Efficacy and safety of regenerated cellulose topical gauze haemostats in managing secondary haemostasis: a randomised control trial

Objective: To compare the efficacy and safety of HemoStyp (United Health Products, US), a neutralised oxidised regenerated cellulose (NORC) and Surgicel (Johnson & Johnson, US), an oxidised regenerated cellulose (ORC), in the management of bleeding of surgical wounds during abdominal, thoracic and vascular surgeries.
Method: This study was a prospective, non-inferiority, multicentre, randomised, open-label trial. Surgical procedures were performed according to expected standard of care and in compliance with all relevant laws and institutional guidelines. Patients who developed Lewis Bleeding Scale grade 1 and grade 2 bleeds not controlled through conventional techniques were randomised to either the NORC or ORC treatment arms. Bleeding was measured every 30 seconds after treatment, ending at five minutes after haemostasis was achieved or at 10 minutes if haemostasis was not achieved.
Results: A total of 236 patients were included in the study. There was a total of seven adverse events in the study, none of which had causality related to either the NORC or ORC. For all surgical procedures, haemostasis was achieved more quickly with the NORC than the ORC ($p<0.0001$). In addition, haemostasis for all patients was achieved in under two minutes for the NORC compared with 81% of patients in the ORC groups. For Lewis Bleeding Scale grade 1 bleeds, the median time to control bleeding was 24 seconds in the NORC group and 51 seconds for the ORC group. For grade 2 bleeds, time to control bleeding was 76 seconds and 116 seconds, respectively.
Conclusion: For patients in this study, haemostasis was achieved more quickly in the NORC treatment group compared with the ORC group, in patients with Lewis grade 1 or 2 bleeds caused by surgical wounds generated during abdominal, thoracic and vascular surgeries.
Declaration of interest: GA is an officer of United Health Products (UHP). GA and RD hold restricted stock in UHP. RS, SN and JC received a small honorarium from UHP to participate in this study but did not receive compensation for drafting, reviewing or otherwise participating in this publication. This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

HemoStyp • haemostasis • haemostat • regenerated oxidised cellulose • Surgicel

Throughout history, topical agents have been used to facilitate haemostasis but have remained largely ineffective until the past century.[1,2] Since their introduction in 1943, multiple commercial oxidised regenerated cellulose (ORC) products have been developed,[1,3] and are frequently used in many surgical procedures.[4] Underscoring the importance of topical haemostats in modern surgery, topical haemostats were used in approximately 30% of all surgical procedures performed in 2010.[5]

Choosing an adjunctive haemostatic agent not only requires evaluation of the patient's current bleeding status, but also consideration of the haemostatic device's efficacy, safety, ease of use, affordability and mechanism of action.[6] The mechanism of action can be explained by both the physical and chemical properties of the material. The most common topical haemostats are regenerated cellulose-based haemostatic agents that initiate clotting by serving as a platform for platelet aggregation. Upon contact with blood, these materials swell, promoting the eventual formation of a fibrin plug at the bleeding site,[7] the end product of the clotting or coagulation cascade.[8] In most cases, bioabsorbable haemostats are more desirable than nonabsorbable haemostats because they do not have to be removed from the wound, which often results in rebleeding. This is especially true for intraoperative use, where the consequences of rebleeding are more severe, and it is much easier and safer to leave the haemostat on the wound where it can be eventually absorbed by the body.

This paper describes an evaluation of the efficacy and safety of two topical haemostats, HemoStyp (United Health Products, Inc., US), a neutralised oxidised regenerated cellulose (NORC) and Surgicel (Johnson & Johnson, US), an oxidised regenerated cellulose (ORC), as an adjunct for managing secondary haemostasis during open surgery. Both products were evaluated for the treatment of mild to moderate bleeding on the

