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Comparison of an Intraoperative Application of a Haemostatic Agent (PerClot®) with Conventional Haemostatic Procedure after Thyroid Resection

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Abstract

Background: Postoperative hemorrhage remains an uncommon but potentially life-threatening complication of thyroid surgery. The aim of this case-controlled study was to compare the effectiveness of PerClot® hemostatic agent with hemostasis by conventional technique (HCT) in thyroid surgery. Methods: The thyroid resection was performed from November 2009 to February 2010. Exclusion criteria were applied. There were 30 patients in the HCT group and 30 patients in the PerClot® group. The outcome parameters were postoperative bleeding, the drainage volume 24 hours postoperatively and adverse events according to PerClot®. Results: There was no postoperative hemorrhage in both groups. We found no significant difference between the control and PerClot® group with regard to total drainage volume after 24 h (51 ml ± 36.9 control group/53 ml ± 39.5 PerClot® group (p = 0.79)). There were no adverse events in the PerClot® group. Conclusions: Routine use of PerClot® hemostatic agent has no advantage over conventional hemostasis technique (HCT) in thyroid surgery. In addition, PerClot® is safe and well tolerated.

Keywords

Hemostatic Agent, Thyroid Resection, Drainage Volume, Post-Operative Hematoma, PerClot®

1. Introduction

Thyroidectomy was a common procedure with more than 100,000 operations performed in Germany [1]. Con-

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ventional thyroid surgery routinely produces successful outcomes and is known to have a high safety profile [2] [3]. Since the development of the capsular dissection by Thomson *et al.* [3] [4], morbidity rates even decreased. Surgical technique and experience of the surgeon in the field of thyroid surgery are important for an uncomplicated perioperative course [5] [6]. The major complications of thyroidectomy are the laceration of the parathyroid glands, the injury of the recurrent laryngeal nerve (RLN), and a postoperative hemorrhage [7] [8]. Nevertheless, postoperative haemorrhage remains an uncommon but potentially life-threatening complication of thyroid surgery. The risk for a postoperative hemorrhage to happen ranges from 0.5% and 6.5% [5] [7] [9] [10].

The conventional techniques for hemostasis are suture ligation and electrocoagulation. However, thermal damage to the surrounding structures can occur in the areas of electrocoagulation [7]. Also, it is difficult to satisfy oozing-type bleeding near vulnerable anatomic structures, such as the RLN and the parathyroid glands [7]. In recent years, various topical haemostatic agents have been widely used in thyroid surgery as in other surgical disciplines [6] [7] [11]-[15]. PerClot® (Starch Medical, Inc.; San Jose, CA) consists of dry, sterile, polysaccharide particles manufactured from purified plant starch using proprietary modification processes [16] [17]. The use of PerClot® in primary arterial anastomoses and anastomoses with synthetic prostheses has been reported in the literature [17]. Also it is believed that PerClot (®) can improve the wound healing, which might involve an increase in the activity of fibroblasts and increased release of TGF-β1 [16].

The aim of this prospective, non-blinded, monocentric case-controlled study was to compare the effectiveness of PerClot® as a haemostatic agent in thyroid surgery versus hemostasis by conventional technique (HCT). To our knowledge, this is the first controlled study testing the effectiveness of polysaccharide particle in thyroid surgery.

2. Materials and Methods

2.1. Material and Patients

Sixty patients were included in this study. These patients underwent a routine thyroid resection at the academic teaching hospital of the Ludwig-Maximilians-University in Agatharied, Hausham, Germany, from November 2009 to February 2010. All procedures were performed under general anesthesia and by the same two surgeons with more than 10 years experience in thyroid surgery. All patients gave their written informed consent. Exclusion criteria were the inability or unwillingness to consent, an age of less than 18 years and a known allergy against polysaccharide particles. Patients with suspicion of thyroid cancer, neck dissection, or planned sternotomy were also excluded just as those affected by disorders of hemostasis.

Surgery loupe glasses (factor 2.5 magnification) were routinely used to identify RLN and parathyroid glands. In addition, neuromonitoring of the RLN was performed (AVALANCHE®, Dr. Langer Medical GmbH, Waldkirch/Germany). Depending on the disease morphology, hemithyroidectomy or thyroidectomies were performed. Hemostasis was achieved by ligation of vessels during the surgical procedures or by bipolar electrocautery. After resection and before wound closure the lungs were inflated by positive pressure >35 mmHg for detection of unrecognized bleeding. All patients were examined preoperatively and postoperatively by the same independent laryngologist. Routine haematological tests were determined preoperatively and postoperatively (Hb, Wbc, Thrombos, Mean PTT, PTT, Ca, Crea).

