The Impact of Gelatin-Sealant in the Access Tract after Tubeless Percutaneous Nephrolithotomy: A Randomized Controlled Trial

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Objective: *To determine safety and efficacy of gelatin-sealant filled in the access tract after tubeless percutaneous nephrolithotomy (PCNL).*
Material and Method: *A randomized control trial study. 82 patients were divided into 2 groups, 41 patients for each group of with and without gelatin-sealant filled in the access tract. Changing of hemoglobin, blood transfusion, and post-operative complications were compared.*
Results: *Decreasing of hemoglobin was 1.2 g/dl in group of gelatin-sealant and 1.5 g/dl in the other (p = 0.26). Blood transfusion was less in gelatin-sealant group than the other (2 units vs. 4 units, p = 0.63). Urethral catheter time was shorter in gelatin-sealant group (2 days vs. 3 days, p = 0.02). Others were not different.*
Conclusion: *Gelatin-sealant in access tract after tubeless PCNL is safe to be an option to prevent bleeding in selected patients.*

Keywords: *tubeless PCNL, gelfoam, gelatin sealant hemostatic agent, postoperative bleeding*

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Percutaneous nephrolithotomy (PCNL) is a minimally invasive procedure to remove kidney or proximal ureteral stone by a small puncture wound through the skin. It was first performed in1976, and had become the procedure of choice for management of large, complex, and/or multiple renal calculi[1]. Tubeless PCNL (avoidance of a nephrostomy tube) was initially described by Wickham and colleagues more than 20 years and many trial has shown that benefit to omission of nephrostomy tube in the terms of reduced analgesic requirement and decrease length of hospitalization[2,3].

Hemorrhage is the most common significant complication of PCNL with the transfusion rates about 1 to 10%. Some surgeons reduced bleeding by sealing the nephrostomy tract with various hemostatic agents (Surgicel[4], fibrin glue[5,6] and gelatin matrix[7,8]) but the results were uncertain[9]. One study shown that gelatin-sealant technique in tubeless PCNL had advantage in lower blood transfusion rate, shorter hospitalization, and less analgesic requirement[10]but some had shown no difference[11].

In this prospective randomized study, our objective is to evaluate the safety, efficacy and benefit of absorbable gelatin after placing in access tract following tubeless PCNL.

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Material and Method

Patients selection

From June 2014 to July 2015, 90 patients with renal and/or proximal ureteric calculi who underwent tubeless PCNL in Siriraj Hospital were recruited. Exclusion criterias were shown in the Table 1. 8 patients were excluded because the accesses were more than 1 tract (5 cases), pelvocalyceal perforation (2 cases), and significant intraoperative bleeding (1 case).

A total of 82 patients were eligible in this study. The patients were prospectively randomized into two groups. 41 patients received gelatin-sealant in the access tract after PCNL (study group) and 41 patients were not (control group). All patients had been informed, and the study was approved by Siriraj institutional review board.

Preoperative evaluation

All the patients underwent routine history taking and physical examination.Blood sampling for CBC, serum Cr, urinalysis, and urine culture were obtained.Plain KUB film was done in all patients, included ultrasound, intravenous pyelography, and/or CT scan.

Surgical technique

Under general anesthesia, ureteric catheter was inserted cystoscopically. A 16 Fr Foley catheter was indwelled. Then, patient was changed to prone position. Percutaneous access was obtained under fluoroscopic guidance and guide-wire was inserted. Skin incision was done and nephrostomy tract was initially dilated with fascial dilators from 6 Fr. to 16 Fr., and then balloon dilator with pressure 10 ATM for 5 minutes. Clear Amplatz sheath with radio opaque stripe 30 Fr. was placed. This type of Amplatz sheath allowed us to visualize surrounding tissue clearly. Stone disintegration was achieved with ultrasonic device. A 6 Fr. JJ stent was placed at the end of procedure.

In gelfoam group, nephroscope and Amplatz sheath was carefully withdrawn to the junction between collecting system and renal cortex. A gelfoam size 7x5x1 cm. was rolled like a "Cigar-shaped" (Fig. 1) and then inserted by stone forceps to the tip of radio opaque strip of Amplatz sheath. Fluoroscopy to confirm the proper position of gelfoam. Amplatz sheath and safety guide-wire were removed. Without nephrostomy tube, skin was closed with 2-0 nylon, single stitch. In control group, Amplatz sheath was removed without gelfoam in access tract and the wound was closed in the same fashion.

Post-operative evaluation and statistical analysis

All patients were received routine postoperative care. Post-operative CBC, renal function test, Electrolyte was obtained in post-operative day 1. Urine color was evaluated with Hematuria Grading Scale (with the scale from 0-10)[12] for post-operative day 1-3. Total analgesic usage, urethral catheter time, length of hospital stay were obtained. Film KUB or ultrasound was done at 2 week and DJ stent was taken off in 2-4 weeks postoperatively.