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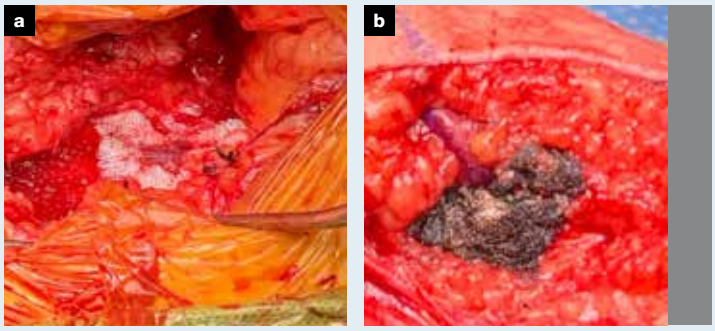
Fig 1. Example of regenerated cellulose-based haemostatic agents used during vascular surgery. A single layer of a pH neutralised oxidised regenerated cellulose (NORC) (**a**) or oxidised regenerated cellulose (ORC) (**b**) was applied to an anastomosis site. Both agents could control mild to moderate bleeding. However, the NORC agent's neutral pH is compatible with the addition of potentially beneficial acid-sensitive compounds or drugs to the bleeding site. In contrast, the acidic pH of the ORC agent lyses red blood cells, turning the ORC agent into a brownish gel, which delays resorption and can delay wound healing



Lewis bleeding scale (grades 1 and 2)[9] that arises during abdominal, thoracic and vascular surgeries.

The NORC used in this study is a Class II medical device registered with the US Food and Drug Administration (FDA) to control bleeding in open wounds and in body cavities (Fig 1). It is a patented, bioabsorbable haemostatic gauze made from neutralised oxidised regenerated cellulose. The product is natural and bacteriostatic, containing no harmful chemicals or animal byproducts. Pre-clinical research and laboratory testing has shown that the NORC is safe, with a low bioburden, lack of significant immunogenicity, as well as other beneficial chemical properties such as rapid dissolution within 24 hours into predominantly sodium and chloride ions and very low concentrations of boron, magnesium and potassium ions. It has a pH of 7.21 and haemostatic performance testing demonstrated it to be non-haemolytic at 0.08% compared with a control (independent testing data available upon request from the authors). This is unlike the hypothesised mechanism of action for the ORC used in this study.[10] Because of these properties, the authors hypothesised that the NORC used in this study is unlikely to alter the pH at the implanted site or lead to an inflammatory response from the surrounding tissue. If correct, this would allow the NORC to be administered or combined with antibiotic irrigation solutions or with acid-sensitive drugs or biological products, such as thrombin, that could further increase haemostatic efficacy.

The oxidised regenerated cellulose (ORC) product used as a comparison in this study is an absorbable oxidised cellulose gauze, used in surgery as a haemostatic agent to control mild bleeding or optimise ligature coagulation or when electrocoagulation is insufficient (Fig 1).[10] The material is deposited on the surgical bed and is usually reabsorbed during the following 7–14 days. The core mechanism of action for the ORC is hypothesised to be due to the acidic pH (pH 2.5) of the material that promotes a haemostyptic reaction resulting in haemolysis of red blood cells, thus initiating a clotting reaction. The haemolytic effect of the ORC on red blood cells causes the product to turn into a brownish gel after initiating a clotting reaction.[7] Because the product is not quickly resorbed, there have been reports of complications in recent years, some described as secondary to compression of surrounding anatomic structures causing the formation of granulation tissue as a foreign body reaction.[11] Although the low pH of the ORC has an antimicrobial effect against miscellaneous pathogenic organisms, the low pH can decrease the pH of its surroundings, resulting in a strong inflammatory response at the implanted site that can delay wound healing. For this reason, the ORC is not used in orthopaedic surgeries.[12]

Methods

Study design

This study, (NCT03654560, clinicaltrials.gov) was a prospective, non-inferiority, multicentre, randomised, open-label trial to compare the efficacy and safety of the NORC with the ORC in the management of bleeding

Table 1. Surgery categories for the intention-to-treat population

	Overall	NORC	ORC
Number of surgeries	236	118	118
Surgery type (%)			
Abdominal	72 (30.5)	35 (29.7)	37 (31.4)
Thoracic	70 (29.7)	32 (27.1)	38 (32.2)
Vascular	94 (39.8)	51 (43.2)	43 (36.4)
Lewis bleeding scale grade (%)			
Grade 1	134 (56.8)	61 (51.7)	73 (61.9)
Grade 2	102 (43.2)	57 (48.3)	45 (38.1)

