclosan eluting stent, antibiotics eluting stent, and Metallic stent, although they are quite expensive and there are still no stent that can prevent stones encrustation[5-8].

The aim of this study is to further understand stone formations and compositions in non-stone formers, since new ureteral stent technology are expensive, and there are no stents available that can prevent stone encrustations. Results from this study could be of assistance in further planning for the prevention of encrustations on ureteral stents in non-stone formers, and also improving patient quality of life in the future.

Ureteral stent encrustation is a side effect which occurs after ureteral stents have been inserted for a period of time. According to present studies, there is no ureteral stent that has the ideal properties, which are: easy insertion, mechanism to prevent disconnection, does not provoke inflammatory response in the body, suitable for a long period of insertion, prevents ureteral stent encrustation, helps with a sufficient and better flow of urine, the patient can undergo stent insertion comfortably, can be seen clearly using radiological imaging, easy to be replaced, can be widely used, and is inexpensive.

One theory on how encrustation occurs is that the cause is the ureteral stent itself, because it is inserted in the exact position where chemical components from the urine, of which there are several types of anti-inflammation protein produced can attached to its surface. There is also bacteria encrusting, multiplying itself, and producing biofilm on the surface. The change in pH level also causes other high concentration components in the urine to solidify and crystallize. Hence, ureteral stent encrustation occurs[9,10]. The risk factors influencing ureteral stent encrustation are a long duration of ureteral

stent insertion, a urinary tract infection which produced enzymes and catalyzed urea, urinary stones, and pregnancy. In stone forming patients, longer durations of ureteral stent insertion increase encrustation rates on the stent[2,11,12]. In patients with a stone formation history, encrustation of stones on the ureteral stent occurs 9.2% in 6 weeks, 47.5% in 6-12 weeks, 76.3% in 12 weeks and up[1] and 100% after 10 weeks of insertion, according to a study conducted by M.M. Tunney et al[12]. Stone compositions found are calcium oxalate, calcium phosphate, and ammonium magnesium phosphate[1,2].

According to our experience, there was less stone encrustation on the ureteral stent in the non-stone forming patients, and occasionally the stones disappeared after medication, or after using potassium sodium hydrogen citrate. Therefore, we are interested in the formation of stones in non stone forming patients, in order to determine the composition, and study it further.

Materials and methods

This research is a cross-sectional observational descriptive study; 93 ureteral stents were collected from adult patients aged 18 and up who had their ureteral stents replaced with no diagnosis history of urolithiasis at the Division of Urology, Department of Surgery, Chulalongkorn Hospital between November 2012 and January 2013. Patients with urolithiasis were excluded (17 stents). Profiles and treatment history were collected, including KUB X-ray film, ultrasonography of Kidneys, intravenous pyelogram (IVP), X-ray computed tomography (CT scan) or magnetic resonance imaging system (MRI). Radiological imaging used to investigate the cause of the obstruction were the CT scan, ultrasound, KUB film and IVP. Presently, the CT scan is known to possess 100% sensitivity and specificity in diagnosing urinary tract calculi. A study by Tomás Ripollés et al.[13] was conducted using the ultrasound combine with KUB film and comparing the result with the CT scan, in order to diagnose urinary tract calculi. The result showed 78.6% and 100% in diagnosis sensitivity and specificity, respectively. On the other hand, for obstructive uropathy cases, sensitivity increased to 100%. IVP results showed 52-69% sensitivity. But if cases with obstructive signs were taken into consideration, sensitivity increased to 90%. Meanwhile, sensitivity in urinary tract calculi diagnosis was 45-66% and 12-93% in KUB film and the ultrasound respectively. Thus, imaging diagnosis methods used in this study were the CT scan, IVP, and the ultrasound combine with KUB film to determine whether a stone had already formed in patients due to their high sensitivity. Imaging methods excluded from this study were plain film KUB or ultrasonography of the KUB tract or MRI alone, since each of them has insufficient sensitivity to diagnose stones in the urinary tract. Five stents were excluded from this study due to the insufficient sensitivity of the radiological imaging methods that were used. The encrustations on the remaining 48 stents were analyzed. Normally, these stents cannot be reused and must be disposed of as infectious waste. The process of analysis was:

