BİLİM VE TİCARET PLATFORMU

YAZARLAR;
MUSTAFA OKAN ISTANBULLUOĞLU
ILYAS TUNCER

EKİM 2024

ANKAFERD : TÜRKİYENİN İLK RUHSATLI İLACI

Yayın Ekibi

YAZARLAR

MUSTAFA OKAN ISTANBULLUOĞLU
ILYAS TUNCER

DERGİ DİREKTÖRÜ

M. UBEYD KORBEY

İÇERİK DİREKTÖRÜ

SEDA YAĞMUR MERT

SANAT DİREKTÖRÜ

TÜLAY KURT

FOTOĞRAF

SEHER KURT

YAYIN YERİ

BILIMVETICARET.ORG.TR

Dijital Dergi

İLETİŞİM
0536 744 0441
WWW.BILIMVETICARET.ORG.TR

GENEL BAŞKAN

Ümit Korkmaz

BİLİM VE TİCARET PLATFORMU

BİLİM VE TİCARET PLATFORMU, hayatta tek değişmeyen olgunun değişim olduğu prensibi ile ülkemizin hem bilime hem ticarete yönelik inovatif projeler üretilmesini, araştırma ve geliştirme yapılmasını desteklemek, teşvik etmek bu alanda kadınlarımızın da kalkınmasına daha fazla destek olmak, onların katılımını sağlamak, bu yönde çalışmaları sürdürmek için kurulmuştur. Bu hedeften yola çıkarak toplumun gelişmesine katkı sağlama yönünde, sosyal alanlar, kültür, sanat, spor, eğitim, sağlık, çevre bilinci, tüketici bilinci, insan hakları, iş hayatı, ekonomi, demokrasi ve siyaset gibi konularda bu alanda bireyleri teşvik ederek Değişim, İnovasyon, proje, araştırma, geliştirme konularına toplumun ilgisini çekme farkındalığını meydana getirip, bilim ile ticaretin birbirini desteklediği oluşumlara gerekli kaynak ve desteğin sağlanmasına öncülük etmek temel amaçtır.

Tüm bunların ışığında, Bilim ve Ticaret Platformu olarak yenilik içeren projelerin hayata geçmesini mevcut durumdan çok daha geniş kapsamlı desteklenmesini amaçlanmaktadır. Özellikle kadınlarımızın kalkınmasına destek sağlamak amacıyla daha fazla bu değişim ve inovasyon eksenli çalışmalar, bilim ve ticari hayatın içinde olmaları ön planda dikkate alınır. Tüm hedefler ulaşmak için etkili ve sürdürülebilir faaliyetler, seminer, konferans, yayın ve sosyal medya gibi iletişim vasıtaları ile geniş kitlelere ulaştırmayı, kamuoyu oluşturup, kamu kurumlarının duyarlılığını artırmayı da hedeflemektedir.

GENEL KOORDİNATÖR

Seda Yağmur Mert

Bilim ve Ticaret Platformu, ülkemizin bilimsel kökenli üretimlerini, ticari hayat ile buluşturup, bunların sadece belgelerde kalmadan, ciddi ekonomik getirileri olacak projeler olarak hayata geçirmek için çalışır. Ayrıca, hali hazırda ilmi yönü incelenmemiş, ancak uygulamada kendine yer edinmiş, birçok faaliyetin, bilimsel alanda incelenmesine ön ayak olarak, bilimsel kapasitemizin yükselmesine katkı sağlayarak ülkemizde ve dünyada bu alanlarda değişimi başlatıp, bunun sürdürülebilir olmasını amaçlamaktadır.

BİLİM VE TİCARET
PLATFORMU

İÇERİKLER

DÜNYADA KANAMA DURDURUCULAR:

SENTETİK DURDURUCULARA KARŞI DOĞAL ANKAFERD

“Ankaferd BloodStopper ürününün içeriği tamamen bitkiseldir.”

Kaynak: https://tr.wikipedia.org/wiki/Ankaferd_BloodStopper

Ankaferd BloodStopper, vücut dışı yaralanmalar, travmatik kesikler, diş operasyonları, spontan ya da cerrahi girişimler sonrası oluşan minör ve majör kanamaların durdurulmasında kullanılan tıbbi bir üründür.

Selüloz Bazlı Hemostatikler ; Okside selülozdan imal edilen bu hemostatik ajan öncelikli olarak kanayan dokuya tampon amacıyla geliştirilmiştir. Pıhtı oluşumuna uygun ortamı sağlamak için dokuyu uyarma (indüklemek) amacıyla tasarlanan selüloz bazlı bu kanama durdurucu ajanlar, sadece küçük kanamaların lokal yönetiminde yardımcı olarak kullanılır.

Mikrofibriler Kollajenler; 1970 yılında geliştirilen ve hammaddesi sığır alt derisi olan, topikal olarak kanama bölgesinde düzensiz yüzeylere yapışarak hemostatik etki oluşturan kanama durdurucu türüdür. Beyaz, yumuşak görünen kuru toz halde bir malzemedir

Anastomotik Yapıştırıcılar; Cerrahi işlemlerde ve travmada hemostaz olarak kullanılan anastomik yapıştırıcılar; jelatin, trombin ve fibrinojen içeren ajanlar olmak üzere üçe ayrılır.

Hemostatlar veya bilinen diğer adıyla kanama durdurucular, bir doku veya organda meydana gelen kanamayı durdurmak için kanamanın oluştuğu bölge üzerinde kullanılan hemostatik ajanlardır. Kanamanın durma süreci ise hemostaz olarak tanımlanır.

Kitin ve Kitosan Esaslı Hemostatik Ajanlar; Hayvanlar üzerinde elde edilen veriler etken madde olarak kitosan asetat içeren hemostatların kanamayı azalttığı gözlemlenmiştir. Günümüzde medikal alanda oldukça önem kazanan kitosan, yara tedavisini %30 oranında hızlandırdığı için hayvan ve insanlar için yara bandı yapımından, kanama durdurucu hemostatik madde yapımına kadar birçok alanda ham madde olarak kullanılmaktadır.