The data was analyzed by using SPSS computer program ver. 18. The quantitative datas were analyzed statistically using independent sample T-test. While the categorical datas were analyzed with Pearson Chi-square test in this study. A *p*-value of 0.05 or less was considered statistically significant.

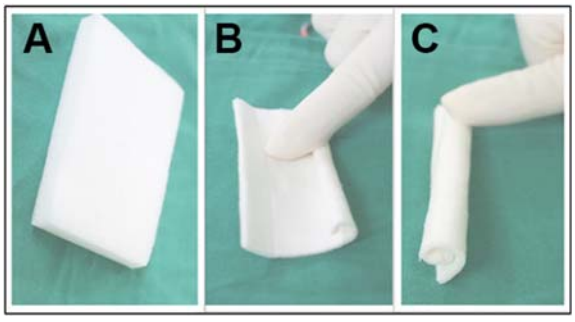

Fig. 1 Gelfoam (Spongostan®; size 7x5x1 cm) rolled in a cigar shape (A-C).

Results

Demographic data of 82 patients were shown in the Table 2. The average age of the patients was 52.7 year-old (range 31-78 year-old) in the gelfoam group and 54.6 year-old (range 27-79 year-old) in control group.There was no difference in age, gender, BMI, co-morbidity, antiplatelet usage, history of UTI, indwelling JJ stent, degree of hydronephrosis, and serum creatinine. There was no difference in preoperative hemoglobin between gelfoam and control group (13 mg/dL (9.5-16.7) and 13 mg/dL (9.8-18.6 mg/dL)) respectively ($p = 0.24$).

Stone surface area was calculated by summary of area of the stone in KUB film (width x height, mm^2). In gelfoam group, stone surface area was 843 mm^2 and 730 mm^2 in control group. Opaque stone was found 75% in both group. Staghorn stone was 53% in gelfoam group and 44% in another. Renal access was majority at upper calyx and infra-costal in both group. Stone location, operative time, estimated blood loss were not statisticallydifferent ($p = 0.37$, 0.24, 0.07 respectively).

From table 3, mean decreasing of hemoglobin was 1.2 and 1.5 mg/dl in gelfoam and control group respectively ($p = 0.26$). Blood transfusion was lower in gelfoam group (2 units versus 4 units) but not statistically significant ($p = 0.63$). At post-operative

Table 1. Exclusion criteria

Exclusion criteria
Age <18 years
>1 puncture site
Pelvocalyceal perforation
Excessive bleeding
Gelatin allergy
Active urinary tract infection (UTI)
Uncontrolled coagulopathy

Table 2. Demographic data and operative data

	Gelfoam (n = 41)	Control (n = 41)	*p*-value
Age (mean)	52.7	54.6	0.45
Sex (M/F)	19/22	23/18	0.38
BMI (kg/m^2)	25.0	26.5	0.15
DM	10	16	0.15
Chronic kidney diseasease (CKD)	4	4	1
Antiplatelet usage	2	2	1
Previous UTI	12	11	0.81
Previous DJ stent	6	3	0.48
Hydronephrosis			
Mild/moderate/severe	19/10/2	17/14/0	0.43
Preoperative Hb (mean; mg/dl)	13	13	0.24
Serum cr. (mean; mg/dl)	1.12	1.25	0.39
Stone surface area (mean; mm^2)	843	730	0.50
Side (Lt./Rt.)	19/22	22/19	0.51
Stone characteristic			
Staghorn stone	22	18	0.37
Renal pelvis stone	14	12	
Calyceal stone	5	11	
Stone opaque/non-opaque	31/10	31/10	1
Access tract			
Infracostal	34	32	0.58
Supracostal	7	9	
Operative time (mean; min)	71.5	81	0.24
Estimate blood loss (mean; ml)	153.3	93.1	0.07

Table 3. Post-operative variables

	Gelfoam gr. (n = 41)	Control gr. (n=41)	*p*-value
Hb decrease (mean; g/dl)	1.2	1.5	0.26
Blood transfusion (units)	2	4	0.63
Hematuria grading scale (0-10)			
- Day 1 (mean; scale)	3.1	4	0.03
- Day 3 (mean; scale)	2.4	2.6	0.46
Length of hospital stay (mean; days)	5	5	0.13
Urethral catheter time (mean; days)	2	3	0.015
Morphine usage (mean; mg)	2	1	0.70
Stone free rate (%)	67%	76%	0.25
- Size of residual stone (mean; cm)	11.2	9.2	0.25

day1, Hematuria Grading Scale was less in gelfoam group, significantly (grade 3 vs. 4, $p = 0.03$). While it was not different at post-operative day 3 (grade 2.4 vs. 2.6, $p = 0.46$). Time to without urethral catheter was shorter in gelfoam group (2 vs. 3 days, $p = 0.015$). Length of hospital stay, analgesic requirement (morphine usage) was not statistically different in both groups. Stone free rate after PCNL was similar in both groups (67% vs. 73%, $p = 0.25$) and mean residual stone-size was not different.

