Translational Research in Urology

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Original Article

Homeostatic Efficacy of Microporous Polysaccharide Hemosphere in Post-Operative Complications Reduction of Tubeless Percutaneous Nephrolithotomy

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HIGHLIGHTS

- Several new agents are considered to reduce bleeding and transfusion during several surgery processes.
- It is reported that using different hemostatic agents prevents bleeding and urinary leakage immediately after PCNL.
- The microporous polysaccharide hemosphere did not affect bleeding reduction, hemoglobin decline, and postoperative blood transfusion, and hospital stay.

ARTICLE INFO

Receive Date: 15 June 2020
Accept Date: 15 July 2020
Avaliable online: 16 August 2020
DOI: 10.22034/TRU.2020.257231.1047

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ABSTRACT

Introduction
Current hemostatic agents are needed to reduce bleeding and transfusion during several surgery processes. Plant-based absorbable surgical hemostatic agents (microporous polysaccharide hemospheres) are proposed for use in surgical wound sites as an absorbable hemostat and in this study, we checked its efficacy.

Methods
This study was run under the Tehran University of Medical Science Ethics Committee observation based on the clinical trial registry criteria (IRCT20190624043991N1). Total numbers of 42 percutaneous nephrolithotomies (PCNL) patients were enrolled, 21 cases hemostatic powder and 21 controls. Hemostatic powder pumped into Amplatz sheath before its extraction.

Results
The mean age of the case and control groups was 42.1±19.5, and 42.1±18.5 years, respectively. The median stone size was 11.3±1.85cm. Overall, the differences between sex, age, stone size, and the location were not statistically significant in the two groups (p-value>0.05). Serum hemoglobin reduction following PCNL was significant in both groups compared to the serum level before surgery (p-value<0.001). However, the difference was not significant between case and control groups postoperatively (p-value=0.727). Yet, postoperative serum creatinine reduction was not significantly different between the two groups compared to preoperative serum levels (p-value>0.05).

Conclusions
The present study showed that microporous polysaccharide hemosphere (MPH) did not affect bleeding reduction, hemoglobin decline, and postoperative blood transfusion, and hospital stay.

Keywords: Hemostatic Agents; Percutaneous Nephrolitotomy; Tubeless Surgeries; Microporous Polysaccharide Hemospheres

Introduction

Hemostasis during the surgery depends on the type of surgery and local surgical hemostasis by the surgeon but some absorbable hemostatic agents are demanded controlling Intra and postoperative bleeding. Therefore, different hemostatic agents have been used several times

and one of the newest ones is microporous polysaccharide hemosphere (MPH). MPH is a local absorbable plant-derived polysaccharide powder hemostat (1). It creates a molecular network leading to the absorption of blood fluid components through polysaccharide hemispheres. Consequently, it concentrates and condenses red blood cells, platelets, and proteins that play a role in forming a coagulation cascade. These processes cause mechanical barrier and natural coagulation products accumulation and prevent bleeding through hemostatic plug formation (1). Compared to a hemostatic matrix-like gelatin absorbable bovine thrombin, MPH has a larger volume, lower weight, and density so covers a bigger surface and absorbs faster (1, 2). The application of the usual technology in controlling bleeding is approved by the food and drug administration (FDA) and is studied in various surgeries (1, 3). Although the effectiveness of the material in hemostasis is reported in some studies, there is confidential evidence. One study discusses the application of the technology in urological surgery explaining its impact on decreasing the incidence of lymphocytes following robotic prostatectomy and lymphadenectomy (4). The findings of the study were not significant and there is no evidence on its impact on bleeding reduction. Percutaneous nephrolithotomy (PCNL) is the common urological surgery for treating large, complicated kidney stones. Every surgery may be accompanied by complications and preventing them can reduce the risk of morbidity and mortality. Intra or postoperative bleeding is one of the most significant complications of PCNL. Different transfusion rates ranging from 1% to 34% are reported in this surgery (5). The risk of delayed bleeding remains for a few weeks postoperatively and 1% of the patients would need angiographic treatment (5). In addition to preoperative measures, intra, and postoperative techniques, and details, several studies have investigated the application of ant fibrinolytic and hemostatic agents in reducing the risk of bleeding (6, 7). Currently, the surgery is usually tubeless and there is no evidence on the effect of nephrostomy hemostatic agent's tract on reducing bleeding (5). No study has evaluated the effect of MPH in tubeless surgeries on bleeding control yet; however, different studies have demonstrated the impact of MPH on bleeding control in various surgeries. Thus, in the present study, we aim at examining the effect of this technology on bleeding control in tubeless PCNL.