Zeolit Kanama Durdurucu Ajan; Zeolit, doğada doğal bir mineral olarak bulunan ve ekzotermik reaksiyonla hasar gören doku üzerindeki suyu emerek işlev görmesinden dolayı, pıhtılaşma faktörlerinin ve kemik iliği dokusunda bulunan hücrelerin olgunlaşmasının ardından kana geçerken parçalanması sonucu oluşan trombositlerin yoğunluğunu arttırarak pıhtı oluşumunu indüklemektedir.

A NEW HEMOSTATİC AGENT (ANKAFERD BLOOD STOPPER) İN TUBELESS PERCUTANEOUS NEPHROLİTHOTOMY: A PROSPECTİVE RANDOMİZED STUDY

YAZAR : MUSTAFA OKAN ISTANBULLUOĞLU, MD,1 MEHMET KAYNAR, MD,2 TUFAN ÇİÇEK, MD,3
MURAT KOŞAN, MD,3 BÜLENT ÖZTÜRK, MD,3 AND HAKAN ÖZKARDEŞ, MD4

Abstract Purpose: The present study evaluates the efficiency and reliability of a hemostatic agent ABS (Ankaferd Blood Stopper) in tubeless percutaneous nephrolithotomy (PCNL). Patients and Methods: A total of 90 patients were divided into two subgroups. The first group had ABS applied during the intervention, whereas the control group underwent regular tubeless PCNL in this prospective randomized study. Age, stone size, operative time, postoperative hemoglobin change, renal parenchyma thickness, postoperative ureteral catheter removal time, access number, nephroscope time, blood transfusion rate, serum creatinine change, complication rate, visual analogue scale (VAS), and hospitalization time were compared between the two groups. Results: Preoperative and postoperative data obtained from both groups were compared. No statistically meaningful differences were found related to variables of mean age, stone size, access number, serum creatinine change, operative time, renal parenchyma thickness, VAS scores, and hospitalization period. Whereas the nephroscope time (minutes) was longer in the ABS group (Group 1 [G1]:3, 33 – 1, 72 vs G2:2, 62 – 1, 43, P = 0.035), hemoglobin (Hb) decrease, and urine clarity time were statistically lower compared with the control group. Hb decrease was (mg/dL) (G1: 1.40 – 1.04 vs G2: 1.84 – 1.15, P = 0.034), and urine clarity time was (hour) (G1: 9.60 – 5.50 vs G2: 11.95 – 4.71, P = 0.012), respectively. Complications were encountered in three (6.6%) patients of the ABS group and in four (8.8%) of the control group. Conclusion: ABS is an efficient and reliable hemostatic agent in tubeless PCNL. Comparative studies are needed, however, with other hemostatic agents that might be applied in tubeless PCNL.

Introduction Percutaneous nephrolithotomy (PCNL) is a wellestablished technique for the management of urinary stone disease. Nephrostomy catheters of various diameters are used after standard PCNL operations to provide renal drainage and to tamponade bleeding. In many tubeless PCNL applications, to safeguard against extravasation and hemorrhage, a Double-J or ureteral catheter is used. In stone-free and other cases without serious bleeding and perforation in the collecting system during the operation, totally tubeless PCNL can be safely applied.1 The aim of various management options of PCNL is to make it more reliable and less morbid, and hence tubeless PCNL might be opted for because it decreases the required hospitalization period and time to return to normal activities, as well as analgesia requirements.2 One of the requirements for tubeless PCNL is low bleeding, and therefore various hemostatic agents have been used (fibrin glue, gelatin matrix, oxidized cellulose purified gelatin, etc.) Thus, tubeless PCNL interventions were considered to be more reliable and safe.3–5 The present study is about the use of ABS as a hemostatic agent in tubeless PCNL interventions. ABS is a combination of five plant extracts that have been known in Turkish folkloric medicine as hemostatic agents for centuries. The basic action mechanism of ABS is the formation of an encapsulated protein network that provides focal points for vital erythrocyte aggregation.6 ABS is patented with the number 2007-0-114485, produced by BirgiMefar Group, (www.mefar.com), and marketed all over the world by Ankaferd _ Ilac, Kozmetik A.Sx In this prospective randomized study, we evaluated the safety and efficacy of ABS as a hemostatic agent in tubeless PCNL interventions. To our best knowledge, this is the first study on the use of ABS in urolithiasis.

