

Tiroid Cerrahisinde Oksitlenmiş Selüloz Kullanımının Postoperatif Hipokalsemi Üzerine Etkisi

The Effect of Oxidized Cellulose Use on Calcium Metabolism for Haemostatic Procedures in Thyroid Surgery

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Özet

Amaç: Hipokalsemi, tiroid cerrahisi sonrası hastalarda sık görülen bir komplikasyondur. Özellikle kalıcı hipokalsemi en sık görülür ve önemli morbiditeye neden olabilir. Ayrıca postoperatif hemoraji, tiroid cerrahisinin nadir görülen, hayatı tehdit eden bir komplikasyondur. Bu çalışmanın amacı tiroid cerrahisinde oksitlenmiş rejener selüloz gazlı bez (OC) ile konvansiyonel hemostaz tekniklerinin kullanımının postoperatif hipokalsemi gelişimi açısından karşılaştırılmasıdır.

Gereç ve Yöntemler: Deneyimli cerrahi servis tarafından yapılan ameliyatların sonuçlarının tek merkezde retrospektif karşılaştırması yapıldı. Okside selüloz (OC) ve ya geleneksel hemostaz, tüm total ve totale yakın tiroidektomi vakalarında kullanılmıştır. Preoperatif ve postoperatif Ca düzeyleri, operasyon süresi, hastanede kalış süresi, komplikasyonlar (kanama, rekürren laringeal sinir yaralanması, hipokalsemi) değerlendirildi.

Bulgular: İki yüz seksen sekiz hasta iki gruba ayrıldı: Grup 1 (144 hasta) konvansiyonel hemostaz, grup 2 (144 hasta) Okside selüloz + konvansiyonel hemostaz. Gruplar arasında cinsiyet, ameliyat öncesi ve sonrası Ca düzeyleri, hastanede kalış süresi, kanama, tekrarlayan sinir yaralanması açısından anlamlı fark yoktu. Ortalama yaş grup 1'de grup 2'ye göre anlamlı olarak daha yüksekti (52,4 yıla karşı 49,6 yıl, p <0,05). Grup 2'de operasyon süresi grup 1'e göre anlamlı olarak daha düşüktü (77,2 dk vs 87,2 dk, P <0,05).

Sonuçlar: Klasik hemostaz yöntemlerine kıyasla hemostaz OC'nin kullanımının postoperatif hipokalsemi oluşumunda pozitif-negatif fark yaratmadığını ve operasyon süresini kısaltırken komplikasyon oranlarında fark oluşturmadığını düşünüyoruz.

Anahtar Kelimeler: Tiroid cerrahisi, Selüloz yama, Hemostaz, Hipokalsemi

Abstract

Objective: Hypocalcemia is a frequent complication in patients after thyroid surgery. Especially permanent hypocalcemia is the most common complication and it can cause significant morbidity. Also postoperative haemorrhage is uncommon life-threatening complication of thyroid surgery. The aim of this study is to compare regenerated cellulose gauze (OC) and conventional haemostasis in thyroid surgery in terms of postoperative hypocalcemia development.

Material and Methods: A single center retrospective comparison of the outcome of surgeries performed by experienced surgeons. The Oxidized cellulose or conventional haemostasis were used in all total and near total thyroidectomy cases. Preoperative and postoperative Ca levels, operation time, hospital stay, complications (bleeding, recurrent laryngeal nerve injury, hypocalcemia) were evaluated.

Results: Two hundred and eighty eight patients were divided in to two groups: Group 1 (144 patients) conventional haemostasis, group 2 (144 patients) Oxidized cellulose + conventional haemostasis. There was no significant difference between groups in sex, preoperative and postoperative Ca levels, hospital stay, bleeding, recurrent nerve injury. The average age was significantly higher in group 1 compared to group 2 (52,4 years vs 49,6 years, p < 0,05). The operation time was significantly lower in group 2 compared to group 1 (77,2 min. vs 87,2 min., p < 0,05).

Conclusion: Compared with conventional haemostasis methods, we think that addition Oxidized Cellulose gauze for haemostasis does not create a positive-negative difference in calcium metabolism and does not make a difference in complication rates, while shortening the operation time.

