

Does BLOODCARE Powder Prevent Postoperative Chylous Ascites After Lymphadenectomy for Gynecological Malignancies?

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Objective: The aim of this study was to evaluate the effect of an intraoperative hemostatic cellulose agent (BLOODCARE powder [Life Line, Brno, Czech Republic]) on reducing the incidence of postoperative chylous ascites (PCA) after complete pelvic and para-aortic lymphadenectomy (PPALN) in patients with gynecological cancers treated with laparotomy.

Methods: This case control study reviewed 150 patients with gynecological cancer who underwent PPALN. In the study group (n = 75), BLOODCARE powder was applied below the left renal vein and bilateral obturator fossa. In the control group (n = 75), no sealant agent was used after the procedure, such as fibrin glue or a hemostatic cellulose agent.

Results: The demographic and surgical characteristics of the patients in both groups were similar. Chylous ascites occurred in 9 cases (6%). The incidence of PCA was lower in the study group (1 [1.3%] vs 8 [10.7%]; $P = 0.03$). Logistic regression analysis indicated that using BLOODCARE powder during the surgery independently protected against the development of PCA.

Conclusions: Using BLOODCARE powder during retroperitoneal surgery may prevent PCA. This simple, effective agent should be used after PPALN for gynecological cancers.

Key Words: BLOODCARE powder, Chylous ascites, Gynecological cancers, Lymphadenectomy

Received April 13, 2017, and in revised form June 15, 2017.

Accepted for publication June 26, 2017.

(*Int J Gynecol Cancer* 2017;00: 00–00)

Postoperative chylous ascites (PCA) has an incidence of approximately 0.1% to 9% after gynecological oncology operations, including lymph node dissection.^{1,2} Postoperative chylous ascites is the pathological leakage of triglyceride-rich lymphatic fluid into the peritoneal cavity.³ It is associated with significant morbidity, such as delayed wound healing, malnutrition, dehydration, electrolyte imbalance, and immunosuppression or septic complications due to superinfection.^{1–3} Therefore, prevention of PCA after retroperitoneal surgery is important. Moreover, because PCA is

relatively rare, little is known about it, and treatment of PCA usually relies on experience.

A few English-language case reports describe the treatment of chylous ascites with fibrin glue with or without hemostatic cellulose.^{4–7} However, no study has evaluated the intraoperative use of hemostatic cellulose to prevent PCA after lymphadenectomy. Therefore, we examined the effect of an intraoperative hemostatic cellulose agent on reducing the incidence of PCA after systematic pelvic and para-aortic lymphadenectomy (PPALN) in patients with gynecological malignancies.

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The authors declare no conflicts of interest.

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 ISSN: 1048-891X
 DOI: 10.1097/IGC.0000000000001093

METHODS

This retrospective case-control study examined data from 3 gynecological oncology departments: Tepecik Education and Research Hospital (İzmir, Turkey), Muğla Sıtkı Koçman University Education and Research Hospital (Muğla, Turkey), and İstanbul Bakırköy Sadi Konuk Education and Research Hospital (İstanbul, Turkey). The study was approved by the local ethics committees and was conducted in accordance with the tenets of the Declaration of Helsinki.

In this study, 150 patients with gynecological cancer who underwent PPALN between September 2013 and November 2016 were reviewed. Women were excluded if they underwent only pelvic lymphadenectomy, pelvic lymphadenectomy with para-aortic lymphadenectomy up to the inferior

mesenteric artery, or hyperthermic intraperitoneal chemotherapy following the surgery.

In the control group (group A, $n = 75$) systematic PPALN was performed by 3 expert surgeons (K.G., A.I.O., M.G.). In the study group (group B, $n = 75$), the same technique was used for the lymphadenectomy, and BLOODCARE powder (Life Line, Brno, Czech Republic) was applied below the left renal vein and bilateral obturator fossa. Each patient was given 2 packets of powder.