Patients and Methods Patients In this prospective randomized study, we evaluated 90 patients who had undergone PCNL because of renal and/or upper ureter stones. Of these patients, 45 underwent tubeless PCNL with the use of ABS as a hemostatic agent (group 1 [G1]), whereas the remaining ones underwent tubeless PCNL without ABS (group 2 [G2]). The study was approved by the local ethical committee, and patients signed an informed consent form in order to be enrolled in the present study. Before the interventions, complete blood cell count, serum creatinine level, and urine culture were performed. Radiologic evaluation was performed with ultrasonography, intravenous urography (except those with a raised serum creatinine level), and noncontrast CT. Inclusion criteria were stone free or clinically insignificant residual fragments (CIRF) (<4 mm) at the end of the procedure and an intact pelvicaliceal system. Solitary kidney, kidneys with congenital anomalies, patients who underwent bilateral simultaneous PCNL, more than two accesses within a single session, persistent severe hemorrhage, and pelvicaliceal sytem perforation were exclusion criteria in the present study. Prophylactic wide-spectrum antibiotics were administered to patients before the procedure. Patients with bacteriuria were treated according to culture and sensitivity results and underwent tubeless PCNL afterward. Surgical technique The appropriate calix was determined approximately before renal access, and parenchyma thickness was measured using noncontrast CT. Under spinal anesthesia, with cystoscopy aid, a 7F ureteral catheter was placed into the ipsilateral ureter and then attached to the urethral Foley catheter. After that, the patient was brought to the prone position. All percutaneous accesses were performed in the prone position. Access to the selected calix was performed with the aid of Carm fluoroscopy and an 18-gauge needle. After entering the collecting system with a guidewire, dilation was performed using Amplatz dilators, and a 30F Amplatz sheath was placed through which a 26F rigid nephroscope was inserted; stone fragmentation was conducted using a pneumatic lithotripter. At the end of the operation, stone-free patients and patients with CIRF (<4 mm) were determined fluoroscopically and with a flexible scope and in the the postoperative period using plain radiography. The distal end of the ureteral catheters were inserted into the Foley catheters to enable drainage. All the patients who underwent the above described procedure were randomized into two groups in the operating room on completion using systematic sampling technique. Forty-five patients in G1 were administered ABS tamponade, whereas 45 patients in G2, the control group, were not. A 4 · 6 cm sheath sponge soaked with ABS was rolled. To pull the sponge back, the proximal end of the sponge was fixed on No. 1 surgical silk. To determine the position of the rolled sponge, the 2 cm distal end was soaked in dilute urography solution. The prepared sponge was sent with a forceps through the sheath into the kidney. The sponge was visualized with the nephroscope and kept in the kidney for 2 minutes in the parenchyma to enable tamponade (Fig. 1). After 2 minutes, the sponge and the sheath were withdrawn. In G2, the sheath was kept in the access site like the ABS soaked tamponade for 2 minutes for the sheer tamponade effect of the sheath itself and then withdrawn before the operation was concluded. In both groups, patients' skins were closed with a single silk stitch.

Evaluation Age, stone size, operative time, postoperative hemoglobin (Hb) change, renal parenchyma thickness, ureteral catheter removal time, access number, blood transfusion rate, creatinine change, complication rate, visual analogue scale (VAS) scores, and hospitalization time of the groups were compared statistically. In all patients, the Hb level was checked 16 hours after the operation and in doubt regarding hemorrhage or urinoma driven perinephric collection, ultrasonography was performed. Ureteral and Foley catheter removal decision was made based on patients' urine color (light pink-tinged fluid in the urobag). Urine color was observed by the clinical nurse, blind edto both groups, at regular intervals. Differences in percentages (qualitative variables) were analyzed using the chi-square test. Differences between means were evaluated with the Student t test and Mann-Whitney U test. Statistical analyses were performed using the SPSS 15.0 package program. P value of <0.05 was considered to be statistically significant.

Results G1 consisted of 29 men and 16 women patients and G2 of 33 men and 12 women. Mean patient age in G1 and G2 was 49, 84 – 15, 08 (range 21–71) and 49, 86 – 11, 83 (range 25–76) years, respectively (P = 0.994). Stone location in G1 was lower calix (n = 9), pelvis (n = 7), multiple calices (n = 16), upper ureter (n = 12), and upper calix (n = 1) and in G2, lower calix (n = 11), pelvis (n = 6), multiple calices (n = 16), upper ureter (n = 10), and upper calix (n = 2). Supracostal access (between the 11th and 12th ribs) was performed in seven patients in G1 and in eight patients in G2 (Table 1). No significant changes were found between the groups in terms of mean stone volume, operative time, mean hospitalization time, access number, renal parenchyma thickness, and VAS scores (Table 2). Hemoglobin drop and hematuria loss and catheter removal times were significantly shorter in G1, however (P < 0.05). Nephroscope time, however, was significantly longer in G1 (P < 0.05). Complications were encountered in G1 in three (6.6%) and in G2 in four (8.8%) patients. One patient with hematuria in G1 received a diagnosis of pseudoaneurysm on renal angiography. Angioembolization was performed to control bleeding. In two patients, a minimal pleural effusion was determined. Of the four patients in G2, colic emerged in two patients on the third day of the postoperative period. Of these two patients, one was considered to have a blood clot.

Conservative treatment was applied in the former and in the latter, a stone was defined in the ureter; ureteroscopy was performed. In another patient of G2, minimal pleural effusion was seen, and in a further one during the second postoperative day, continuing abdominal pain from a perirenal urinoma was diagnosed and treated conservatively. Blood transfusion was needed only in the patient with pseudoaneurysm.