There was no difference of septic complications and pleural injury between 2 groups as shown in Table 4 ($p = 0.20$). 7 patients had post-operative sepsis and 1 patient developed septic shock which was able to treat with intravenous antibiotics. 5 patients had mild pleural effusion in procedural site. There was no major pleural complication which required intercostals drainage and none had gelatin allergy.

In this study, stone analysis was performed with FTIR method (Fourier transform infraredspectro

Table 4. Postoperative complications

	Gelfoam gr.	Control gr.	*p*-value
1. Fever	19	15	0.20
2. SIRS	1	6	
3. Septic shock	1	-	
4. Mild pleural effusion	3	2	

SIRS = Systemic inflammatory response syndrome

photometry). The components were calcium oxalate monohydrate (35%), calcium oxalate dihydrate (18%), calcium phosphate (33%), uric acid (5%), struvite (5%), and ammonium urate (3%).

Discussion

Acute hemorrhage is a common complication after PCNL, the incidence of hemorrhage was 6-20%. Most hemorrhage occurs from renal parenchymal bleeding. This topic is major concerned especially in tubeless PCNL which omit nephrostomy tube in the access tract. In some articles, various hemostatic agents have been used after tubeless PCNL to decrease urinary leakage, bleeding and morbidity.

Gelfoam (Spongostan™) is a purified absorbable porcine gelatin for application to the bleeding surfaces as a hemostatic. It is a water-insoluble, nonelastic, porous, pliable product preparation. The mechanism of action is 1) by absorbing fluid and then expanding to form an artificial clot which also tamponade the nephrostomy tract and 2) by clotting reaction which platelets entering the sponge and contact with the wall of many interstices and release thromboplastin, which interacts with prothrombin and calcium to generate thrombin and activate clotting cascade[13]. When placed in soft tissues, gelfoam is usually absorbed completely within four to six weeks, without inducing excessive scar tissue. One study of gelfoam implants in canine kidneys and reported that it assisted in healing, with no marked inflammatory or foreign-body reactions[14].

The factors that may reduce blood loss and transfusion rate are ultrasound-guide access, the use of Amplatz or balloon dilatation, reducing the operative time and staging procedure in case of large stone burden or intraoperative complication[15]. Dah-Shyong Yu et al. described the use of gelatin packing intracortical tract with the necessity for blood transfusion was much lower in the gelatin packing tubeless group than standard PCNL with tube drainage group (6.6% vs. 26.7%; $p = 0.013$)[10]. In that study, they used internal urethrotomy to dilate the access tract that had more chance of bleeding than the blunt dilation. In our study, there was less blood transfusion in gelfoam group but it was not statistically significant (4.8% vs. 9.7%, totally 2 units vs. 4 units; $p = 0.63$). While we used the balloon dilator that caused less tissue injury surrounding to the access tract. Therefore gelfoam may not has much role in case of balloon dilation, even though for tubeless PCNL. However, our study revealed less hematuria according to the hematuria grading scale at postoperative day 1 in the group of using gelfoam filled in the access tract. Urethral catheter time was shorter in gelfoam group because less hematuria as well. Other variables, morphine usage and stone free rate were not affected directly with utilizing of gelfoam. These two variables were not different in both groups.

Postoperative complication was considered especially the infection because gelfoam was a foreign body that left in the wound. As aforementioned, the property of gelfoam was absorbable agent, therefore the septic complication was not different between two groups.

Conclusion

By placing gelatin-sealant in the access tract is safe and available for a tubeless PCNL. It could promote hemostasis with the advantage in urine clarity, urethral catheter time.We suggest that gelfoam may be an alternative adjunct for hemostasis in the case of unusual bleeding.

What is already known on this topic?

Nowadays the standard treatment for large renal calculi is percutaneous nephrolithotomy and postoperative bleeding is the most common complication of this procedure (transfusion rate ~ 1-10%). One study (Yu et al, 2006) show that necessity for blood transfusion was significantly lower in gelatin packing group compared to tube-drainage group. But in other study (Iqbal et al, 2008) show no difference in hematocrit drop, however there are advantage in lower hospital stay and analgesic requirement among gelfoam-sealant group.

What this study adds?

In our prospective randomized study which compared with and without gelfoam-sealant in access tract after tubeless PCNL showed that gelfoam-sealant is safe and has benefit in better urine clarity, lower

urethral catheter time. Blood transfusion rate was lower in gelfoam-sealant PCNL tract but not statistically significant. We suggest that gelfoam is an alternative adjunct for hemostasis in the case of unusual bleeding from the access tract.