2.2. Study Design

The first 30 consecutive patients represented the control group. These patients underwent a standard procedure (HCT) without any additional treatment after thyroid resection. The second 30 patients were placed in the treatment group. These patients received 1 g of PerClot® to the operative site following resection of the thyroid gland (**Figure 1**). PerClot® was applied at the end of the surgical procedure and therefore it had no impact on the visualization of the correct surgical anatomy (**Figure 2**). Perclot® is available in different dosages (1 g, 3 g and 5 g). In order to carry out cost-effective surgery, we decided to use the smallest dose of 1 g. In both groups, suction drains were placed in resection site (one drain in hemithyroidectomy, two drains in total thyroidectomy) to objectify the amount of postoperative bleeding.

PerClot® (Starch Medical, Inc.; San Jose, CA) consists of dry, sterile, polysaccharide particles manufactured from purified plant starch using proprietary modification processes [16] [17]. The final product is a sterile, white powder that can be applied directly to a bleeding wound to help control blood loss. The purified polysaccharide

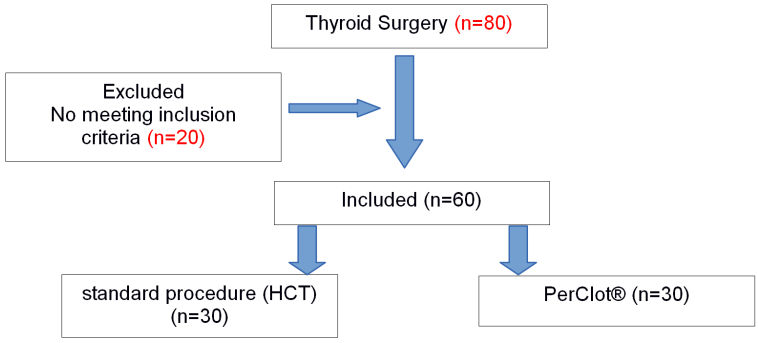

Figure 1. Flowchart of the trail design.

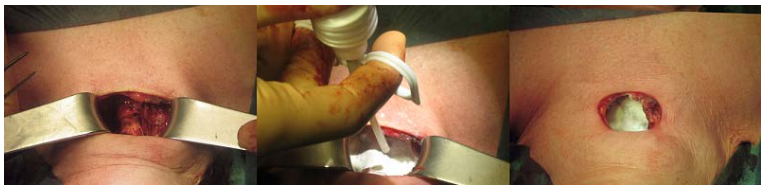

Figure 2. Application of PerClot® after resection of the thyroid gland.

particles contain no human or animal components. The haemostatic effect of the particles is produced by the rapid dehydration of blood and subsequent concentration of solid blood components (*i.e.*, thrombin, fibrinogen, platelets, etc.) which accelerates the normal, physiological clotting cascade [16] [17]. The concentration of serum proteins and red blood cells produces a viscous gel. Normal platelet activation and fibrin deposition within the congealed blood then produces a clot and adhesive matrix that limits further bleeding.

The primary outcome was postoperative hemorrhage, the drainage volume 24 hours postoperatively. Secondary outcome measures were adverse events concerning the use of PerClot® haemostatic agent like foreign body reaction, wound infection, edema and nerve entrapment. Additionally, the incidence of postoperative complications, *i.e.*, transient hypoparathyroidism, seroma, RLN palsy, duration of surgical procedure and the length of hospital stay were measured.

2.3. Statistical Analysis

The Sample size was estimated, using a power calculation based on a 50% reduction in drainage volume in the PerClot® group. It was calculated that after using PerClot® at least 12 or more patients per group would be required to detect a significant difference (power level 80%, alpha error of 5%). SPSS® 20 is used for statistical analysis. Kolmogorov-Smirnov-Test proves the normal distribution of our data (0.99). T-test and Chi square-test are used for comparison of the groups as the data are normal distributed.

3. Results

The mean age was 60.1 ± 11.2 years (range 38 - 83 years) and 76.67% of participants were female. The two groups were homogeneous for age, gender, ASA-score, type of procedure, reason for surgical intervention, size of the resected specimen and preoperative use of anticoagulant agents (**Table 1**). Routine hemogram, blood chemistry, and coagulation parameters were within normal ranges in all patients preoperatively (**Table 2**). In this study, 15 hemithyroidectomy and 45 thyroidectomy were included.

Mean operative time was 141.5 min ± 43.3 with no significant difference between the two groups: 141.3 min ± 49.8 PerClot® group and 141.7 min ± 43.5 control group ($p = 0.98$). The length of hospital stay was 2.4 days ± 0.7 by mean with so significant difference between the two groups: 2.5 days ± 0.7 control group and 2.4 days ± 0.7 PerClot® group ($p = 0.59$).