Key words: Thyroid surgery, Cellulose patch, Haemostasis, Hypocalcemia

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INTRODUCTION

Thyroid gland, as one of the best blood supplied organs in human organism. Thyroid surgery has been accepted as a surgery avoided by high hemorrhagia complication and mortality rate, in old times. Thyroid surgery maintains its importance as a primary treatment model in many thyroid diseases. In recent years, decreasing rates in morbidity and mortality were achieved, with the extracapsular method and ligating the arterial blood supply at the beginning of surgery (1,2). The most common complications of thyroidectomy are recurrent laryngeal nerve damage and hypocalcemia due to hypoparathyroidism (3). The rate of transient hypoparathyroidism is reported between 0.3- 49% in different studies, and the rate of permanent hypoparathyroidism between 0-13%. (4). Hemostasis is very important in thyroid surgery (3,5). Postoperative hemorrhage may cause respiratory distress, asphyxia, respiratory arrest as result over the pressure on respiratory tract (5). Some studies reported: postoperative bleeding occurs between 0.5- 4.3% after thyroidectomy(1).

Oxidized cellulose gauze (OC) is frequently used in surgical interventions to provide haemostasis because it is cheaper and easier to use than many other haemostatic gels and similar materials. It is preferred by many surgeons to provide haemostasis during thyroidectomy (6). Platelet activation and aggregation accelerates, fibrin clot formation increases with the application of OC to the bleeding area (5). The aim of this study is to compare thyroidectomy patients with conventional +OC haemostasis and thyroidectomy patients conventional haemostasis for the development of postoperative hypocalcemia and to examine the role of OC in possible hypoparathyroidism.

MATERIALS and METHODS

We retrospectively reviewed the data of 362 patients who had undergone thyroidectomy for, in the the General Surgery Department of Evliya Celebi Hospital, Kütahya Health Sciences University between March 2015 and December 2019. Ethical issue was aproved by local ethic commite of Kütahya Health Sciences University (2020/09-11, 04.06.2020). According to Helsinki declaration, personal identities of the patients were not shared in this article. Informed constents were obtained from all patients.

Total thyroidectomy and near total thyroidectomy patients for benign thyroid nodules were included in the study. Age, sex, operation time, hospital stay, complications (bleeding, recurrent laryngeal nerve injury, hypocalcemia), preoperative and postoperative 24 hour Ca levels were determined. To evaluate the hypocalcemia and usage of OC, patients were divided into two groups: group 1-control (conventional haemostasis) and group 2- conventional+Oxidized cellulose (c+OC) haemostasis. For conventional haemostasis, monopolar, bipolar electrocautery, Harmonic ACE (Ethicon Endo Surgery) scissors and ligament suturing were performed. All thyroidecto-

mies were done by experienced endocrine general surgeons.

Exclusion criterias were pediatric age group (<18 years old), lobectomies, parathyroid gland autotransplantation patients, parathyroid gland excision patients, hypo-hyperparathyroid diseases, calcium disorders, hyperthyroidism and malignant thyroid disorders and incomplete data. Flow chart is presented in **Figure 1**.

Statistical Analysis

The information obtained was evaluated by using IBM SPSS (Statistical Package for Social Sciences) Statistics 20 statistical program, using Descriptive Statistics, Frequency Tables, Cross Tables, Independent Two-Sample t Test and Chi-square test. $P < 0.05$ was considered statistically significant.

RESULTS

In this study, we evaluated a total of 362 patients. On the other hand 74 patients' datas excluded from study due to exclusion criterias. The basic demographic features and clinical outcomes of 288 patients are presented in **Figure 1** and **Table 1** respectively.

The number of female patients was higher in both groups. There were 113/144 (78.5%) female patients in group 1, and 115/144 (79.9%) female patients in group 2. There was no significant difference in both groups in terms of sex distributions ($p = 0.77$). When the ages of the patients were evaluated, the average age in group 1 was 52.4 years and the average age in group 2 was 49.6 years. There was a statistical difference between both groups. ($p < 0.05$) (**Table 1**)

When preoperative and postoperative calcium values were examined, and the mean calcium values in both groups were found to be close to each other. There was no significant difference between the two groups both preoperatively ($p = 0.245$) and postoperatively ($p = 0.222$) (table 1). Transient hypocalcemia was detected in 29 patients (20.1%) in group 1, and in 23 patients (16%) in group 2. There was no statistically difference between the two groups ($p = 0.358$). Permanent hypocalcaemia was present in an equal number of patients (2.8%) in both groups ($p > 0.05$) (**Table 1-2**).