Methods

This Trial study conducted at Sina Hospital from January 23, 2016, to October 11, 2018. Patients eligible for entering the study signed the written consent following the approval of the Ethical Committee of Tehran University of Medical Sciences (IR.TUMS.VCR.REC.1398.347 and IRCT20190624043991N1). The inclusion criteria were PCNL candidates with the middle, upper calyx, and pelvis stones>2cm and lower calyx stones>1cm or patients with extracorporeal shock wave lithotripsy failure (it was defined as the presence of stone fragments larger than 1 cm in computed tomography (CT) scan one month after the procedure). Also, anti-coagulants and antiplatelet discounted for the patients with the permission of the physician 10 days before the operation. Patients without the said parameters and/or with a positive history of hepatic disease or coagulopathy excluded from the study. Additionally, all surgeries were tubeless conducted by an experienced urologist using fluoroscopy in the prone position so the patients who experienced intraoperative complications such as pelvis perforation, excessive bleeding, the significant residual stone that preclude tubeless PCNL, were excluded before final analysis. The position and size of the stones were determined via CT scan without contrast preoperatively. Moreover, all patients underwent preoperative kidney-ureter-bladder radiography (KUB); all stones were opaque and radiolucent stones were excluded from the study. In cases of numerous stones, the total size is considered. In cases of individual stones, the biggest was included in the classification. All patients underwent a preoperative physical examination and primary tests including blood count, biochemistry, reticulocyte count, and coagulation profile. Following the termination of surgery and removing the stones, kidneys were examined by nephroscope again. In the case group, the hemostatic powder was pumped into Amplatz sheath before its extraction and at the time of extraction on the trace (3gr plant base absorbable hemostatic agent) and it sutured by one single silk suture and non-pressure dressing maintained.

Patients were divided into two groups regarding MPH administration based on a blocked randomization method: group A (with hemostatic powder) and group B (without hemostatic powder). They underwent blood count, biochemistry and reticulocyte count tests 24 hours postoperatively. The number of wet gases recorded after the surgery. Patients' hematuria was classified into four groups; none, mild, moderate, and high hematuria according to CMYK global criteria (8). This scoring system used a cyan, magenta, yellow, and black color model. This tool applied 5 points to a sample with pure red color and a score of 0 to 4 to samples with different degrees of saturation regarding different values of M and Y, with constant intervals of 80%, 60%, 40%, 20%, and 0%. Scores of 6 to 10 are applied to pure red samples with different degrees of brightness regarding constant intervals of K values of 20%, 40%, 60%, 80%, and 100%. This score was used from 1-4 on the day after surgery and 3 days postoperatively. Pelvicalyceal system obstruction is evaluated by patients' symptoms and if

needed postoperative CT scans. Demographic and clinical information including age, sex, number, size and location of the stone, duration of hospitalization, postoperative complications, postoperative pain, needing blood, creatinine, hemoglobin and hematocrit changes, retic count, and extravasation were recorded in questionnaires. The collected data entered into SPSS. Qualitative variables are demonstrated as frequencies and percentages. As the quantitative data were not normal based on statistical tests, non-parametric tests were used for data analysis. Statistically significant was considered as p-value<0.05.