- Cleansed by water until no blood stains remained.
- Patted dry. Stored in bags and labeled.
- Analyzed stone composition by scraping all encrusted contents from outer and inner surfaces [Figure 1].
- Crushed the scraped contents and mixed with potassium bromide until blended. Compressed the mixture into pellets using the Carver hydraulic press with a clamping pressure of 10 tons [Figure 2].
- Used Fourier-transform infrared spectroscopy [Figure 3,4] to analyze the compound struc-

tures of the pellets according to the principle of infrared absorption. The energy from the absorption will be transformed into the energy from the rotation or vibration of the molecules which is the characteristic of the compounds. Molecules in each compound show a unique spectrum of the chemical bonds in the molecules. Compared the results with the sample compound to determine whether it was organic or inorganic, and which had the highest sensitivity for diagnosis and a high reliability. Then interpreted the results.

Patient profile and history, such as congenital

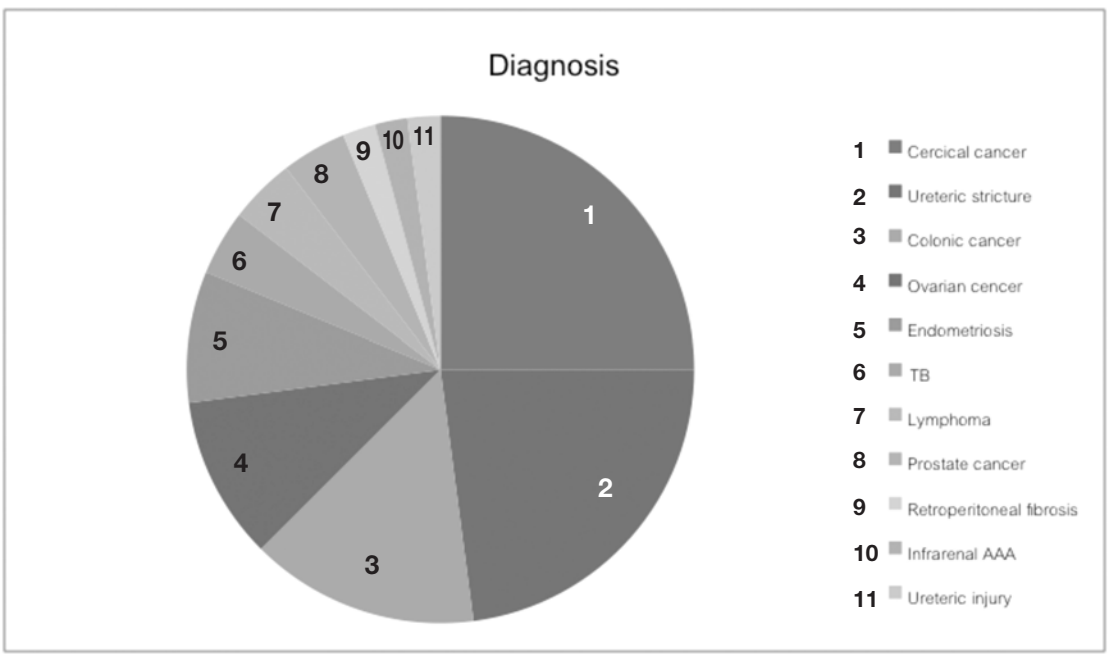


Figure 1 *Diagnosis of the patients*

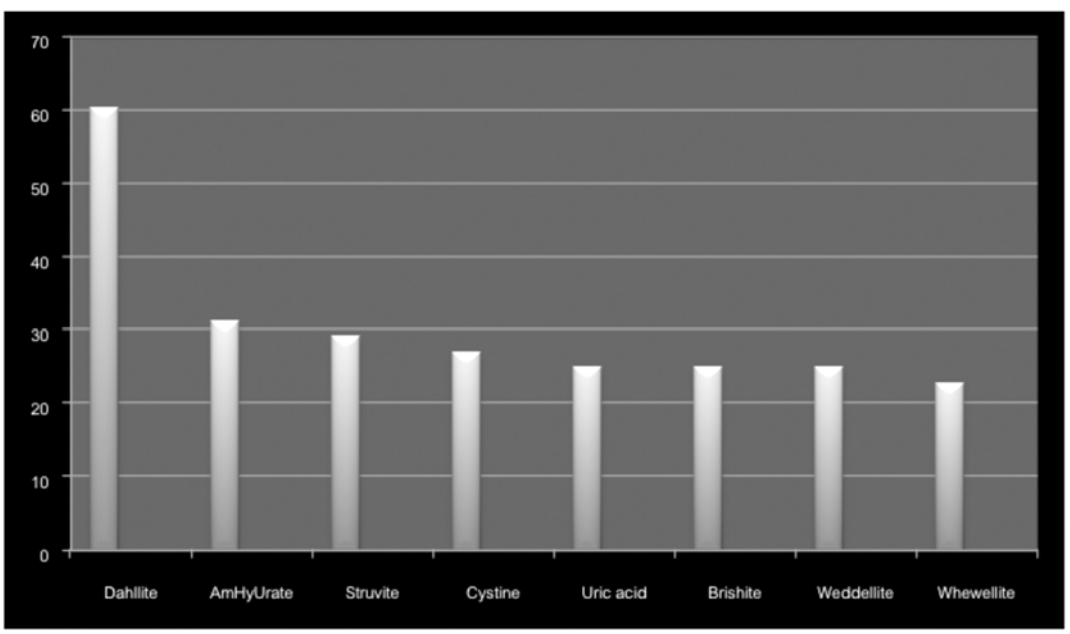


Figure 2 *Prevalence of the stone components*

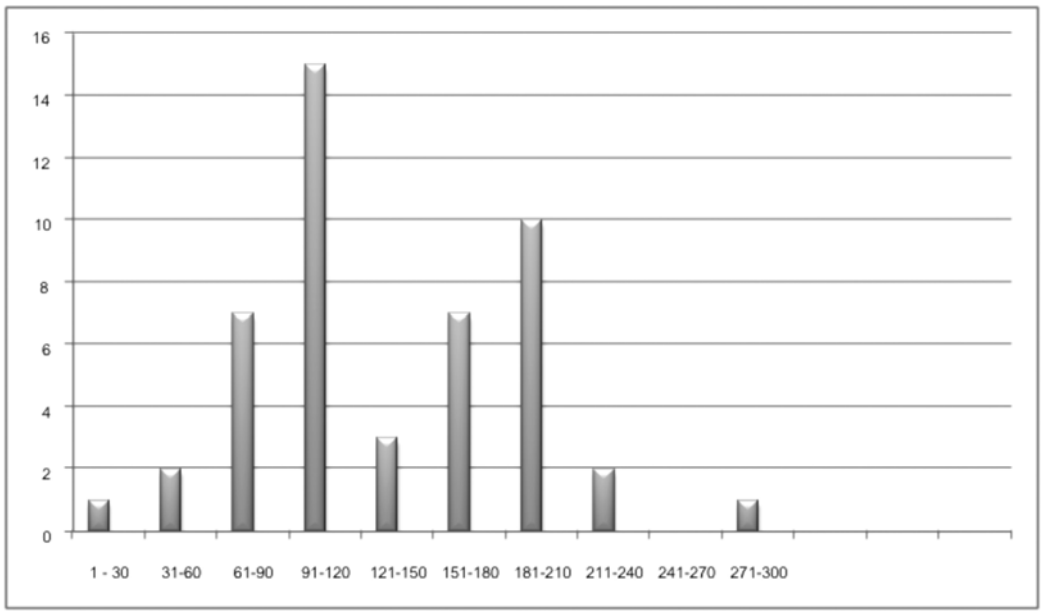


Figure 3 *Duration of stent insertion in the patients*

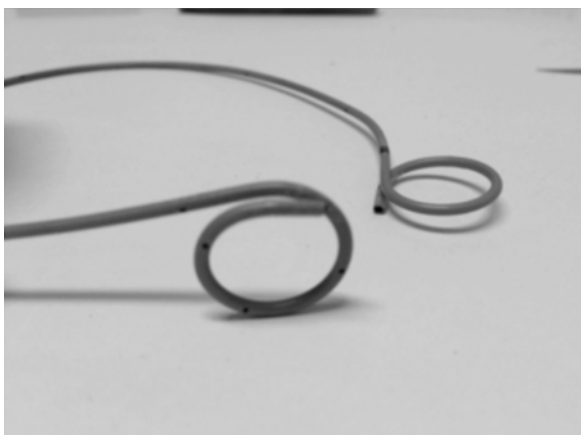


Figure 4 *Mild stent encrustation*

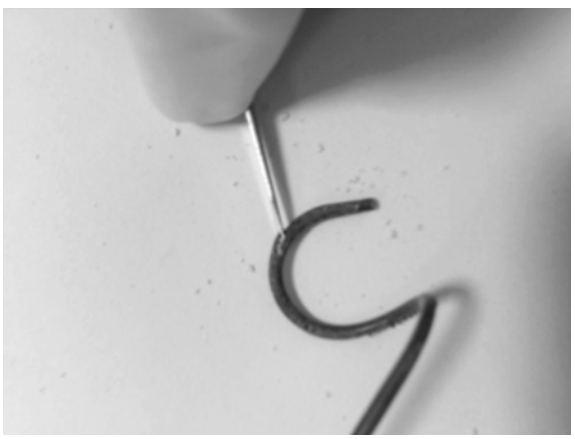
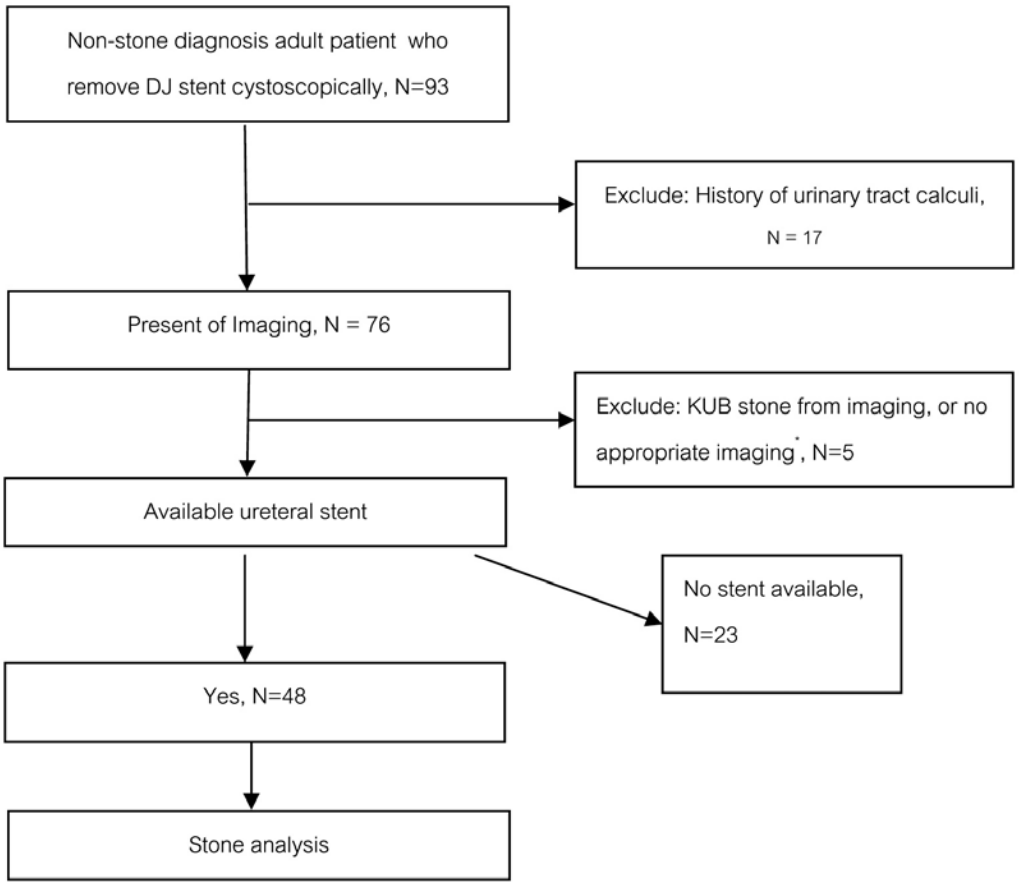