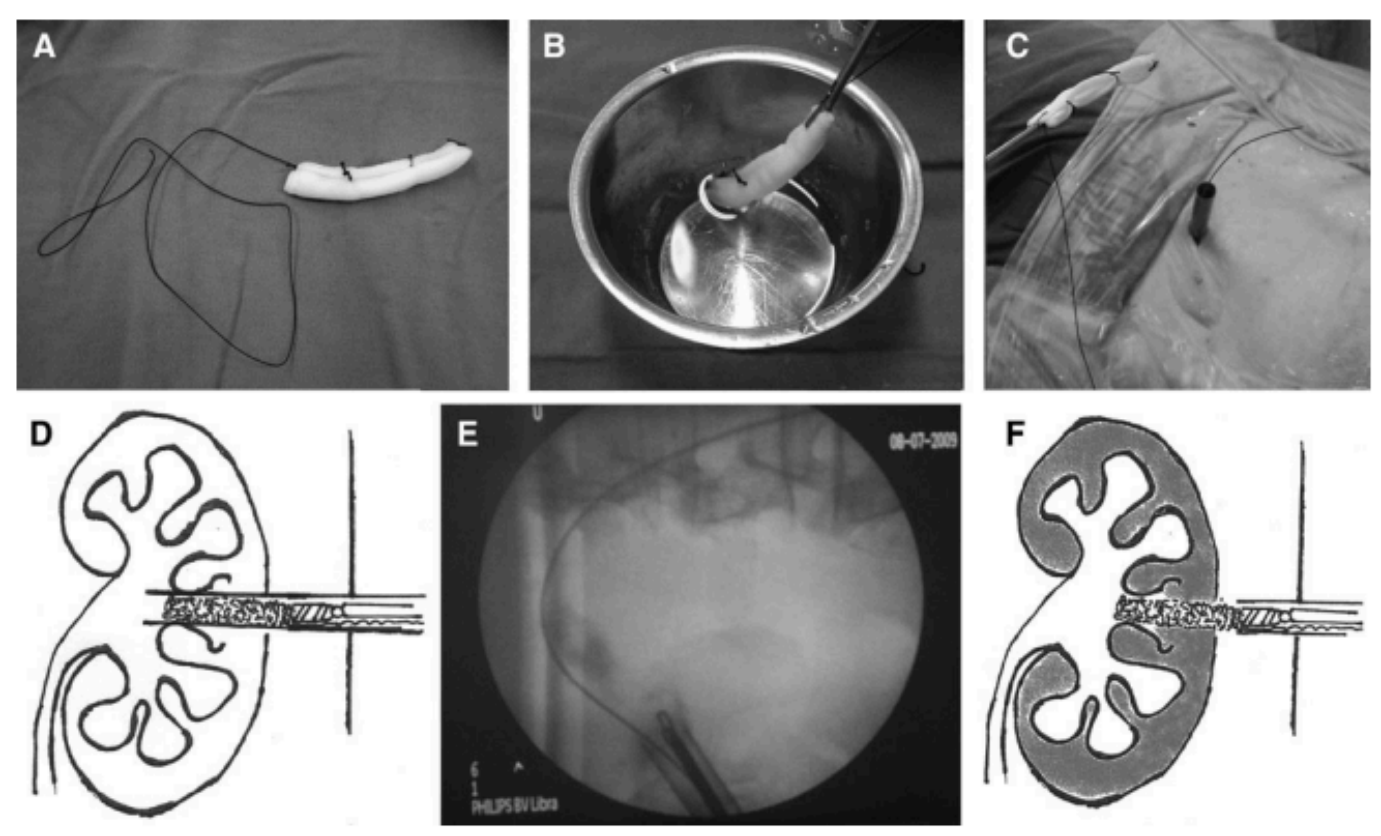

FIG. 1. Enrolled sponge fixed with silk suture (A); Ankaferd Blood Stopper and contrast fluid soak (B); placement into parenchyma through the sheath using forceps (C); nephroscopic and schematic image of the parenchyma with prepared sponge (D, E, F).

Discussion The European Association of Urology guideline suggests that in uncomplicated cases, tubeless (without nephrostomy tube) or totally tubeless (without nephrostomy tube and without ureteral stent) is a safe alternative with a shorter hospitalization period.7 Bellman and associates2 have also determined tubeless percutaneous renal surgery as a safe, efficient, and costeffective treatment modality because of decreased analgesia requirement, hospital stay, and recovery time.2 Many endourologists still consider tubeless PCNL as adventurous and risky, however, and thus hinder its widespread adoption in clinical practice.8 In particular, some risks, such as urinary leakage and bleeding in the access tract, are considered complex by endourologists and thus they prefer tubeless or totally tubeless PCNL only in painstakingly chosen cases. In some articles, the advantages and disadvantages of hemostatic agents that have been used after tubeless PCNL to decrease urinary leakage, bleeding, and morbidity are discussed.9–12 In the present study, ABS has been used as a hemostatic agent. ABS comprises a standardized mixture of the plants Thymus vulgaris, Glycyrrhiza glabra, Vitis vinifera, Alpinia officinarum, and Urtica dioica.6 Each of these plants has some effect on the endothelium, blood cells, angiogenesis, cellular proliferation, vascular dynamics, and cell mediators. ABS represents its unique hemostatic effect by promoting the very rapid (<1 second) formation of a protein network, which acts as an anchor for vital physiologic erythrocyte aggregation mechanism of action independent of clotting factors.6 ABS, 100 mL, comprises a standardized mixture of plants, including 5 mg T vulgaris, 9 mg G glabra, 8 mg V vinifera, 7 mg A officinarum, and 6 mg U dioica. It has been used in Turkish traditional medicine as a hemostatic agent in Anatolia for centuries. It has been approved by the Ministry of Health in Turkey and is a licensed hemostatic agent acting as a topical hemostatic agent for mucocutaneous hemorrhages (www.ankaferd.com). Studies investigating the hemostatic effects and ultrastructural and morphologic analyses have revealed that when ABS was added to plasma or serum, it induced a very rapid formation of a protein network and erythrocyte aggregation without affecting the levels of coagulation factors II, V, VII, VIII, IX, X, XI, and XIII. After ABS addition, plasma fibrinogen activity and antigen levels decreased, in parallel with the prolonged thrombin time.

