Int J Clin Exp Med 2014;7(1):274-279
www.ijcem.com /ISSN:1940-5901/IJCEM1311013

Original Article

Does adrenaline spraying over thyroidectomy area reduce bleeding?

Yeliz E Ersoy[1], Erhan Aysan[1], Aysenur Meric[2], Huseyin Kadioglu[1], Merve B Cengiz[1], Suleyman Bozkurt[1], Naim Memmi[1], Gokhan Cipe[1], Mahmut Muslumanoglu[1]

[1]Department of General Surgery, Faculty of Medicine, Bezmialem Vakif University, 34306 Vatan Caddesi, Fatih, Istanbul, Turkey; [2]Department of Head and Neck Surgery, Faculty of Medicine, Bezmialem Vakif University, 34306 Vatan Caddesi, Fatih, Istanbul, Turkey

Received November 14, 2013; Accepted December 12, 2013; Epub January 15, 2014; Published January 30, 2014

Abstract: Background: Means to prevent and control intra- or postoperative bleeding remain a topic of utmost importance in thyroidectomy. In this randomised clinical trial, we used adrenaline spraying to see if it helps bleeding control and reduces drainage and hematoma formation after thyroidectomy. Methods: After total thyroidectomy, 1 mg/ml adrenaline solution in 10 ml saline was sprayed all over the operation area by a syringe in 40 patients of "Adrenaline (+) Group". In the other 40 patients in "Adrenaline (-) Group", only standart total thyroidectomy was performed. Drainage amounts of 24 hours were recorded. Results: Among 80 patients, 66 (82.5%) were female and 14 (17.5%) were male. The daily drainage amounts of the Adrenaline (+) Group were found statistically significantly lower than the Adrenaline (-) Group ($p<0.05$). In both of the groups, thyroid volumes were significantly correlated with the drainage amounts. "*p*" values were 0.008 and <0.001 in Adrenaline (+) and Adrenaline (-) Groups, respectively. Conclusions: Preliminary experience using adrenaline has been encouraging and it is useful as an adjunct to thyroid surgery in order to prevent hemorrhagia and give up drain placement. But prospective randomized trials using adequate patient numbers are still needed to validate efficacy and safety.

Keywords: Adrenaline, thyroid, bleeding, thyroidectomy, hematoma

Introduction

Thyroidectomy is one of the most commonly performed operative procedures in general surgery. Hematoma is a significant complication after thyroid surgery given the vascularity of the thyroid and the proximity of the thyroid bed to the airway [1]. Whilst uncommon, postoperative hematoma formation following thyroidectomy remains a potentially life threatening complication. It is important to recognise the more subtle signs of hematoma and to exercise a low threshold for surgical re-intervention to evacuate the haematoma [2].

Post-thyroidectomy haemorrhage has a variably reported incidence in the literature between 0.49 [3] and 4.3% [4].

Along surgical history, numerous technical advances have emerged in hemostasis. Ties, suture ligatures, Bovie's invention of monopolar/bipolar diathermy, vessel ligating clips, innovative hemostatic devices such as the electrothermal bipolar vessel sealing system and ultrasonically activated shears, topical haemostatic agents/sealants or tissue adhesives like oxidized cellulose (Surgicel), antifibrinolytics, surgical patches coated with human coagulation factors, Ankaferd Blood Stopper, hydroxilated polyvinyl acetal tampons, fibrin and collagen sealants have all been used to prevent postoperative hematoma formation [5-9].

But, as far as we know, there is not a study in the literature about the use of adrenaline after thyroidectomy to reduce bleeding. The vasoconstrictor effect of adrenaline is well known and infiltration of its solutions in saline is used in various interventions including nasal, breast, ophtalmic, urologic, orthopedic operations and endoscopic procedures.

For this reason, we decided to use adrenaline spraying to see if it helps bleeding control and reduces drainage after thyroidectomy and

hoped that it would help us to give up our traditional habit of using drains after thyroid surgery.

Materials and methods

The study was designed prospectively including 80 patients who were undergone total thyroidectomy for suspicion of malignancy as a result of fine needle aspiration biopsy at Bezmialem Vakif University, Medical Faculty, General Surgery Department. The study protocol was approved by the local ethics committee of Bezmialem Vakif University. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008, and informed consent has been obtained.

Patients were computer randomised and allocation was done on a sequential basis. Inclusion criterias were; patients who would undergo total thyroidectomy, no previous thyroid or any kind of neck operation, patients between 18-70 years old, without a previous history of disorders like hyperthyroidism, dysrhythmia, hypertension, angina pectoris, incompatiblity of adrenaline with the anaesthetic drugs, etc., and willing to participate in the study. On the other hand, exclusion criterias were; patients who had any kind of thyroid or neck operations previously, previous history of disorders like hyperthyroidism, dysrhythmia, hypertension, angina pectoris, incompatiblity of adrenaline with the anaesthetic drugs, etc., unwilling to participate in the study, patients who were pregnant or mentally retarded, patients under 18 and over 70 years old, ubnormal INR, and use of anticoagulant drugs.