Figure 5 *Severe stent encrustation*

disease history, infection prevention medication history, urinary tract infection history, urine sampling and culture history during the insertion of the ureteral stents, were collected from medical records.

Results

Fundamental data were gathered and analyzed. All 48 stents were analyzed for stones, 9 from male (18%) and 39 female (82%) patients with an average age of 59.1±18.29 years old (ranging from 18-83). Thirty six patients (75%) were from the central region, and 7 patients (25%) were from the eastern region. Twelve patients (25%) were diagnosed with cervical cancer, while 11 patients (22.92%) with urethral stricture, 7 patients (14.58%) with colon cancer, and 5 patients (10.42%) with ovarian cancer. Lymphoma cancer, prostate cancer and tuberculosis were each found in 2 patients. Number of patients diagnosed with aortic aneurysm and ureteric injury were 1 each, according to Table 2. Figure 1 shows that



** Imaging methods, were plain KUB film, Ultrasonography of KUB tract, or Magnetic Resonance Imaging system (MRI) due to insufficient sensitivity to diagnose urinary tract stones.*

stone composition in all stent encrustation were mixed stone (100%); 32 patients (66.67%) were diagnosed with two compositions, while 16 patients (33.33%) were diagnosed with three compositions. By determining the characteristic compounds of stone compositions (the proportion of the characteristic compounds of stone compositions were more than 70% according to the stone analysis results of each ureteral stent), dahllite was found the most often, in 16 out of 48 stent samples (33.33%); cystine, ammonium hydrogen urate, and uric acid were found 16.67%, 8.33%, 6.25% respectively [Table 3]. The prevalence of each stone composition indicates that dahllite was found the most in 29 out of 48 stent samples (60.42%); other compositions, include ammonium hydrogen urate, struvite, cystine, uric acid, brushite, weddellite, whewellite (31.25%, 29.17%, 27.08%, 25%, 25%, 25%, 22.92% respectively), were also found [Table 4]. Figure 2 Mixed stones found were dahllite+weddellite in 6 samples (12.5%), dahllite+struvite and ammonium hydrogen urate+uric acid in 4 samples each, dahllite+whewellite in 3 samples, and dahllite+brushite, dahllite+cystine, ammonium hydrogen urate+struvite in 2 samples each [Table 5]. Average duration of the ureteral stent insertion was 131.85±53.61 days (ranging from 43-276 days), divide into time periods. Twenty two patients (45.83%) received stent insertion for a duration of 61 to 210

Table 1 Demographic data of the patients

Characteristics	Number	Part of the country					
		North-East	North	Central	East	West	South
Number of stent	48						
Gender							
Male(%)	9(18%)	-	-	7(14.53%)	-	1(2.08%)	1(2.08%)
Female(%)	39(82%)	1(2.08%)	1(2.08%)	29(60.42%)	7(14.53%)	1(2.08%)	-
Age (years) Mean±SD	59.1±18.29	37	32	66.33	60	59.5	80