NORC—neutralised oxidised regenerated cellulose; ORC—oxidised regenerated cellulose

Table 2. Validated bleeding severity scale

Grade	Visual presentation	Anatomic appearance	Qualitative description	Visually estimated rate of blood loss (ml/min)
0	No bleeding	No bleeding	No bleeding	≤1.0
1	Ooze or intermittent flow	Capillary-like bleeding	Mild	>1.0–5.0
2	Continuous flow	Venule and arteriolar-like bleeding	Moderate	>5.0–10.0
3	Controllable spurting and/or overwhelming flow	Noncentral venous- and arterial-like bleeding	Severe	>10.0–50.0
4	Unidentified or inaccessible spurting or gush	Central arterial- or venous-like bleeding	Life threatening*	>50.0

*Systemic resuscitation required (for example, volume expanders, vasopressors, blood products, etc.). The bleeding severity scale is designed and validated for use in clinical studies to generate clinically meaningful labelling claims. The scale is a Likert-type scale in which the user assigns a grade based on the overall agreement of the items listed. Source: Lewis, et al., 2017[9]

during abdominal, thoracic and vascular surgeries. All procedures were approved by Western Institutional Review Board (an independent review board accredited by the Association for the Accreditation of Human Research Protection Programs) and performed in compliance with all relevant laws, institutional guidelines and the Declaration of Helsinki. At time of surgery, patients had to have Lewis grade 1 and grade 2 bleeds, based on the validated Lewis bleeding scale (also known as the ViBe SCALE),[9] that could not be controlled by conventional surgical techniques. Patients were screened and provided their written informed consent during evaluation for their elective surgical procedure.

We sought to enrol a total of 236 patients between December 2018 and September 2019, and randomise them in a 1:1 ratio to either the NORC or ORC treatment arms. Assuming a drop-out rate of 10%, this would achieve 80% power to compare the efficacy of the two haemostatic products. Treatment randomisation was stratified according to bleeding severity, using the Lewis bleeding scale, by each individual study centre (two centres in total) and generated before study initiation. Patients were randomly distributed to either the NORC or the ORC treatment arm so that approximately equal numbers of patients were included in each intervention arm for each surgery type (abdominal, thoracic and vascular) (Table 1).

The primary outcome measure was median time to achieve haemostasis. The study objective was to assess whether the NORC is non-inferior to the ORC in terms of the key parameter of median time to achieve

Table 3. Demographic characteristics of the intention-to-treat population

	Overall	NORC	ORC
Patients, n	236	118	118
Age, years			
Mean±SD	60.19±16.32	58.89±16.13	61.48±16.48
Median	62	62	63
Min–max, range	20–94	20–93	22–94
Sex: male, n (%)	139 (58.9)	66 (55.9)	73 (61.9)
Race, n (%)			
Asian	16 (6.8)	10 (8.5)	6 (5.1)
Black or African American	8 (3.4)	5 (4.2)	3 (2.5)
Native Hawaiian or Other Pacific Islander	2 (0.8)	1 (0.8)	1 (0.8)
White	160 (67.8)	74 (62.7)	86 (72.9)
Other	50 (21.2)	28 (23.7)	22 (18.6)
Ethnicity—not Hispanic or Latino, n (%)	179 (75.8)	87 (73.7)	92 (78.0)

NORC—neutralised oxidised regenerated cellulose; ORC—oxidised regenerated cellulose; SD—standard deviation; min—minimum; max—maximum

Table 4. Time to haemostasis by NORC and ORC for the intention-to-treat population

	NORC	ORC
Total, n	118	118
Events, n	118	112
Censoring, n	0	6
Median, seconds	36	67
95% CI for median, seconds	31, 47	57, 89
	Estimate±SD	**95% CI**
HR of NORC to ORC*	2.6±0.14	1.97, 3.46

*Estimate and 95% CI from Cox regression model; SD—standard deviation; CI—confidence interval; HR—hazard ratio; NORC—neutralised oxidised regenerated cellulose; ORC—oxidised regenerated cellulose

haemostasis at the target bleeding site. This study also evaluated the percentage of patients achieving haemostasis every 30 seconds after treatment, ending at five minutes after haemostasis was achieved or at 10 minutes if haemostasis was not achieved. In addition, the percentages of patients with rebleeding events during surgery and any post-surgical events requiring additional surgery during a 30-day follow-up period were evaluated.