There was no significantly difference ($p = 0.79$) between the two groups in the mean postoperative suction drainage volume during the first 24 hrs (51 ml ± 36.9 for control group and 53 ml ± 39.5 for PerClot® group) (**Figure 3**). In all 60 performed thyroid resections, no postoperative bleeding or formation of a seroma with the

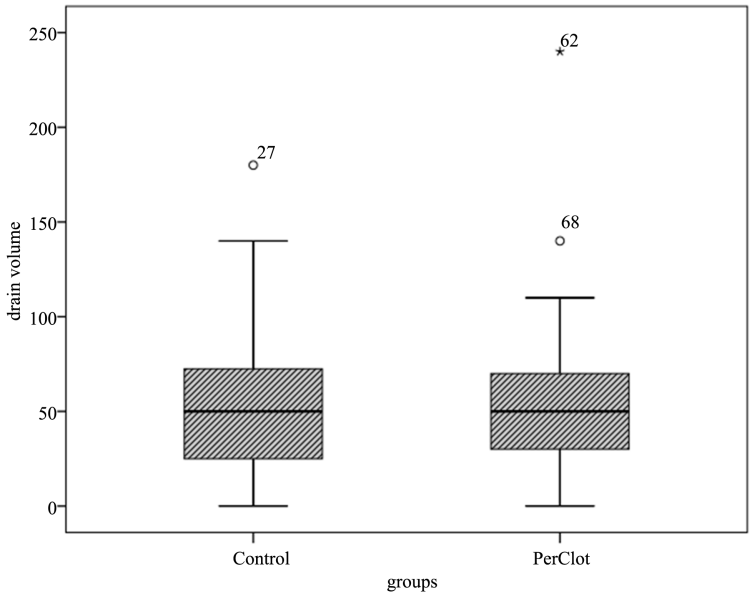

Figure 3. Drainage volume 24 hrs after thyroid resection.

Table 1. Patient demographics.

	Total (n = 60)	PerClot® (n = 30)	Control (n = 30)	P-value
Age, mean ± SD	60.1 ± 11.2	62.7 ± 11.2	57.4 ± 10.7	0.07
Male/female	46/14	25/5	21/9	0.22
ASA-Score, No				0.38
ASA 1	27	13	14	
ASA 2	26	15	11	
ASA 3	7	2	5	
Morphology				0.23
Nodular goiter	52	24	28	
Adenoma	6	4	2	
Papillary cancer	2	2	0	
Solitary nodule	0	0	0	
Mean specimen size, ml (Min-Max)	68.7 (8 - 430)	57.2 (8 - 146)	80.3 (14 - 430)	0.15
Lobectomy/Thyroidectomy	15/45	7/23	8/22	0.77
Mean operative time, min	141.5 ± 43.3	141.3 ± 49.8	141.7 ± 43.5	0.98
Mean duration of hospital stay	2.4 ± 0.7	2.4 ± 0.7	2.5 ± 0.7	0.59

ASA = American Society of Anesthesiologists; PTT = Partial Thromboplastine Time.

need for needle aspiration or surgical intervention occurred.

There was no operative mortality in any group. In the PerClot® group, there were no allergic reactions or adverse events (**Table 3**). In five cases (8%), transient hypocalcemia occurred (four control group and one PerClot® group). One RLN-palsy occurred in the control group. In a follow-up clinical examination it turned out to be a temporary one. No significant difference could be found for complication rates between control and PerClot® groups (**Table 2**).

Table 2. Laboratory values.

	Total (n = 60)	PerClot® (n = 30)	Control (n = 30)	P-value
Hb (g/dl) [12.5 - 17.5]	13.05	12.92	13.18	0.37
Wbc (x10E3/ul) [4.4 - 11.3]	10.32	10.15	10.49	0.63
Thrombos (/nl) [193 - 366]	251.92	263	240.83	0.18
Mean PTT, % [70 - 120]	103.7	105.5	102.3	0.39
PTT (sec) [29 - 45]	31.39	32.36	30.43	0.03
Ca (mmol/l) [2.00 - 2.60]	2.08	2.13	2.04	0.49
Crea (mg/dl) [0.60 - 1.13]	0.82	0.84	0.79	0.12

Hb = hemoglobin, Wbc = White blood cells, Thrombos = platelets, PTT = Partial thromboplastin time, Ca = Calcium, Crea = Creatinine.

Table 3. Complications/adverse events.

	Total (n = 60)	PerClot® (n = 30)	Control (n = 30)	P-value
Complications				0.58
Postoperative bleeding	0	0	0	
Seroma	0	0	0	
Hypocalcaemia	5	1	4	
RLN-palsy	1	0	1	
Adverse events				1.0
Allergic reactions	0	0	0	
Wound healing disorders	0	0	0	
Damage to the RLN	0	0	0	

RLN = Recurrent Laryngeal Nerve.