Table 2 Diagnosis of the patients

Diagnosis	Number, N=48
Cervical cancer	12
Ureteric stricture	11
Colonic cancer	7
Ovarian cancer	5
Endometriosis	4
Lymphoma	2
Prostate cancer	2
TB	2
Retroperitoneal fibrosis	1
Infrarenal AAA	1
Ureteric injury	1

Table 3 Stone composition regarding to major component of the patients

Stone composition	Number	%
Dahllite	16	33.33
Cystine	8	16.67
Ammonium Hydrogen Urate	4	8.33
Uric acid	3	6.25
Whewellite	1	2.08
Struvite	1	2.08

Table 4 Prevalence of the stone components

Stone component	Number	%
Dahllite	29	60.42
Ammonium Hydrogen Urate	15	31.25
Struvite	14	29.17
Cystine	13	27.08
Uric acid	12	25.00
Brushite	12	25.00
Weddellite	12	25.00
Whewellite	11	22.92

Table 5 Prevalence of the stone components (mixed stone)

Mixed stone component	Number	%
Dahllite+Weddellite	6	12.5
Dahllite+Struvite	4	8.33
AmmoniumHydrogenUrate + UricAcid	4	8.33
Dahllite + Whewellite	3	6.25
Dahllite + Brushite	2	4.17
Dahllite + Cystine	2	4.17
AmmoniumHydrogenUrate + Struvite	2	4.17

days, and 17 patients (35.42%) for 151 to 210 days [Table 6]. Figure 3 indicates that 100% antibiotic prophylaxis, ciprofloxacin was used in 24 patients (50%), cefixime in 2 patients (4.17%), amoxicillin-clavulanic acid in 2 patients, and imipenem-cilastatin, ampicillin, meropenem, piperacillin-tazobactam in 1 patient each [Table 7]. Results indicate that there were urinary tract infections during the ureteral tract insertion, which were diagnosed due to abnormal urination patterns and urine test results, indicating the presence of leukocytes in 11 patients (22.92%) [Table 8] (Urine tests found a white blood cell count of 20-30/hpf in 1 patient, 50-100/hpf in 1 patient, 100-200/hpf in 3 patients, and numerous white blood cell count in 6 patients). The average urine pH = 7.41±0.86. Eight patients underwent urine culture, the results showed *E.coli* in 4 patients, *E.feacalis* in 2 patients, *K.pneumoniae* in 1 patient, and *A.baumanii* in 1 patient [Table 9, 10]. In cases with no infection, there were no urine test results in 5 patients, and there were urine test results in 32 patients. According to Table 11, the average urine pH = 7.02±0.85 from all urine test results. The ureteral stent used was a colored polyurethane double-J stent (Percuflex 4.8 Fr, 6 Fr, StretchVL 4.8 Fr, 6 Fr, COOK 4.7 Fr, Microvasive 4.8 Fr) [Table 12].

Discussion

Ureteral stent encrustation, is a side effect which causes obstruction, inability to remove stent, infection, and ureteric injury. The actual cause of encrustation is still being debated, but it is believed that

Table 6 Duration of stent insertion in the patients

Days	Number, N=48
1-30	1
31-60	2
61-90	7
91-120	15
121-150	3
151-180	7
181-210	10
211-240	2
241-270	0
271-300	1

Table 7 Antibiotics Prophylaxis in the patients

Antibiotics	Number, N=48
Ciprofloxacin	24
Cefixime	14
Cefdinir	2
Ceftriaxone	2
Amoxicillin-Clavulanic acid	2
Imipenem-Cilastatin	1
Meropenem	1
Ampicillin	1
Piperacillin-Tazobactam	1