Inclusion/exclusion criteria

Patients were included in the study if they were having an elective procedure (non-laparoscopic abdominal, thoracic or vascular surgery); at the time had mild to moderate soft tissue, vascular or parenchymal bleeding present at the target bleeding site after primary standard conventional surgical haemostatic methods were proven to be ineffective or impractical; were 18 years of age or older; and were willing and able to sign the consent.

Patients were excluded if they had a physical or psychological condition which would impair study participation; had indications for emergency surgery; had preoperative laboratory findings of a haematologic disorder; had a history of moderate to severe allergies; were undergoing minimally invasive laparoscopic surgery; would require fresh frozen plasma or platelet transfusions; were pregnant or breastfeeding at the time of surgery; were taking P2Y12 platelet inhibitor (clopidogrel) <5 days before surgery, warfarin or Xa inhibitors not withheld per standard protocols for the management of anticoagulants preoperatively; or had a coagulation disorder, thrombocytopenia, liver disease, or anti-thrombin therapy.

Surgical procedures

Surgical procedures were performed in a surgical suite, according to the expected standard of care and practices, guided by the surgical specialty guidelines and institutional standard operating procedures at the study sites. A specific bleeding area/site was designated as the target bleeding site when it was determined by the investigator that control of bleeding by conventional surgical techniques (including suture, ligature and cautery) would be ineffective or impractical, and that control of bleeding would require an adjunct treatment to achieve haemostasis. When the target bleeding site was identified, the investigator rated the intensity of the bleeding at the target bleeding site according to the validated Lewis bleeding scale (Table 2). Only patients with a target bleeding site qualitative description of mild or moderate severity (grade 1 or grade 2) were randomised. Each study treatment (NORC or ORC) was applied in accordance with the manufacturer's instructions provided to each investigator. Upon application of the study treatment at the target bleeding site, a stopwatch was started with inspection for bleeding occurring every 30 seconds after treatment, ending at five minutes after haemostasis was achieved to ensure that rebleeding did not occur or at 10 minutes if haemostasis was not achieved.

Assessments of bleeding

The investigating surgeons were trained on a video library of different bleeding rates for intraoperative recruitment of patients.[9] These videos were verified using gravimetric measurements of blood loss. Inter- and intra-rater reliability was assessed before protocol participation. Inter- and intra-rater concordance exceeded 90% for a bleeding grade of 0 (haemostasis) and a bleeding grade of 3 (severe bleeding).

Endpoints and safety assessments

The primary endpoint was time to haemostasis from the start of treatment with the study product at the target bleeding site. Secondary endpoints were the percentage of patients achieving haemostasis at the target bleeding site at two, five and 10 minutes following the application of the study product; percentage of patients with intraoperative haemostasis at the target bleeding site; percentage of patients with intraoperative rebleeding from the target bleeding site post-haemostasis; and postoperative rebleeding from the target bleeding site requiring surgical re-exploration up to 30 days after surgery. Safety assessments included evaluation of the frequency and nature of adverse events and adverse device effects up to 30 days after treatment application.

Recording of screen failures

Patients who did not have mild to moderate soft tissue, vascular or parenchymal bleeding (Lewis grade 1 and 2 bleeds) present at the target bleeding site after conventional primary haemostatic intervention were recorded as screen failures.