Total protein, albumin, and globulin levels decreased after the addition of ABS as well. These findings suggest that ABS stimulates the formation of an encapsulated protein network that provides focal points for erythrocyte aggregation on contact with blood.6 In various studies, the hemostatic effect of ABS has been investigated and used.13–15 In tonsillectomy,16 partial nephrectomy,17 and gastrointestinal bleeding,18 it has been used safely and efficiently without any reported local adverse effect or systemic toxicity. Because the hemostatic effect of ABS is unrelated to coagulation factors and platelets, it can also be used to control acute bleeding.6,19 It is available in different commercial forms such as tampon (2.5 cm · 7 cm-3 mL), (5cm · 7.5cm-10 mL), (20 cm · 20 cm100 mL), spray 5 mL, 10 mL, 25 mL, 50 mL, and 100 mL, and ampules 24 units · 2 mL per box without any known adverse effects or adverse interactions with drugs used by patients. Moreover, it is also known to be hypoallergenic. Shah and colleagues5 used fibrin glue (TISSEEL) sealant as a hemostatic agent in their study. There was no difference in the hematocrit decrease and blood transfusion requirement in the two groups. The patients who received fibrin glue, however, reported less postoperative pain and needed less analgesia. The underlying cause might be less retroperitoneal blood and urine oozing resulting in less postoperative pain. In the present study, hemoglobin drop and urine color clarity time were significantly shorter in G1 compared with G2 ($P < 0.05$). Nephroscope time of G1, however, was longer than that of G2. Hb drop and urine color clarity time can be explained with the hemostatic effect of ABS. The reason for the prolonged nephroscope time of G1 is the use of the scope for control during the placement of the ABS soaked sponge into the parenchyma. The prolonged nephroscope time can be considered as the disadvantage of the present study. Therefore, it has to be considered that endoscopy time is not within the nephroscope time. Nephroscope time, in the present study, is the time measured after access to the kidney and thus defines the fluoroscopy time. The study of Singh and coworkers4 conducted with absorbable porcine gelatin (SPONGOSTAN) revealed no statistically significant differences in the control and study group regarding hematocrit drop and time to return to work. Hospitalization, urinary extravasation, and analgesia requirement were, however, significantly lower in the patients who had undergone gelatin sealant assisted tubeless PCNL. Another study concluded that hemostatic gelatin matrix remained as a fine particulate suspension in both normal and sanguineous urine.20 Because SPONGOSTAN is totally absorbable in the human body within a long period, 4 to 5 weeks, the Double-J stents were removed after 4 to 6 weeks because of the expectancy that such agents may block and obstruct the pelvicaliceal system, hinder drainage, and trigger even future stone formation. The underlying reason of low urinary extravasation is not clear, because it might be a result of absorbable gelatine hemosealant use or the presence of an ureteral catheter. They found that hospitalization and analgesia requirement was significantly lower. This might be related as in other studies to the lack of nephrostomy tubes.2,21 One of the major advantages of our method is the low existence of one of the major complications of PCNL, namely hemorrhage. The lack of a statistically significant VAS in both groups is related to the nonexistence of a nephrostomy tube in both groups. Urinoma was seen in one patient of G2. Aghamir and colleagues9 used oxidized cellulose (SURGICEL) to seal the nephrostomy tract after totally tubeless PCNL; however, sealing the nephrostomy tract with oxidized cellulose after totally tubeless PCNL did not decrease bleeding or extravasation. Because their study was conducted with small groups, larger groups are needed to determine the reliability of the hemostatic effect of oxidized cellulose. The gel matrix hemostatic sealant (FLOSEAL) 22,23 was used in tubeless PCNL and mini-PCNL, resulting inreduced postoperative pain and analgesic requirement. The risk of bleeding or urinary leakage was not reduced, however. In their randomized control study, Cormio and associates3 defined the efficacy and safety of absorbable equine collagen matrix (TachoSil). Like in other studies, it was used as a hemosealing agent for the PCNL tract and compared with nephrostomy tube placement. With regard to analgesic requirement, VAS scores, and Hb decrease, there was not any difference in their control and study group. TachoSil, however, provided better tract control (bleeding and urinary leakage) and a shorter hospitalization period compared with nephrostomy tube placement. In percutaneous nephrolithotomy, parenchyma thickness is among the factors having an impact on bleeding. Atrophic parenchyma is associated with reduced blood loss.24 Yet, in the above mentioned studies, this issue was not addressed. In the present study, it was measured and compared because of its possible effect on hemorrhage. There was no statistically significant difference regarding parenchyma thickness in G1 and G2, however. In the present prospective randomized study, there was not a statistically significant difference between G1 and G2 between VAS scores and analgesia requirement. The present study is prospective, because studies randomized at the end of a procedure could introduce selection bias into the study design and will create results favoring one technique over another. Hence, in the present study, patients were randomized and divided as G1 and G2 before the intervention Hb decrease between G1 and G2 were statistically significant. In the other studies, parenchyma thickness was not considered; however, although we considered parenchyma thickness and access number, there was not a statistically significant difference in both groups. We consider that the hemostatic agents used in other studies might have a sealant or a mechanic tamponade effect on urinary leakage and bleeding until they are absorbed; ABS might, because of its hemostatic effect ,be more suitable in tubeless PCNL.

Conclusion Hb drop and hematuria, considered to be among the major complications of tubeless PCNL, are decreased with the use of ABS in the present study. Because there were not any differences in the access numbers and parenchyma thickness, among the perioperative hemorrhage factors, was considered as the effect of ABS. The disadvantage of the study was prolonged nephroscope time. Interestingly, compared with other studies, there was not a difference in VAS scores or analgesia requirement and hospitalization period in G1 and G2. It has to be considered that Hb drop and hematuria decrease might be attributed to the hemostatic effect of the sponge as well. Although further studies are needed to compare the efficiency of ABS to other hemostatic agents as well as to the tamponade effect of sponge per se, we believe that it is a safe and reliable one in tubeless or totally tubeless PCNL interventions leading to expectations that these procedures might find widespread use among endourologists. Disclosure Statement No competing financial interests exist.