All operations were performed by laparotomy. In all patients, type III bilateral pelvic lymph node dissection was performed according to the classification of Cibula and Abu Rustum.⁸ The para-aortic lymph nodes were dissected, and all lymph node-bearing tissues were harvested from the lateral, medial, anterior, and posterior aspects of the inferior vena

TABLE 1. Patient characteristics

	Control (n = 75)	Study (n = 75)	P
Age,* y	56.9 ± 9.0	58.2 ± 8.6	0.39
Gravida*	2.3 ± 1.1	2.2 ± 1.2	0.73
Body mass index,† kg/m ²	27.8 ± 3.9	27.7 ± 4.6	0.79
Ethanol use†	1 (1.3)	–	1.00
Tobacco use†	7 (9.3)	5 (6.7)	0.76
Primary tumor site†			0.071
Endometrium	45 (60.0)	49 (65.3)	
Ovary	28 (45.3)	25 (33.3)	
Fallopian tube	2 (2.7)	1 (1.3)	
Omentectomy	54 (72.0)	44 (58.7)	0.12
Peritonectomy	18 (24.0)	11 (14.7)	0.21
Colon resection	6 (8.0)	9 (12.0)	0.58
No. LNs removed*			
Pelvic	25.4 ± 10.1	26.1 ± 9.8	0.67
Para-aortic	22.3 ± 3.7	21.2 ± 5.4	0.33
LN status‡			
Only pelvic LN positive	4 (2–8)	3 (2–8)	0.70
Only para-aortic LN positive	2 (1–3)	3 (2–3)	0.47
Pelvic and para-aortic LN positive	9.5 (2–22)	9 (5–20)	0.85
LN status*			
Only pelvic LN positive	7 (9.3)	8 (10.7)	1.00
Only para-aortic LN positive	2 (2.7)	3 (4.0)	1.00
Positive pelvic and para-aortic LN	8 (10.7)	7 (9.3)	1.00
Chylous ascites†	8 (10.7)	1 (1.3)	0.03
Time to onset,‡ d	3 (2–4)	3	0.75
Time to resolution,‡ d	7 (3–9)	5	0.29
Daily volume of ascites,‡ mL	1900 (2100–1400)	850	0.01
Vascular anomalies†	–	1 (1.3)	1.00
Time to drain removal,* d	11 (8–13)	6	0.058

*Mean ± SD.

†Number (percentage).

‡Median (range).

LN, lymph node.

cava and aorta up to the left renal vein. The inferior mesenteric artery was visualized and preserved. The lymphatic tissues were dissected using several methods, including a harmonic scalpel and monopolar and bipolar electrocautery. Absorbable suture or hemoclips were used to ligate all vascular and lymphatic channels during the dissection. No sealant agent, such as fibrin glue, was used after the procedure. Intra-abdominal 10F or 12F drains were routinely placed to obtain early information about postoperative bleeding or leakage. All of the patients were given a single intravenous dose of antibiotics for prophylaxis and low-molecular-weight heparin based on the patient's weight and individual risk of thrombosis.

The following clinical data were collected from the patients' medical and surgical reports: demographic characteristics, type of surgery, number of pelvic and para-aortic lymph nodes harvested, stage of disease, number of metastatic lymph nodes, development of chylous ascites during the postoperative period and further treatment, and length of hospital stay.

The diagnosis of chylous ascites was based on the presence of noninfected milky or creamy peritoneal fluid with a volume of 100 mL/d or greater and with a triglyceride concentration of 110 mg/dL or greater. The drainage catheters were left in place until the daily output was less than 300 mL, and the fluid became clear and pink (serosanguineous). White blood cells were counted and body temperature measured to exclude infected ascites fluid (particularly bacterial peritonitis). The time to onset of chylous ascites was defined as the interval between the end of surgery and collection of chylous ascites in the drainage bag. The time to the resolution of chylous ascites was defined as the number of days between first diagnosis and resolution.

The normality of the distribution of variables was examined using the Kolmogorov-Smirnov test. The χ^2 and Fisher tests were used to compare categorical variables; Student *t* test was used to compare normally distributed continuous variables, and the Mann-Whitney *U* test was used to compare non-normally distributed variables. Odds ratios were estimated using Cox proportional hazard modeling. The statistical analysis was performed using MedCalc software (version 16.4). $P < 0.05$ was considered significant.

RESULTS

Table 1 summarizes the characteristics of the patients in the study and control groups. The demographic and surgical

characteristics of the patients in both groups were similar, including mean age, types of surgical procedures, and numbers of harvested and metastatic lymph nodes.