Potential conflicts of interest

None.

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การศึกษาผลจากการใส่วัสดุช่วยห้ามเลือดชนิดเจลาตินในรูที่เจาะจากผิวหนังถึงเนื้อไตหลังทำหัตถการเพื่อลดภาวะเลือดออกภายหลังการเจาะผิวหนังเพื่อส่องกล้องสลายนิ่วในไต: การวิจัยเชิงทดลองแบบสุ่ม

สกลรัฐ ทิตอร่าม, ไชยยงค์ นวลยง, ธวัชชัย ทวีมั่นคงทรัพย์, ศิรส จิตประไพ, เอกรินทร์ โชติกวาณิชย์

วัตถุประสงค์: เพื่อศึกษาประสิทธิผลและความปลอดภัยของการใส่วัสดุช่วยห้ามเลือดชนิดเจลาติน (Gelfoam) ในรูที่เจาะส่องกล้องหลังจากการทำผ่าตัดเจาะผิวหนังส่องกล้องสลายนิ่วในไตแบบไม่ใส่สายระบายปัสสาวะจากไต Tubeless percutaneous nephrolithotomy, tubeless (PCNL)

วัสดุและวิธีการ: ดำเนินการโดยใช้รูปแบบการวิจัยเชิงทดลองแบบสุ่มประชากรที่ใช้เป็นกลุ่มผู้ป่วยที่มีโรคนิ่วในไตที่มีข้อบ่งชี้ในการผ่าตัดเจาะผิวหนังส่องกล้องสลายนิ่วในไตจำนวน 82 รายและได้รับการสุ่มโดยระบบคอมพิวเตอร์ เพื่อแบ่งประชากรออกเป็น 2 กลุ่มคือ กลุ่มผู้ป่วยที่ได้รับการใส่วัสดุช่วยห้ามเลือดชนิดเจลาตินในรูที่เจาะจากผิวหนังถึงเนื้อไต และกลุ่มผู้ป่วยที่ไม่ใส่เจลาติน เพื่อเปรียบเทียบผลของการช่วยห้ามเลือดโดยประเมินจากผลเฉลี่ยของระดับที่ค่าความเข้มข้นเลือดที่ลดลง (ฮีโมโกลบิน), ปริมาณเลือดที่ผู้ป่วยได้รับภายหลังการผ่าตัด, ระดับสีของน้ำปัสสาวะ รวมถึงศึกษาผลแทรกซ้อนจากการใส่สารช่วยห้ามเลือดชนิดนี้

ผลการศึกษา: ผลของการวิจัยพบว่าข้อมูลพื้นฐานของผู้ป่วย, ปริมาณและขนาดนิ่วของทั้ง 2 กลุ่มไม่ต่างกันในเชิงสถิติ ระดับความเข้มข้นของเลือดที่ลดลงหรือปริมาณเลือดที่สูญเสียภายหลังการผ่าตัดในกลุ่มที่ใส่วัสดุช่วยห้ามเลือด มีแนวโน้มน้อยกว่ากลุ่มตัวอย่าง (1.2 กรัมต่อเดซิลิตร เทียบกับ 1.5 กรัมต่อเดซิลิตร ตามลำดับ) ($p = 0.26$) กลุ่มที่ใส่วัสดุ ช่วยห้ามเลือดได้รับเลือดหลังผ่าตัดน้อยกว่า (2 ยูนิต จากผู้ป่วยทั้งหมด 41 คน เทียบกับ 4 ยูนิต จากผู้ป่วยทั้งหมด 41 คน; $p = 0.63$) สีของปัสสาวะหลังผ่าตัดวันแรก จางลงเร็วกว่าในกลุ่มที่ใส่สารช่วยห้ามเลือด ($p = 0.03$) ระยะเวลาในการผ่าตัด, ระยะเวลาในการนอนโรงพยาบาล, โอกาสที่นิ่วเหลือค้าง และผลแทรกซ้อนภายหลังการผ่าตัดไม่ต่างกันในทั้ง 2 กลุ่ม

สรุป: การใส่วัสดุช่วยห้ามเลือดชนิดเจลาตินในรูที่เจาะจากผิวหนังถึงเนื้อไตภายหลังการเจาะส่องกล้องสลายนิ่วในไต โดยไม่ใส่สายระบายจากไตมีความปลอดภัย และอาจใช้เป็นตัวเสริมเพื่อช่วยลดระดับการเสียเลือดภายหลังการผ่าตัด ในกรณีที่สงสัยว่ามีภาวะเลือดออกจากรูเจาะส่องกล้องมากผิดปกติภายหลังการเจาะผิวหนังส่องกล้องสลายนิ่วในไต