References 1. Istanbulluoglu MO, Ozturk B, Gonen M, et al. Effectiveness of totally tubeless percutaneous nephrolithotomy in selected patients: A prospective randomized study. Int Urol Nephrol 2009;41:541–545. 2. Bellman GC, Davidoff R, Candela J, et al. Tubeless percutaneous renal surgery. J Urol 1997;157:1578–1582. 3. Cormio L, Perrone A, Di Fino G, et al. TachoSil() sealed tubeless percutaneous nephrolithotomy to reduce urine leakage and bleeding: Outcome of a randomized controlled study. J Urol 2012;188:145–150. 4. Singh I, Saran RN, Jain M. Does sealing of the tract with absorbable gelatin (Spongostan) facilitate tubeless PCNL? A prospective study. J Endourol 2008;22:2485–2493. 5. Shah HN, Hegde S, Shah JN, et al. A prospective, randomized trial evaluating the safety and efficacy of fibrin sealant in tubeless percutaneous nephrolithotomy. J Urol 2006;176: 2488–2493. 6. Go¨ker H, Haznedaroglu IC, Erc¸etin S et al. Haemostatic actions of the folkloric medicinal plant extract Ankaferd BloodStopper. J Int Med Res 2008;36:1447–1448. 7. Tu¨rk C, Knoll T, Petrik A, et al. Guidelines on Urolithiasis. European Association of Urology 2012. Available at: http://www.uroweb.org/gls/pdf/20_Urolithiasis_LR%20March %2013%202012.pdf. Accessed: July 13, 2013. 8. Shah HN, Kausik VB, Hegde SS, et al. Tubeless percutaneous nephrolithotomy: A prospective feasibility study and review of previous reports. BJU Int 2005;96:879–883. 9. Aghamir SM, Khazaeli MH, Meisami A. Use of Surgicel for sealing nephrostomy tract after totally tubeless percutaneous nephrolithotomy. J Endourol 2006;20:293–295. 10. Lee DI, Uribe C, Eichel L, et al. Sealing percutaneous nephrolithotomy tracts with gelatin matrix hemostatic sealant: Initial clinical use. J Urol 2004;171:575–578. 11. Mikhail AA, Kaptein JS, Bellman GC. Use of fibrin glue in percutaneous nephrolithotomy. Urology 2003;61:910–914. 12. Noller MW, Baughman SM, Morey AF, Auge BK. Fibrin sealant enables tubeless percutaneous stone surgery. J Urol 2004;172:166–169. 13. Kilic O, Gonen M, Acar K, et al. Haemostatic role and histopathological effects of a new haemostatic agent in a rat bladder haemorrhage model: An experimental trial. BJU Int 2010;105:1722–175. 14. Huri E, Akgu¨l T, Ayyildiz A, et al. Hemostatic role of a folkloric medicinal plant extract in a rat partial nephrectomy model: Controlled experimental trial. J Urol 2009;181:2349–2354. 15. Tokgo¨z H, Karakaya K, Hanci V, et al. Protective value of a folkloric medicinal plant extract against mortality and hemorrhage in a life-threatening renal trauma model. Urology 2010;75:1515–1519. 16. Teker AM, Korkut AY, Gedikli O, Kahya V. Prospective, controlled clinical trial of Ankaferd Blood Stopper in children undergoing tonsillectomy. Int J Pediatr Otorhinolaryngol 2009;73:1742–1745. 17. Huri E, Akgu¨l T, Ayyildiz A, et al. First clinical experience of Ankaferd BloodStopper as a hemostatic agent in partial nephrectomy. Kaohsiung J Med Sci 2010;26:493–495. 18. Karaman A, Baskol M, Gursoy S, et al. Endoscopic topical application of Ankaferd Blood Stopper in gastrointestinal bleeding. J Altern Complement Med 2012;18:65–68. 19. Kurt M, Oztas E, Kuran S, et al. Tandem oral, rectal, and nasal administrations of Ankaferd Blood Stopper to control profuse bleeding leading to hemodynamic instability. Am J Emerg Med 2009;27:631. 20. Uribe CA, Eichel L, Khonsari S, et al. What happens to hemostatic agents in contact with urine? An in vitro study. J Endourol 2005;19:312–317. 21. Agrawal MS, Agrawal M, Gupta A, et al. A randomized comparison of tubeless and standard percutaneous nephrolithotomy. J Endourol 2008;22:439–442. 22. Borin JF, Sala LG, Eichel L, et al. Tubeless percutaneous nephrolithotomy using hemostatic gelatin matrix. J Endourol 2005;19:614–617. 23. Nagele U, Schilling D, Anastasiadis AG, et al. Closing the tract of mini-percutaneous nephrolithotomy with gelatine matrix hemostatic sealant can replace nephrostomy tube placement. Urology 2006;68:489–494. 24. Kukreja R, Desai M, Patel S, et al. Factors affecting blood loss during percutaneous nephrolithotomy: Prospective study. J Endourol 2004;18:715–722.

INSTANT CONTROL OF FUNDAL VARİCEAL BLEEDİNG WİTH A FOLKLORİC MEDİCİNAL PLANT EXTRACT: ANKAFERD BLOOD STOPPER

YAZAR : ILYAS TUNCER, MD, LEVENT DOGANAY, MD, OGUZHAN OZTURK, MD

Variceal bleeding is one of the fatal complications of portal hypertension.1 As many as 33% of the patients with cirrhosis have gastric varices, and one fourth of them will bleed within 2 years.2 Gastric variceal bleeding, compared with bleeding from esophageal varices, has a poorer prognosis, is associated to more blood loss, and has higher rebleeding and mortality rates.3 Ankaferd Blood Stopper (ABS) (Ankaferd Sag˘lik U¨ru¨nleri, A.S¸., Istanbul, Turkey), a standardized mixture of 5 plants, has been used historically as an hemostatic agent, yet its mechanism of action remains unknown.4The simplicity of its application and its effectiveness make it an attractive alternative treatment for miscellaneous hemorrhagic conditions. Its use is approved in Turkey for external hemorrhage and dental surgery bleeding. The local ethics committee at our institution approved its use in GI hemorrhage. As of May 2009, according to our English MEDLINE search, there are only 3 case reports demonstrating the effects of ABS in GI hemorrhage.5-7 Here we present a case of fundal variceal hemorrhage that was managed with endoscopic administration of this novel agent.