Chylous ascites developed in 9 cases (6%). The incidence of chylous ascites was lower in the study group compared with the control group (1 [1.3%] vs 8 [10.7%]; $P = 0.03$), as was the median daily volume of ascites (850 vs 1900 mL; $P = 0.01$). Logistic regression analysis indicated that using BLOODCARE powder after PPALN independently protected against the development of chylous ascites (Table 2). No adverse effects of BLOODCARE powder were seen in the study group.

In all 9 patients, the chylous ascites improved after conservative treatment. In 2 patients (1 patient in each of the study and control groups), a high-protein, low-fat, medium-chain-triglyceride diet was initiated. In the patient treated with BLOODCARE powder after PPALN, chylous ascites was diagnosed on postoperative day 3 and resolved by diet on postoperative day 5. Seven patients in the control group discontinued oral intake, because large volumes of fluid continued to drain (more than 1000 mL/24 h), and total parenteral nutrition was administered. One of these 7 patients was given octreotide, a somatostatin analog (0.1 mg/mL) in the total parenteral nutrition, and it was also administered subcutaneously 3 times a day for 5 days (Table 1). None of the patients showed evidence of recurrent chylous ascites.

DISCUSSION

This case-control study examined how to prevent PCA after lymphadenectomy. To our knowledge, this is the first study to investigate this. Postoperative chylous ascites is a complication of gynecological cancer surgery. It develops as a result of leakage from the lymphatic channels in pelvic and para-aortic lesions.^{1–5} Han et al¹ reported that 7 (0.17%) of 4119 patients developed PCA after laparotomic lymphadenectomy in the management of gynecological cancer. Recently, Thiel et al⁸ reported a 3.0% incidence in a cohort of 931 patients who underwent lymphadenectomy in gynecological cancer. In our cohort, the incidence of PCA was 6%. The markedly higher incidence in our trial may be related to use of a more extensive and meticulous systematic lymphadenectomy (type III pelvic lymphadenectomy and para-aortic lymphadenectomy up to the left renal vein) in all cases. Another possible reason for our high PCA incidence is

TABLE 2. Logistic regression analysis of risk factors for chylous ascites after gynecological malignancy surgery

Variable	Odds Ratio	95% Confidence Interval	<i>P</i>
Only pelvic LN positive	1.4	1.7–1.2	0.0001
Only para-aortic LN positive	14.2	1.8–100	0.009
Pelvic and para-aortic LN positive	29.4	6.2–136.9	<0.0001
No. pelvic lymph nodes removed	1.05	0.9–1.1	0.21
No. para-aortic lymph nodes removed	1.1	0.9–1.2	0.10
No BLOODCARE powder used	8.8	1.0–72.5	0.01

LN, lymph node.

that we routinely use peritoneal drainage tubes, whereas other gynecological oncology centers do not generally use drains or remove them before commencing oral food intake.

Prevention of PCA is important after lymphadenectomy, because chyle in the peritoneal cavity can lead to serious complications, such as sepsis, a prolonged hospital stay, and sudden death. In the only case report on prevention of PCA, fibrin glue was used.⁶ We used BLOODCARE powder to prevent PCA and found that it reduced the incidence of PCA after PPALN. Although our series was small, only 1 patient developed PCA in the BLOODCARE group, and the volume of PCA was less than that in the control group.

BLOODCARE powder is a cellulose-based hemostatic agent that is used to control minor bleeding, such as oozing from the liver or pelvic organs. After lymphadenectomy, BLOODCARE powder may stimulate coagulation factors in the lymphatic canals, such as factors VIII and V, fibrinogen, and von Willebrand factor, and block lymph oozing.⁹

Limitations of our study included its retrospective nature and the small sample size. Retrospective cohort studies are subject to both selection and recall biases and the effects of unknown confounding variables, which may in turn negatively affect the accuracy of the results. Despite these limitations, the similarities in the demographic and surgical characteristics of our study groups, availability of good follow-up data, and use of the same surgical techniques suggest that our results are valid, mitigating any possible weaknesses.

In conclusion, using BLOODCARE powder after PPALN may prevent PCA. Furthermore, the use of hemostatic cellulose reduced the volume of lymphatic ascites and showed a statistical tendency toward a decreased number of days of

drainage required. This simple, effective agent should be used after lymphadenectomy for gynecological malignancy.

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