When the operative times were evaluated in both groups, the mean operative time in group 1 was 82.7 minutes, and in group 2 was 77.2 minutes. Compared to group 1, group 2 was found to have shorter operative times ($p < 0.05$). When the length of hospital stay was evaluated, the mean duration of stay in both groups was measured as 2.65 days in group 1 and 2.4 days in group 2, and was not statistically significant ($p > 0.05$). In the postoperative period, only 1 patient (the conventional + OC (c + OC) haemostasis group) developed bleeding and requiring reoperation. However, it was not statistically significant ($p > 0.05$). Recurrent nerve injury developed only in one patient in group 2 and was not statistically significant (**Table 2**).

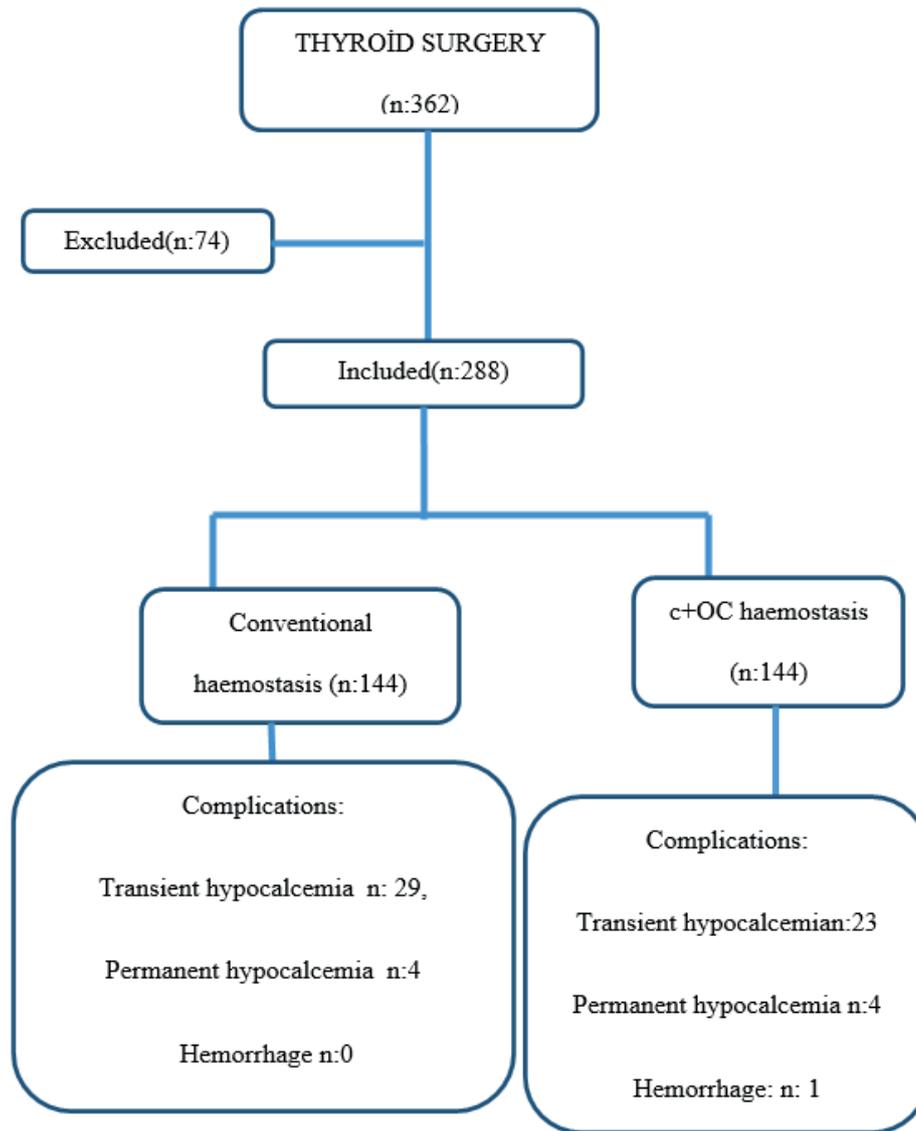


Figure1. Population samples disturbance in the study

Table 1. Baseline characteristics of 288 patients undergoing total and near total thyroidectomy