Statistical analysis

The primary analysis was the test of non-inferiority of the NORC compared with the ORC. Cox proportional hazards regression or log-rank test were used for the analysis of

Table 5. Efficacy parameters to achieve haemostasis for the NORC and ORC in abdominal, thoracic and vascular surgeries

Surgery type	NORC	ORC	p*
Abdominal (n=72)			
Total, n	35	37	<0.0001
Events, n	35	37	
Censoring, n	0	0	
Median, seconds	26	49	
95% CI for median, seconds	21, 29	44, 57	
	Estimate±SD	**95% CI**	
HR of NORC to ORC**	4.87±0.27	2.87, 8.26	
Thoracic (n=70)			
Total, n	32	38	<0.0001
Events, n	32	38	
Censoring, n	0	0	
Median, seconds	32.5	53.5	
95% CI for median, seconds	26, 39	49, 86	
	Estimate±SD	**95% CI**	
HR of NORC to ORC**	2.56±0.25	1.57, 4.19	
Vascular (n=94)			
Total, n	51	43	<0.0001
Events, n	51	37	
Censoring, n	0	6	
Median, seconds	76	114	
95% CI for median, seconds	61, 84	105, 139	
	Estimate±SD	**95% CI**	
HR of NORC to ORC**	6.33±0.29	3.59, 11.16	

SD—standard deviation; CI—confidence interval; HR—hazard ratio; NORC—neutralised oxidised regenerated cellulose; ORC—oxidised regenerated cellulose; *p compares the NORC and ORC treatment arms using a log-rank test; **estimate and 95% CI from Cox regression model

non-inferiority. The NORC was concluded to be non-inferior to the ORC if the lower bound of the 95% confidence interval (CI) of hazard ratio (HR) was >0.8. Once the criteria for non-inferiority were satisfied, a superiority analysis was performed. Cox proportional hazards regression or log-rank test were used for the analysis of superiority and for all subgroup analyses (i.e., surgical type, bleeding severity, sex). The NORC was concluded to be superior to the ORC if the lower bound of the 95% CI of HR was >1.

Table 6. Percentage of haemostasis at two, five and 10 minutes in the intention-to-treat population

Haemostasis, minutes	NORC (n=118) n (%)	ORC (n=118) n (%)	Difference in % (95% CI)	p*
2	118 (100)	96 (81.4)	18.6 (10.8, 26.5)	<0.0001
5	118 (100)	110 (93.2)	6.8 (1.4, 12.2)	0.007
10	118 (100)	112 (94.9)**	5.1 (0.3, 9.9)	0.03

NORC—neutralised oxidised regenerated cellulose; ORC—oxidised regenerated cellulose; *p in terms of haemostasis at two minutes is from z-test, p in terms of haemostasis at five and 10 minutes are from Fisher's exact test; **six patients in the ORC treatment arm did not achieve haemostasis by 10 minutes

Table 7. Efficacy of NORC and ORC in Lewis bleeding scale grade 1 and grade 2

Lewis bleeding scale	NORC	ORC
Grade 1 (n=134)		
Total, n	61	73
Events, n	61	73
Censoring, n	0	0
Median, seconds	24	51
95% CI for median, seconds	21, 28	47, 55
	Estimate±SD	**95% CI**
HR of NORC to ORC*	6.87±0.21	4.55, 10.39
Grade 2 (n=102)		
Total, n	57	45
Events, n	57	39
Censoring, n	0	6
Median, seconds	76	116
95% CI for median, seconds	63, 84	109, 139
	Estimate±SD	**95% CI**
HR of NORC to ORC*	7.80±0.28	4.56, 13.38

*Estimate and 95% CI from Cox regression model; SD—standard deviation; CI—confidence interval; HR—hazard ratio; NORC—neutralised oxidised regenerated cellulose; ORC—oxidised regenerated cellulose

Table 8. Efficacy of NORC and ORC in male and female patients

Patients	NORC	ORC
Male (n=139)		
Total, n	66	73
Events, n	66	67
Censoring, n	0	6
Median, seconds	37	89
95% CI for median, seconds	29, 53	62, 105
	Estimate±SD	**95% CI**
HR of NORC to ORC*	3.71±0.20	2.49, 5.51
Female (n=97)		
Total, n	52	45
Events, n	52	45
Censoring, n	0	0
Median, seconds	36	54
95% CI for median, seconds	29, 74	49, 82
	Estimate±SD	**95% CI**
HR of NORC to ORC*	1.65±0.21	1.09, 2.50

*Estimate and 95% CI from Cox regression model; SD—standard deviation; CI—confidence interval; HR—hazard ratio; NORC—neutralised oxidised regenerated cellulose; ORC—oxidised regenerated cellulose