Table 8 Prevalence of urinary tract infection in the patients

UTI	N=48
Yes	11
No	37

Table 9 Urinary tract infection proved by urine culture

Urine culture result	Number, N=8
E.coli	4
E.feacalis	2
K.pneumoniea	1
A.baumanii	1

Table 10 Case profile of the patients with urinary tract infection

	Diagnosis	Duration (days)	Antibiotics prophylaxis	Bacteria	Stone type
1	Prostate cancer	174	ampicillin	E.faecalis	Dahllite + Weddellite + Whewellite
2	Ureteric stricture	213	cefixime	E.faecalis	Dahllite + Cystine
3	Rectal cancer	159	ciprofloxacin	A.baumanii	Struvite + Dahllite + Ammonium Hydrogen Urate
4	Rectal cancer	85	meropenem	K.pneumoniae	Ammonium Hydrogen Urate + Uric acid + Dahllite
5	Ureteric Stricture	99	cefixime	E.coli	Weddellite+Ammonium Hydrogen Urate
6	Cervical cancer	153	ciprofloxacin	E.coli	Whewellite+Weddellite + Uric acid
7	Ureteric Stricture	276	Piperacin-tazobactam	E.coli	Ammonium Hydrogen Urate + Brushite
8	Ureteric Stricture	87	Imipenem-cilastatin	E.coli	Dahllite+Struvite+Brushite
9	Ureteric stricture	162	ciprofloxacin	-	Uric acid+Ammonium Hydrogen Urate
10	Cervical cancer	97	cefixime	-	Dahllite+Struvite
11	Rectal cancer	99	cefixime	-	Dahllite+Ammonium Hydrogen Urate

several factors influence encrustation. According to the study, results of stone analysis show that phosphate stones are usually diagnosed along with a urinary tract infection, include dahllite (60%) and carbonate apatite as a mixed stone, found in alkaline urine along with the infection. Calcium oxalate and struvite-brushite (25%), calcium hydrogen phosphate and struvite (29.17%), and magnesium ammonium phosphate hexahydrate are also occasionally found. The infection concerning the ureteral stent was caused by bacterial biofilm on the equipment, due to bacteria with urease enzyme which catalyzed uric acid in the urine, producing ammonia and carbondioxide. In an alkaline state, ammonium will create a chemical reaction to water, increasing alkaline levels, and the chemical reaction between water and carbon-dioxide will produce carbonic acid, creating two positive charges of hydrogen and carbonate. While hydrogen-phosphate in an alkaline state produces phosphate, both phosphate and carbonate cause stone formation due to infection (struvite: $MgNH_4PO_4$-$6H_2O$, hydroxy apatite:$Ca_5(PO_4)_3OH$, carbonate apatite:$Ca_5(PO_4)_3CO_3$) which is believed to be the cause of stone encrustation,even in the cases of non-stone formers. But results from the pH test level were alkaline, which is likely to be the cause of the infection and stone formation, and might be an underlying infection. According to this study, the urinary tract infection rate is 22.92%. In medication using antibiotics prophylaxis, there are studies of using cioprofloxacin which can be absorbed through the surface of the stent and help reduce the occurrence of conditioning film temporarily, although it is effective for only a short period of time after medication has been ceased,