	Conventional haemostasis (Grup1)	c+OC haemostasis (Grup 2)
Age (mean±s.d)	52,48±13,17	49,69±11,23
Sex(%)(male/female)	21,5/78,5	20,1/79,9
Preoperative Ca(mean±s.d) mg/dL	9,40±0,37	9,45±0,42
Postoperative Ca(24. hour) (mean±s.d) mg/dL	8,87±,57	8,96±0,57
Operation time (mean±s.d)minute	82,70±10,85	77,22±11,01
Hospital stay(mean±s.d)day	2,62±0,85	2,47±0,71

Table 2. Postoperative morbidity in 288 patients undergoing total and near total thyroidectomy.

Complications	Conventional haemostasis(grup1)	c+OC haemostasis(Grup 2)
Recurrent nerve injury %	2,8	0,7
Transient hypocalcemia(%)	2,8	2,8
Permanenet hypocalcemia(%)	2,8	2,8
Haemoragia %	0	0,7

DISCUSSION

Providing hemostasis in all surgical procedures is as important as completing the surgical technique required by the indication. Haemostasis is achieved by applying pressure to the hemorrhage area for a while, tying it with simple sutures, closing the vessel with clips, using mono-bipolar cautery, using ultrasonic closure devices, using topical agents. Studies on effective, fast, inexpensive, easy-to-use hemostatic agents are ongoing (7). In this study, we reviewed retrospectively files of patients who underwent total or near total thyroidectomy for benign thyroid disease. The use of oxidized cellulose agent did not make a significant difference when postoperative calcium levels were compared, but a statistical difference was found in operative time.

The use of topical hemostatic agents, dating back to the 1940s, has increased rapidly over the past 30 years. There are many studies on agents that absorb and can stop bleeding quickly (8). Oxidized cellulose (OC) is one of the most commonly used topical hemostatic agents with anti-adhesion properties. In tissue, the hemostatic agent begins its destruction within 24-48 hours, it is wrapped with granulation tissue within 7 days and complete destruction occurs in 4-8 weeks (6). Side effects such as foreign body reaction, wound infection-abscess, edema, suspicious lesion in postoperative imaging, granuloma formation have been reported (6, 9, 10). Severe adhesions extending to the trachea, which causes skin withdrawal in long term, has been reported (11).

The thyroid gland, like all endocrine organs, has a very good blood supply system. The most common endocrine surgery is thyroidectomy (12). Completing the surgery with an extracapsular approach without damaging the thyroid gland reduces the risk of bleeding (2,3). Thyroidectomy procedure has become an outpatient surgery in recent years. Life-threatening bleeding usually develops within 6-8 hours after surgery. Seventeen percent of bleeding develops 24 hours after thyroidectomy (13). Postoperative bleeding rarely develops, and has been reported to be between 0.3% to 2% in some case series (14). With the use of mono-bipolar electrocautery devices, ultrasonic cutter-closer devices in surgical interventions for the last 25-30 years, blood loss in thyroid surgery has decreased and the operation times have been shortened (12,15). It is reported that careless use of mono-bipolar cautery, ultrasonic sealing device, near the parathyroid glands, recurrent laryngeal nerve may cause damage. As a result of sudden bleeding that may develop during dissection, careless and inexperienced use of clamps, clips or other hemostasis devices may cause injuries for parathyroid glands, recurrent laryngeal nerve, esophagus, trachea, carotid arteries, large veins (3). Hemorrhages close to the berry ligament may develop from the capillary branches of inferior laryngeal artery. Bleeding can be stopped with the use of compression and topical hemostatic agents patiently and carefully. In this way, nerve and parathyroid gland damage can be prevented (3).