Results

Defining the intention-to-treat, per protocol and safety populations

A total of 236 patients were enrolled and represent the intention-to-treat analysis population. There were three patients with major protocol violations that occurred in the NORC group due to no 30-day follow up being performed. Thus, the per protocol analysis population was composed of 115 and 118 patients in the NORC and ORC groups, respectively. Because the intention-to-treat and per protocol populations were so closely matched, there was essentially no difference in their results. Therefore, it was elected to highlight the intention-to-treat group data. The per protocol group data is available as supplementary material from the authors. Because all patients received the treatment according to their randomisation assignment, safety analyses were reported according to randomisation assignment (also available as supplementary material from the authors).

Study population demographics and distribution of surgical procedures

Randomisation demonstrated little difference in patient demographics between the NORC and ORC treatment groups and the types of surgery undergone (Table 3). There were no statistically significant differences observed between the NORC and ORC treatment arms with respect to age, sex, race or ethnicity. The surgical types were nearly evenly distributed among abdominal (30%), thoracic (30%), and vascular (40%) surgeries, with 57% and 43% of patients rated grade 1 or grade 2 on the Lewis bleeding scale, respectively (Table 1).

Impact of treatment arm on time to haemostasis

Statistics on time to achieve haemostasis for the NORC and ORC treatment arms for the intention-to-treat population (n=236, 118 per treatment arm) show a clear advantage of the NORC over the ORC (Table 4). Log-rank testing indicates that the NORC is significantly faster than the ORC ($p<0.0001$) in obtaining haemostasis. Median time to achieve haemostasis in the NORC arm was 36 seconds (95% CI: 31, 47); median time to achieve haemostasis in the ORC treatment arm was 67 seconds (95% CI: 57, 89) (Table 4). Additionally, the Cox proportional hazard regression model (NORC versus ORC) used to predict time to haemostasis showed that the hazard ratio of NORC to ORC in achieving haemostasis was 2.61 (95% CI: 1.97, 3.46) (Table 4), indicating the NORC performed better than the ORC. Similar hazard ratios were observed when stratifying outcomes by surgery type, with the NORC achieving haemostasis faster than the ORC in abdominal, thoracic and vascular surgeries. For both treatment arms, haemostasis was achieved first in abdominal surgery followed by thoracic and vascular surgeries. The hazard ratios of the NORC to ORC were 4.87, 2.56 and 6.33 for abdominal, thoracic and vascular surgeries, respectively (Table 5).

When considering outcomes across all surgeries, all patients (n=118) in the NORC treatment arm achieved

haemostasis during the initial two-minute observation period (Table 6). In contrast, 81% (n=96) of patients in the ORC treatment arm achieved haemostasis in the initial two-minute observation period, and 95% (n=112) of patients were able to achieve haemostasis at the 10-minute observation point. A total of six patients in the ORC treatment arm did not reach haemostasis during the observation window and were treated as censored without further information collected beyond the 10-minute observation period. Similar results were obtained for the per protocol population (included in the supplementary material available from the author).

Comparison of treatment efficacy for grade 1 and grade 2 Lewis bleeding scale bleeds

The efficacy of the NORC was compared with the ORC in the time to achieve haemostasis by level of initial bleeding, either Lewis grade 1 or 2. The hazard ratio for treatment group (NORC to ORC) in Lewis grade 1 bleeds was 6.87 (95% CI: 4.55, 10.39), with the median time in the NORC group 24 seconds and the median time in the ORC group 51 seconds (Table 7). The hazard ratio for treatment group (NORC to ORC) in Lewis grade 2 bleeds was 7.80 (95% CI: 4.56, 13.38), with the median time in the NORC group 76 seconds and the median time in the ORC group 116 seconds (Table 7). Taken together, this means that patients with grade 1 bleeding achieved haemostasis faster than those with grade 2 bleeding, even after taking into account surgical procedure, and that the NORC consistently outperformed the ORC in time to achieve haemostasis, regardless of the level of bleeding.