Results

The 42 patients including 21 cases in each group entered the study. The mean age of the case and control groups was 42.1±19.5, and 42.1±18.5 years, respectively. There were 2 women and 12 men in the control group and 11 women and 11 men in the case group. Location of 0.1%, 31%, and 1% of the stones was in the pelvis, calyx, and inter-calyx space, correspondingly. The mean stone size was 11.3±1.85cm. Overall, the differences between sex, age, stone size, and the location were not statistically significant in the two groups (p-value>0.05). Table 1 demonstrates the comparative mean hemoglobin (HB), creatinine, and retic count before and 24 hours after surgery. There was no statistically significant difference between the said variables pre or postoperatively. Bleeding from the incision was found in five and three patients of the case and control groups, respectively. The variable was recorded based on the number of wet gases used on the surgical site. No significant correlation was observed between the case-control and surgical site bleeding (p-value=0.695). Postoperative blood transfusion was administered for four (one unit) and one patient (2 units) in each group. However, there was no significant correlation between the control group and the need for blood transfusion during hospitalization (p-value=0.695). Moreover, the mean hospital stays (p-value=0.705) and hematuria score (p-value=0.150) was not statistically different in the two groups. The postoperative hematuria state of the patients was compared based on the qualitative criteria of "without hematuria, slight, moderate, gross" and no significant correlation was found between the state of hematuria and the case group (p-value=0.582) (Table 2). Postoperative serum retic count increase was significant in the case group using hemostatic powder compared to the information recorded before surgery (p-value=0.010); however, the difference was not significant in the control group (p-value=0.132). The difference was not significant between the two groups after surgery (p-value=0.758) (Table 3). On the other hand, the mean hemoglobin of the patients of both groups was calculated pre and postoperatively. Serum hemoglobin reduction following PCNL was significant in both groups (w/o hemostatic powder) compared to the serum level before surgery (p-value<0.001). The difference was not significant in the two groups postoperatively (p-value=0.727) (Table 4). Yet, postoperative serum creatinine reduction was not significant in any of the groups compared to preoperative serum levels (p-value>0.05).

Discussion

Findings of the present study show using MPH hemostatic powder does not reduce surgical site bleeding, hospital

Table 1. Mean preoperative & postoperative HB, creatinine, retic count

Variable	Number of patients	Minimum	Maximum	Mean	Std. Deviation	p-value
Preoperative Hemoglobin (g/dl)	40	9.80	17.20	14.3425	1.51892	0.39
Postoperative Hemoglobin (g/dl)	40	9.60	16.10	12.8725	1.64363	
Preoperative Retic count	40	0.50	1.30	0.9025	0.26841	0.46
Postoperative Retic count	40	0.50	1.70	1.0575	0.36647	
Preoperative Serum Creatinine (mg/dl)	40	0.70	6.52	1.2780	0.89039	0.98
Postoperative Serum Creatinine (mg/dl)	40	0.80	5.90	1.2625	0.78730	

Table 2. Postoperative hematuria

Hemostatic powder		Number of patients		Total	p-value
		No Hemostatic powder	No Hemostatic powder		
Quality of hematuria	**No hematuria**	3	1	4	0.582
	Slight	7	5	12	
	Moderate	6	7	13	
	Gross	4	7	11	
Total		20	20	40	-

Table 3. Comparing pre-& post-operative retic count in both groups & comparing postoperative retic count between case and control groups

Groups		Retic count mean (percent)	Retic count mean difference	p-value	Comparing pre-& post-operative retic count (p-value)
Using hemostatic powder	**Preoperative**	1.8850	0.19	1.010	0.758
	Postoperative	1.0750			
Not using hemostatic powder	**Preoperative**	1.9200	0.12	1.132	
	Postoperative	1.0400			

Table 4. Comparing pre-& post-operative hemoglobin in each group & comparing postoperative hemoglobin between case and control

Groups		HB mean (mg/dl)	HB mean difference (mg/dl)	p-value	Comparing postoperative HB (both groups)
Using hemostatic powder	**Preoperative**	14.4150	-1.635	<0.001	1.323
	Postoperative	12.7800			
Not using hemostatic powder	**Preoperative**	14.2700	-1.305	<0.001	
	Postoperative	12.9650			