Hypoparathyroidism may develop during thyroidectomy with iatrogenic mechanical or thermal damage, devascularization of the parathyroid gland, excision of the parathyroid gland along with the thyroid gland. Symptomatic and asymptomatic hypocalcemia may be seen (16). In order for hypoparathyroidism to develop, at least 2 parathyroid glands must be damaged (17). Different protocols for calcium, ionized calcium and parathormone measurement have been reported for the detection of hypoparathyroid (16, 18,17).

In this study, we used the calcium measurement values at the 24th hour postoperatively (16). Postoperative 1st day after thyroidectomy is called hypocalcemia, prolonged hypocalcemia if it lasts for 1 month, and permanent hypocalcemia if it continues despite treatment for about 1 year (16,17).

Surgeons are recommended to use C for hemostasis, shortening the operation time and limiting drain use. While there are authors using routine OC, there are those who think that OC use is useless (1,5).

In meta-analysis, which examined 10 research articles involving the use of hemostatic agents in thyroid surgery, the operation time was found to be significantly shorter in only 1 study in hemaostatic agent group (1). In our study, a statistical difference for operation time was detected in group two (77.22 ± 11.01 (min mean \pm sd)) compared to group 1 (82.70 ± 10.85 min (mean \pm sd)) ($p < 0, 05$).

In this study, in parallel with the studies evaluated in meta-analysis, no statistically significant difference was found in patients using both conventional and hemostatic agents for recurrent nerve injury (developed only in one patient in group 2) (1). In 4 studies evaluated in the same article, postthyroidectomy hypocalcemia was evaluated. No statistically significant difference was found in the development of hypocalcemia among groups using conventional hemostasis or hemostatic agent. In our study, in group 1 (20%); In group 2 (16%), the patient developed transient hypocalcemia, but there was no statistical difference between the two groups. The same result was obtained when evaluated in terms of permanent hypocalcemia (1). In metaanalysis, it was determined that the duration of hospital stay was shorter with the use of hemostatic agents compared to patients who underwent conventional hemostasis. In our study, it was found that the length of hospital stay did not differ statistically in both groups (1).

With this study, it was found that the operation time was shortened in patients using an anti-bleeding agent in accordance with the literature. Considering the limitations of our study; Our study is a retrospective and medium volume study and we cannot use parathormone levels because of missing data.

As a conclusion, Regardless of the method to be used for post-thyroidectomy hemostasis, the surgery should be completed carefully. The use of hemostatic agents is safe, does not cause problems affecting calcium metabolism and shortens the duration of the surgery (20).

Conflict of Interest and Financial Status

The authors declare that there is no conflict of interest to declare. The author(s) received no specific funding for this work.

Research Contribution Rate Statement Summary

The authors declare that, they have contributed equally to the manuscript.