Comparison of treatment efficacy by sex

The efficacy of the NORC was compared with the ORC by measuring the time to achieve haemostasis in male (n=139) and female (n=97) patients for each treatment arm. In male patients, the hazard ratio for treatment group (NORC to ORC) was 3.71 (95% CI: 2.49, 5.51), with the median time in the NORC group 37 seconds and the median time in the ORC group 89 seconds (Table 8). In female patients, the HR for treatment group (NORC to ORC) was 1.65 (95% CI: 1.09, 2.50), with the median time in the NORC group 36 seconds and the median time in the ORC group 54 seconds (Table 8). Hence, male and female patients achieved haemostasis at a similar speed with the NORC treatment, whereas female patients were faster to achieve haemostasis than male patients in the ORC group.

Adverse events/adverse device events

Overall, the safety analysis found the number of patients experiencing adverse events during the course of the study was seven (two mild, three moderate and two severe). Per treatment group this was equal to five adverse events in four patients in the NORC group, and one patient experiencing two severe adverse events in the ORC group. In the NORC group, no action was required for three of the adverse events, one required medical treatment, and one required the patient to be hospitalised. For the two severe adverse events in the ORC group, the patient was also hospitalised. No adverse events were related to the treatment, and all but one were considered recovering or resolved at the end of the study period. Another adverse event was considered recovered/resolved with sequelae.

Limitations

The primary limitation of the study was the involvement of only two surgical centres, both located in Los Angeles, US. The inclusion of additional centres, particularly international sites, would be needed to strengthen the general applicability of the findings, and determine if the efficacy and safety of each product may be influenced by surgical technique. Although we do not believe this to be the case in the hands of a skilled surgeon, additional clinical testing would be prudent to definitively rule out this possibility.

Discussion

In reviewing the literature, this is the first head-to-head study of two oxidised regenerated cellulose products. Some marketed topical haemostatic agents claimed comparative efficacy or superiority via meta-analysis.[13] However, the study most similar to that presented in this paper was a comparison of two gelatin and thrombin combination haemostats, which were studied in a porcine liver abrasion model.[14] Floseal VH (Baxter Healthcare Corporation, US) and Surgiflo (Ethicon Inc., US) were the first products studied using the Lewis bleeding scale that measured time to haemostasis at two, five and 10 minutes. In this study, 87.5% of the wounds achieved haemostasis at two minutes, but no values were recorded for less than two minutes.[14]

The predominant findings of this study pertain to the non-inferiority and superior efficacy of the NORC compared with the ORC in controlling mild to moderate bleeding (Lewis bleeding scale[9] grade 1 and grade 2) that occurs during abdominal, thoracic and vascular surgeries. Although both devices were able to control bleeding, the NORC achieved haemostasis faster than the ORC across all surgical types and all levels of bleeding. Importantly, the NORC achieved haemostasis in all patients tested within two minutes, whereas bleeding was not controlled in six patients at the 10 minutes observation point in the ORC group.

In this study, it was found that the efficacy of the

Reflective questions

- How effectively could the neutralised oxidised regenerated cellulose (NORC) or oxidised regenerated cellulose (ORC) haemostats control bleeding from more severe surgical wounds or non-surgical wounds?
- How could using the NORC or ORC as an adjuvant to control bleeding in open surgeries potentially reduce patient risk?
- How could using NORC or ORC as an adjuvant to control bleeding potentially improve patient outcomes?

NORC did not depend on the type of surgical procedure. Across abdominal, thoracic and vascular surgeries, the NORC performed better than ORC in achieving haemostasis. This was reflected in the hazard ratios measured for each surgery type. The NORC also performed better than the ORC across all levels of bleeding tested. In subgroup analysis, both male and female patients achieved haemostasis with a similar efficacy if they received the NORC treatment, whereas female patients achieved haemostasis faster than male patients if they were assigned to the ORC group.

Conclusion

Taken together, the findings of this study showed that the NORC was more effective in controlling low to moderate bleeding that occurs during abdominal, thoracic, and vascular surgeries. The NORC was able to control bleeding within two minutes of application in all cases. Given the other characteristics of the NORC, such as a neutral pH, bacteriostatic and bioabsorbable properties, it should be considered for use as an adjuvant to control bleeding during open surgeries. JWC

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