Table 11 Case profile of the patients without urinary tract infection

Diagnosis	Duration (days)	Antibiotics prophylaxis	Stone type
1. Ureteric stricture	147	ciprofloxacin	Dahllite+Weddellite
2. Sigmoid cancer	185	cefixime	Dahllite+Weddellite
3. Ovarian cancer	99	cefixime	Dahllite+Weddellite
4. Lymphpoma	127	cefixime	Whewellite+Weddellite+Uric acid
5. Endometriosis	162	cefixime	Whewellite+Ammonium Hydrogen Urate+ Dahllite
6. Prostate cancer	162	ciprofloxacin	Dahllite+Whewellite
7. Cervical cancer	225	ciprofloxacin	Dahllite+Brushite+Whewellite
8. Ovarian cancer	99	cefdinir	Ammonium Hydrogen Urate+Brushite
9. Cervical cancer	87	cefdinir	Uric acid+Dahllite
10. Retroperitoneal fibrosis	192	ciprofloxacin	Cystine+Brushite
11. Colonic cancer	80	amox-clavulanic acid	Cystine+Brushite
12. Endometriosis	90	ciprofloxacin	Dahllite+Brushite
13. TB	115	Ceftriaxone	Uric acid+Ammonium Hydrogen Urate
14. Cervical cancer	43	ciprofloxacin	Ammonium Hydrogen Urate+Struvite
15. Cervical cancer	185	ciprofloxacin	Dahllite+Weddellite
16. Ureteric stricture	185	ciprofloxacin	Struvite+Cystine
17. Cervical cancer	183	ciprofloxacin	Dahllite+Struvite
18. Ureteric stricture	92	ciprofloxacin	Dahllite+Cystine
19. Cervical cancer	101	ciprofloxacin	Dahllite+Ammonium Hydrogen Urate
20. TB	97	ciprofloxacin	Dahllite+Cystine
21. Cervical cancer	97	cefixime	Cystine+Uric acid
22. Ureteric stricture	94	ciprofloxacin	Dahllite+Struvite+Brushite
23. Ovarian cancer	99	ciprofloxacin	Cystine+Uric acid
24. Ovarian cancer	85	ciprofloxacin	Dahllite+Weddellite
25. Ovarian cancer	92	ciprofloxacin	Ammonium Hydrogen Urate+Struvite
26. Endometriosis	183	cefixime	Cystine+Weddellite
27. Lymphpoma	183	ciprofloxacin	Cystine+Uric acid
28. Ureteric stricture	209	Ceftriaxone	Dahllite+Struvite+Whewellite
29. Cervical cancer	87	cefixime	Dahllite+Ammonium Hydrogen Urate+Uric acid
30. Ureteric injury	183	ciprofloxacin	Cystine+Brushite
31. Colonic cancer	51	amox-clavulanic acid	Dahllite+Ammonium Hydrogen Urate+Uric acid
32. Cervical cancer	190	cefixime	Dahllite+Struvite
33. Ureteric stricture	22	ciprofloxacin	Dahllite+Struvite+Brushite
34. Rectal cancer	127	cefixime	Struvite+Whewellite+Weddellite
35. Endometriosis	92	ciprofloxacin	Dahllite+Struvite+Brushite
36. InfrarenalAAA	178	cefixime	Cystine+Whewellite
37. Cervical cancer	96	ciprofloxacin	Dahllite+Uric acid

Table 12 Stent type of the patients

Stent type	Number, N=48
Percuflex 6 Fr 1 year	14
Percuflex 4.8 Fr 1 year	8
Stretch VL 6 Fr 6 months	11
Stretch VL 4.8 Fr 6 months	4
COOK 4.7 Fr 6 months	10
Microvasive 4.8 Fr 1 year	1

and still cannot prevent the occurrence of biofilm and encrustation[14]. Meanwhile, the duration of stent insertion is one of the factors influencing the encrustation on the stent. According to this study, it was found that the average duration of insertion was 132.59 days, which is longer than the duration recommended in other studies, which is approximately 90 days. The rate of stent encrustation is 100% [Figure 4,5], which is in accordance with previous studies. Results indicating the presence of cystine stones can be explained by the fact that highly alkaline urine causes more occurrences of chemical substances in the urine than typical urine with a balanced pH. Further studies are required to help prevent infection and reduce stone formations. Appropriate duration of ureteral stent insertion should be investigated further as well.

Conclusion

Dahllite or carbonate apatite:$Ca_5(PO_4)_3CO_3$ is the composition found most frequently in non-stone forming ureteral stent encrustation patients. Prevention of encrustation still requires further study.

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