HB: Hemoglobin

stay, and postoperative hematuria and does not prevent hemoglobin decline when compared to the control group. Moreover, no difference in blood transfusion was observed between the two groups. Findings of a case-control meta-analysis study on 311 patients undergoing tubeless PCNL showed that administering hemostatic agents does not reduce bleeding, though it shortens hospital stays. Studies examined in this meta-analysis did not use MPH (7). It is reported that using different hemostatic agents prevents bleeding and urinary leakage immediately after PCNL (9, 10). Although our study does not refer to this specific case, observations while applying the agent indicates that bleeding immediately stopped at the Amplatz sheath. The agent causes short-lived clot formation, which is absorbed 6 hours after formation (11). Besides, urinary leakage or pelvicalyceal system obstruction was not observed in any of the patients using the agent. Pelvicalyceal system obstruction is a concern in using this agent (12). MPH causes platelet plug formation and blood coagulation by concentrating blood solids. Specific conditions like hypothermia and coagulopathy disturb platelet plug formation. Platelet adhesion does not work well in hypothermic patients (33º-37ºC) (13). Therefore, intraoperative bleeding and the possibility of hypothermia in patients should be taken into consideration while administering such agents because it might affect the effectiveness and proper interpretation of the findings. It is shown that in gross blood loss cases, MPH and tissue fluids cause the absorption of further proteins from Da 410111 to 40,000 Da and is thus hypothetical. This causes the secretion of other proteins into the bleeding site and although this does not disturb coagulation, it prevents multiple reapplications (14). Consequently, this should be taken into consideration to prevent unreliable interpretations of the findings of studies examining the application of the agent in surgery. Some studies cite that fast-absorbing hemostatic agents are appropriate for low-level bleeding conditions (14, 15). MPH is also used in other surgeries and different results are reported. According to the study of Payne et al, this agent did not reduce complications like hematoma formation and wound infection in total knee arthroplasty; instead, blood loss was more in the case group. The said findings are in contrast with ours (1). Findings of a study evaluating the effect of the agent on microsurgical brain tumor resection indicate that it was fast and effective in controlling hemostasis and does not have complications (16). Similar findings were reported in a study evaluating the application of MPH in cardiothoracic surgical procedures. In this study, the agent reduces hemostasis duration, postoperative blood transfusion, and chest tube output (17). Another study reports the agent is not effective in reducing the incidence of postoperative lymphocell in robotic prostatectomy along with lymphadenectomy (4).

Conclusions

Considering different results on the effect of MPH on controlling hemostasis in different surgeries and the lack of similar studies on the effect of the agent on PCNL, the present study was conducted. Our findings showed

that MPH did not affect bleeding reduction, HB decline, postoperative blood transfusion, and hospital stay. Limitations of the study include a small sample size and not considering conditions leading to disturbance of result interpretation. The duration of patients' follows up was also short.

Authors' contributions
All authors contributed equally.

Acknowledgments
Special thanks to Urology Research Center (URC), Tehran University of Medical Sciences (TUMS), and Bita Pourmand.

Conflict of interest
All authors claim that there is not any potential competing or conflict of interest.

Funding
There was no founding.

Ethics statement
The study was under the Tehran University of Medical Sciences Ethical Committee (IR.TUMS.VCR.REC.1398.347 and IRCT20190624043991N1).

Data availability
Data will be provided by the corresponding author on request.

Abbreviations

CT	Computed tomography
FDA	Food and drug administration
HB	Hemoglobin
KUB	Kidney-ureter-bladder radiography
MPH	Microporous polysaccharide hemosphere
PCNL	Percutaneous nephrolithotomy

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How to cite this article
Aghamir SMK, Ramezani Binabaj M, Khatami M, Fattahi B. Homeostatic Efficacy of Microporous Polysaccharide Hemosphere in Post-Operative Complications Reduction of Tubeless Percutaneous Nephrolithotomy. Translational Research in Urology. 2020 Jul;2(2):83-88.
DOI: 10.22034/tru.2020.257231.1047
URL: http://www.transresurology.com/article_119549.html