CASE REPORT

A 70-year-old man was admitted to the hospital with upper GI bleeding. He stated that he had vomited fresh blood. He had cirrhosis caused by hepatitis B for the past 3 years. His blood pressure was 85/50 mm Hg and heart rate was 85 beats per minute. His hemoglobin level was 6.9 g/dL, platelet count was 95,000/mm3 , serum creatinine was 1.9 mg/dL, prothrombin time was 20.4 seconds (upper limit 16 seconds), and international normalized ratio was 1.45. Somatostatin infusion was started, and 2 units of packed red blood cells were transfused. Upper endoscopy was performed at the 10th hour and revealed grade 1-2 esophageal varices without any stigmata of bleeding and actively bleeding and tumor-shaped varices in the fundus (F3, Lg-f; graded according to the Japanese Society for Portal Hypertension8) (Fig. 1A). Before the procedure, informed consent regarding the experimental use of ABS was obtained. Three vials (2 mL each) of ABS were sprayed through the washing pipe over the bleeding site (Fig. 1B). Immediate hemostasis was achieved in 18 seconds without any further treatment (Fig. 1C and D). On day 5, another endoscopic examination was performed and revealed clean surface fundal varices (Fig. 2), and a successful variceal obturation by cyanoacrylate injection was performed. On day 7, at discharge, the patient's final hemoglobin level was 9.5 mg/dL. No further bleeding episode occurred in the hospital or during outpatient follow-up.

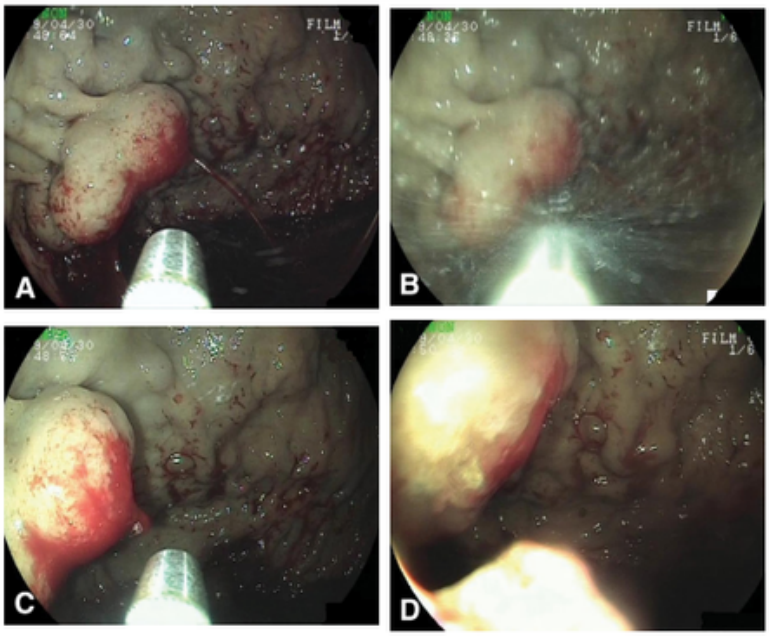

FİGURE 1.
A, SPURTİNG HEMORRHAGE FROM TUMOR-SHAPED FUNDAL VARİCES İS SHOWN.
B, ABS İS SPRAYED OVER THE LESİON THROUGH A WASHİNG PİPE.
C, BLEEDİNG STOPS İN 18 SECONDS.
D, TWO MİNUTES AFTER THE APPLİCATİON OF ABS, A PROTEİN NETWORK, WHİCH GİVES THE YELLOWİSH COLOR, İS FORMED AND COVERS THE BLEEDİNG SİTE. THE HEMORRHAGE İS COMPLETELY CONTROLLED.

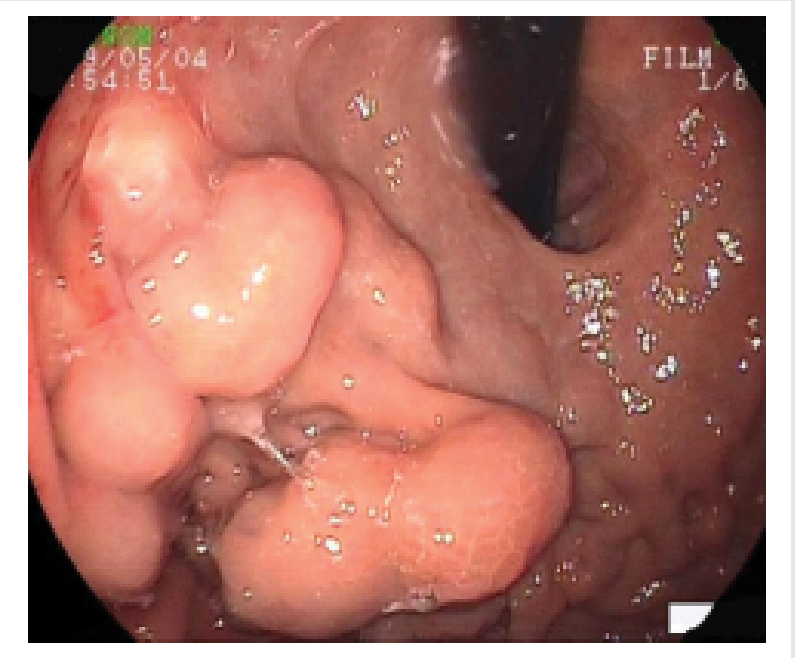

FİGURE 2.
ON DAY 5, A SECOND ENDOSCOPY DEMONSTRATES VARİCES WİTH A CLEAN SURFACE. THE MUCOSA ON THE PREVİOUSLY BLEEDİNG SİTE İS COMPLETELY HEALED. LATER, VARİCEAL OBTURATİON WİTH CYANOACRYLATE WAS SUCCESSFULLY PERFORMED, AND THE PATİENT WAS DİSCHARGED.