REFERENCES

1. Khadra H, Bakeer M, Hauch A, Hu T, Kandil E. Hemostatic agent use in thyroid surgery: a meta-analysis, *Gland Surg* 2018; 34-41.
2. Aleksandar K, Miodagl D, Nebojsa D, Ilija G. Effect of fibrin vs cellulose based haemostatic agents with traditional haemostatic procedures in thyroid surgery. *Pak J Med Sci*. 2017;33(6):1360-1365.
3. Testini M, Marzaioli R, Lissidini G, Lippolis A, Logoluso F, Gurrado A, et al. The effectiveness of FloSeal matrix hemostatic agent in thyroid surgery: a prospective, randomized, control study. *Langenbecks Arch Surg*. 2009;394(5):837-42.
4. Kim JH, Chung MK, Son YI. Reliable early prediction for different types of post-thyroidectomy hypocalcemia. *Clin Exp Otorhinolaryngol*. 2011;4(2):95-100.
5. Amit M, Binenbaum Y, Cohen JT, Gil Z. Effectiveness of an oxidized cellulose patch hemostatic agent in thyroid surgery: a prospective, randomized, controlled study. *J Am Coll Surg*. 2013;217(2):221-5.
6. Royds J, Kieran S, Timon C. Oxidized cellulose (Surgicel) based reaction post thyroidectomy mimicking an abscess: A case report. *Int J Surg Case Rep*. 2012;3(7): 338-9.
7. Lewis KM, Schiviz A, Hedrich HC, Regenbogen J, Goppelt A. Hemostatic efficacy of a novel, PEG-coated collagen pad in clinically relevant animal models. *Int J Surg*. 2014;12(9):940-4.
8. Fischer CP, Bochicchio G, Shen J, Patel B, Batiller J, Hart JC. A prospective, randomized, controlled trial of the efficacy and safety of fibrin pad as an adjunct to control soft tissue bleeding during abdominal, retroperitoneal, pelvic, and thoracic surgery. *J Am Coll Surg*. 2013;217(3):385-93.
9. Tartaglia N, Di Lascia A, Lizzi V, Cianci P, Fersini A, Ambrosi A, et al. Haemostasis in Thyroid Surgery: Collagen-Fibrinogen-Thrombin Patch versus Cellulose Gauze-Our Experience. *Surg Res Pract*. 2016;2016:3058754.
10. Liu J, Hong W, Wu W, Ni H, Zhou M. Delayed Absorption of Oxidized Cellulose (Surgicel) in Post-Thyroidectomy Patients. *J Ultrasound Med*. 2016;35(6):1349-51.
11. Park KS, Lee KE, Ku do H, Kim SJ, Park WS, Kim HY, et al. Antiadhesive effect and safety of oxidized regenerated cellulose after thyroidectomy: a prospective, randomized controlled study. *J Korean Surg Soc*. 2013;84(6):321-9.
12. De Palma M, Rosato L, Zingone F, Orlando G, Antonino A, Vitale M, et al. Post-thyroidectomy complications. The role of the device: bipolar vs ultrasonic device: Collection of data from 1,846 consecutive patients undergoing thyroidectomy. *Am J Surg*. 2016;212(1):116-21.
13. Erdas E, Medas F, Podda F, Fucas S, Pisano G, Nicolosi A, et al. The use of a biologic topical haemostatic agent (TachoSil[®]) for the prevention of postoperative bleeding in patients on antithrombotic therapy undergoing thyroid surgery: A randomised controlled pilot trial. *Int J Surg*. 2015;20:95-100.
14. Rosato L, Avenia N, Bernante P, De Palma M, Gulino G, Nasi PG, et al. Complications of thyroid surgery: analysis of a multicentric study on 14,934 patients operated on in Italy over 5 years. *World J Surg*. 2004;28(3):271-6.
15. Cheng H, Soleas I, Ferko NC, Clymer JW, Amaral JF. A systematic review and meta-analysis of Harmonic Focus in thyroidectomy compared to conventional techniques. *Thyroid Res*. 2015; 1; 8:15.
16. Lorente-Poch L, Sancho JJ, Muñoz-Nova JL, Sánchez-Velázquez P, Sitges-Serra A. Defining the syndromes of parathyroid failure after total thyroidectomy. *Gland Surg*. 2015;4(1):82-90.
17. Oran E, Yetkin G, Mihmanlı M, Celayir F, Aygün N, Çoruh B, et al. The risk of hypocalcemia in patients with parathyroid autotransplantation during thyroidectomy. *Ulus Cerrahi Derg*. 2015;18;32(1):6-10.
18. Albuja-Cruz MB, Pozdeyev N, Robbins S, Chandramouli R, Raeburn CD, Klopper J, et al. A "safe and effective" protocol for management of post-thyroidectomy hypocalcemia. *Am J Surg*. 2015;210(6):1162-8.
19. Kala F, Sarici IS, Ulutas KT, Sevim Y, Dogu A, Sarigoz T, et al. Intact parathormone measurement 1 hour after total thyroidectomy as a predictor of symptomatic hypocalcemia. *Int J Clin Exp Med*. 2015;15;8(10):18813-8.
20. Kocián P, Neumann J, Bavor P, Hoch J. Disekční a koagulační technika - má vliv na výsledky totální tyreoidektomie? [Dissection and coagulation technique in thyroid surgery - is it the key to a successful outcome?]. *Rozhl Chir*. 2014;93(5):255-9.