4. Discussion

According to R. Promberger ea. postoperative bleeding is an important complication after thyroidectomy [9]. Postoperative bleeding is associated with older age, bilateral procedure and operation for recurrent disease [9] [18]. There are several standard techniques for mastery of bleeding complications like suture ligation of individual vessels and electrocoagulation [7]. In addition to these standard techniques, the new haemostatic devices like Ligasure® [19] and Harmonic Scalpel [20] (e.g.) which have proven to decrease the risk for postoperative bleeding and intra-operative blood loss [21], could be useful in the surgical management of postoperative bleeding. It is a well known phenomenon that in case of postoperative bleeding often an active source of bleeding cannot be identified [5]-[7].

For several years, local haemostatic agents are available. Over the last decade the use of haemostatic agents has increased rapidly. Already in 1986 Browder IW and Litwin MS used an absorbable collagen for hemostasis in thyroid surgery [11]. Wright ea. report in their study on 3.633.799 patients that in 30.3% cases a haemostatic agent was used. The abdominal visceral surgery was leading with 47.1% of these cases [22]. Haemostatic agents are already successfully being used in abdominal and thoracic surgery. Rickenbacher *et al.* show the benefits of haemostatic agents concerning the control of diffuse oozing-type bleeding, suture-hole bleeding and in management of organ ruptures [23]. Haemostatic fleeces were shown to be superior to conventional methods in reaching a fast and effective haemostasis in cardiovascular surgery [24]. There are few studies investigating the usage of local haemostatic agents in neck surgery and thyroid surgery [6] [7] [11] [13]-[15] [25] [26]. After a systematic review of the literature, there has been no study that investigated the benefits of PerClot® in the reduction of postoperative bleeding after thyroid resection.

Our study showed no significant differences between the two groups with respect to patient demographics, medical histories, and operative and postoperative parameters. Despite the positive haemostatic characteristics of PerClot®, we found no significant difference in the drainage volume, 24 h postoperatively. The expected reduction of 50% of the drainage volume 24h after surgery as required above was not reached in this study. Furthermore the study fails to reveal any significant difference between the control group and the PerClot® group. Most likely, the amount of 1g used in this study is not sufficient enough to produce a measurable effect [17].

In this study, no adverse events (allergic reactions, wound healing disorders and the possible damage to the recurrent laryngeal nerve) related to the use of PerClot® were monitored. Several case reports describe massive allergic reactions after the application of the local haemostatic agent [27]. However Yanxia Wang *et al.* could prove that PerClot® can improve the wound healing in an animal model. This effect might be related to an increase in the activity of fibroblasts and increased release of TGF-1 [16].

An ideal agent would be effective, inexpensive, bioabsorbable, safe, and easy to use. In literature, however, some adverse events for hemostatic agents have been described, such as, wound infection, edema, nerve entrapment, allergic reaction [14] and misleading appearance on postoperative imaging [28]. The haemostatic effect of PerClot® has been proven [29] and until now no adverse events occur using PerClot®. The results of the present study are not contradictory of these findings but confirm the assumption of complication-free use of polysaccharide particles. Another advantage is the simple way of application. Furthermore the possibility of punctual implementation holds special advantages in comparison to the plane hemostatic agents. Applying polysaccharide particles the whole surgical wound cavity could be easily achieved. A higher dosage of PerClot® applied intraoperatively after thyroid resection could possibly decrease the 24 hrs drainage volume. But from the results of the study in this manuscript, we could not conclude that the use of PerClot® in a dosage of 1 g seems not to be effective. A final statement only can possibly be given after further investigation using a higher dosage like 3 g or 5 g of PerClot®. The cost of the application of 1g PerClot® amounts to 90€. Compared to other haemostatic agents, e.g. FloSeal® (210 €/application [6]) or TachoSil® (9.5 × 4.8 cm 210 €/application [30]), the costs are quite moderate. Further investigations using a higher dosage of PerClot® powder are planned in a similar setting to further explore the haemostatic effect and possible influence on postoperative bleeding complications.

5. Conclusion

PerClot® is easy and simple to use. There are no adverse events. Although our study findings indicate that routine use of a polysaccharide hemostatic agent (PerClot®) has no advantage over conventional hemostasis. To prevent postoperative hemorrhage, a meticulous hemostasis is necessary.

Conflict of Interest

The members of our surgical department are not consultants for Starch Medical, Inc. or CryoLife, Inc. We received no direct compensation for this research. We only received from Starch Medical, Inc. (San Jose, CA 95131, USA) the samples of PerClot® use for this investigation. The authors (Dr. med. Thomas von Ahnen; Dr. med. Martin von Ahnen; Dr. med. Ulrich Wirth; Anna Barisic; Prof. Dr. med. Hans Martin Schardey and PD Dr. med. Stefan Schopf) declare that they have no conflict of interests.

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