DISCUSSION

ABS is a derivate of 5 plants. It is locally active on the bleeding surface. When ABS is applied to the bleeding site, it interacts with plasma proteins, forms an encapsulated protein network, and stimulates erythrocyte aggregation.4 The drug does not require injecting; spraying over the bleeding site is sufficient for hemostasis. Although gastric varices bleed less frequently than esophageal varices, the rebleeding and mortality rates for gastric variceal hemorrhage are higher.3 There is no universal consensus on the treatment of gastric varices. According to guidelines, when bleeding occurs, endoscopic variceal obturation with tissue adhesives is recommended.9 If obturation is not an option or fails, a transjugular intrahepatic portosystemic shunt procedure is recommended. In our case, the spurting fundal variceal hemorrhage was terminated very rapidly, in only 18 seconds. This short bleeding time enables the endoscopist to observe the lesion in detail with a clean view and facilitates appropriate interventions. At our institution, we also observed the immediate hemostatic effect of ABS on arterial bleeding after gastric polypectomy and spurting bleeding ulcers. Those cases did not respond to injection therapy or thermocoagulation. Our experience agrees with that reported previously by Kurt et al.5-7 To date, no significant side effects of ABS have been reported. We did not observe any side effects attributable to the ABS treatment in our patient. Further clinical observations and well-designed studies are required to validate the effectiveness of ABS in GI hemorrhage

DISCLOSURE

All authors disclosed no financial relationships relevant to this publication.

Abbreviation: ABS, Ankaferd Blood Stopper

REFERENCES

1. D'Amico G, De Franchis R. Upper digestive bleeding in cirrhosis. Posttherapeutic outcome and prognostic indicators. Hepatology 2003;38: 599-612. 2. Sarin SK, Lahoti D, Saxena SP, et al. Prevalence, classification and natural history of gastric varices: a long-term follow-up study in 568 portal hypertension patients. Hepatology 1992;16:1343-9. 3. Ryan BM, Stockbrugger RW, Ryan JM. A pathophysiologic, gastroenterologic, and radiologic approach to the management of gastric varices. Gastroenterology 2004;126:1175-89. 4. Goker H, Haznedaroglu IC, Ercetin S, et al. Haemostatic actions of the folkloric medicinal plant extract Ankaferd Blood Stopper. J Int Med Res 2008;36:163-70. 5. Kurt M, Kacar S, Onal IK, et al. Ankaferd Blood Stopper as an effective adjunctive hemostatic agent for the management of life-threatening arterial bleeding of the digestive tract. Endoscopy 2008;40(Suppl 2): E262. 6. Kurt M, Disibeyaz S, Akdogan M, et al. Endoscopic application of ankaferd blood stopper as a novel experimental treatment modality for upper gastrointestinal bleeding: a case report. Am J Gastroenterol 2008; 103:2156-8. 7. Ibis M, Kurt M, Onal IK, Haznedaroglu IC. Successful management of bleeding due to solitary rectal ulcer via topical application of Ankaferd blood stopper. J Altern Complement Med 2008;14:1073-4. 8. Idezuki Y. General rules for recording endoscopic findings of esophagogastric varices (1991) Japanese Society for Portal Hypertension. World J Surg 1995;19:420-2. 9. Garcia-Tsao G, Sanyal AJ, Grace ND, et al. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology 2007;46:922-38.

AR-GE & RUHSAT AŞAMALARI

İLK BİLİMSEL ARAŞTIRMALARI HACETTEPE ÜNİVERSİTESİ
HEMOTOLOJİ ANABİLİM DALI BAŞKANI
PROF. DR. İBRAHİM HAZNEDAROĞLU VE EKİBİ TARAFINDAN YÜRÜTÜLÜREK 2007 YILINDA YÜZLERCE TÜRK BİLİM İNSANININ KATKISIYLA MODERN BİR HEMOSTATİK AJAN OLARAK TIP LİTERATÜRÜNE YERLEŞMİŞTİR VE SAĞLIK BAKANLIĞI'NIN ARA ÜRÜN İZNİ İLE BELGELENDİRİLMİŞTİR.

AYNI YIL THE JOURNAL OF INTERNATİONAL MEDİCAL RESEARCH VE BLOOD DERGİLERİNDE MAKALELERİN YAYINLANMASI ULUSLARARASI BİLİNİRLİĞİNİNBAŞLANGICI OLMUŞTUR.
2012 YILINDA İLK CE (CERTİFİCATİON OF EUROPE) KALİTE BELGESİNİ ALAN FİRMA 2017 YILINDA FAZ ÇALIŞMALARINI TAMAMLAYARAK İLAÇ RUHSATINA SAHİP OLMUŞTUR.

ÜRÜN T.C SAĞLIK BAKANLIĞI'NDAN RUHSATLI İLK VE TEK ORİJİNAL YERLİ İLAÇTIR.

GÜNÜMÜZE KADAR ULUSLARARASI KABUL GÖRMÜŞ YAYINLARDA VE HAKEMLİ DERGİLERDE 350'YE YAKIN BİLİMSEL MAKALESİ YAYINLANMIŞTIR.

T.C. SAĞLIK BAKANLIĞI
TÜRKİYE İLAÇ VE TIBBİ CİHAZ KURUMU
RUHSATNAME

07.11.2017 tarih ve 2017/848 sayılı bu ruhsatname **ANKAFERD BLOODSTOPPER HARİCEN KULLANILMAK ÜZERE ÇÖZELTİ İÇEREN AMPUL** isimli beşeri tıbbi ürün için **İMMÜN GIDA İLAÇ KOZMETİK SANAYİ VE TİCARET LİMİTED ŞİRKETİ** firması adına tahsis edilmiştir.

Eki : Sertifika
Ruhsatname ID : 10000920
İş bu ruhsatname eki sertifika ile geçerlidir

Dr. [illegible] ÜRSOZ
Kurum Başkanı

TİCARİ ÜRÜN

ANKAFERD KANAMA DURDURUCULARI TİCARİ OLARAK BİRÇOK FARKLI SUNUMA SAHİP

EMİLEBİLEN ISLAK TAMPON

PUSH & STOP

ISLAK TAMPON

AMPUL

SPREY

KAMUOYUNU BİLGİLENDİRME

HÜSEYİN CAHİT FIRAT

ÜRETİM VE BİLİMSEL ÇALIŞMALAR
VEDAT FIRAT & PROF. DR. İBRAHİM HAZNEDAROĞLU

BİLİM VE TİCARET PLATFORMU

www.bilimveticaret.org.tr