The operations (total thyroidectomy using capsular dissection without any central or lateral neck dissections) were done by two endocrine surgeons both using the same surgical principles. In 40 patients of "Adrenaline (+) Group", 1 mg/ml adrenaline (Adrenalin 0.5 Mg 10 Amp., Biofarma İlaç Sanayi Ltd. Şti., IST, Turkey) solution in 10 ml saline was sprayed all over the operation area by a syringe, after standart total thyroidectomy and bleeding control. After placement of suction drain, the incision was closed anatomically. 40 patients were in "Adrenaline (-) Group", and only standart total thyroidectomy with drainage was done. No additional procedures such as lymph node dissection was performed in any of the patients. After thyroidectomy, all of the specimens were weighed and drainage amounts of 24 hours were recorded.

Student's t test was used to compare the daily drainage amounts of the two groups and Pearson correlation test was used to estimate the correlation of thyroid volumes and drainage amounts. A value of $p<0.05$ was considered significant.

Results

Included in the study were 80 patients, 66 (82.5%) of whom were female and 14 (17.5%) male. There were 40 patients (34 female, 6 male) in Adrenaline (+) Group and their mean age was 48.75 (range 28-72) years. Weight of the thyroidectomy specimens were 83.33 (range 24-747) grams.

In Adrenaline (-) Group there were 40 patients (32 female, 8 male) and their mean age was 45.38 (range 21-71) years. Weight of their thyroidectomy specimens were 64.80 (range 22-320) grams.

The mean of measured drain amounts for the first 24 hours were 36.65 ml and 51.75 ml in Adrenaline (+) and Adrenaline (-) Groups, respectively.

The daily drainage amounts of the Adrenaline (+) Group were found statistically significantly lower than the Adrenaline (-) Group ($p<0.05$) (**Table 1**).

In both of the groups, thyroid volumes were significantly correlated with the drainage amounts. "*p*" values were 0.008 and <0.001 in Adrenaline (+) and Adrenaline (-) Groups, respectively.

The longest hospital stay was two days in three patients (one with adrenaline, two without adrenaline) with large goiter, because of serohemorrhagic drainage about 100 cc/day. And their drains were withdrawn on the second (one patient, Adrenaline +) and third (2 patients, Adrenaline -) days before they were discharged from hospital. None of the patients had any morbidity including hematoma and wound infection, or mortality. Adrenaline did not have

Table 1. Patient characteristics and comparison of drainage amounts between groups

	Adrenaline (+) (n:40)	Adrenaline (-) (n:40)	p*
Age (years)	45.38	48.75	
Gender	34 F, 6 M	32 F, 8 M	
Weight of thyroid gland (grams)	64.80	83.33	
Drainage/24 hours (ml)	51.75	36.65	0.021

*p (t test), <0.05 is accepted as significant (F: Female, M: Male).

any unwanted effect on hemodynamic stability and wound healing process.

According to the final pathology results 33 patients in the Adrenaline (+) Group and 31 patients in Adrenaline (-) Group had malignancy. There was not any significant difference between the benign and malignant patients of each group in itself on behalf of weight of the thyroidectomy specimens and measured drain amounts ($p>0.05$), but there were significant differences between the benign and malignant patients of the opposed groups ($p<0.05$).

Discussion

With increasing surgical interest in the thyroid gland in the 1800s came mortality rates in the vicinity of 40%; many of these deaths often being related to hemorrhage [2]. Today, despite ongoing refinements in techniques, innovations in surgical instruments and a better understanding of underlying thyroid pathologies, postoperative hemorrhage and hematoma formation are fortunately rare but dreaded and potentially life-threatening complications of thyroid surgery that require immediate reoperation and warrant adherence to a strict protocol to ensure safe management. When life-threatening hematomas occur, they depend on various uncontrolled factors and drainage is often not helpful [2, 10, 11].

Numerous factors contribute towards causing haemorragic complications, such as the technique used for haemostasis, the drainage, and the haemorragic risk factors presented by the individual patient including the hyperthyroidism causing thyroid congestion, tumescence, and increasing thyroid blood supply [12, 13].

Although the rate of bleeding might increase in subtotal thyroidectomy or in Graves disease due to vascularised remnant tissue, in fact, postoperative bleeding has been reported as rare as 0.3%~1% after thyroidectomy [10]. Meticulous haemostasis is important in all surgical procedures. However, the head and neck area is particularly susceptible to bleeding due to rich vascular supply in the area [14, 15]. Each must be securely occluded and divided to perform a safe and expeditious operation [14]. Any surgeon who has routinely been practising thyroid surgery knows that even minor bleeding from small vessels may greatly compromise the view of surgical field, lead to severe difficulties in identifying the anatomical structures and could cause a major complication in thyroid surgery. Furthermore, management of abnormal bleeding exposes the patient to the morbidity of re-operation [9].

Means to prevent and control intra- or postoperative bleeding remain a topic of utmost importance. Numerous manoeuvres and surgical hemostatic agents may be used to minimise the risk of hematoma formation but are no substitute for careful hemostasis [2, 15]. Valsalva manoeuvre and tilting the patient with the head down (Trendelenburg tilt) may reveal occult bleeding vessels by increasing venous pressure, or washing the wound with hydrogen peroxide may make bleeding points more evident [15]. Hemostasis in thyroid surgery is achieved by means of conventional clamp-and-tie technique, diathermy, and haemostatic clips, tampons, fibrin sealant, and gauzes [7, 9]. In the last 10 years major improvements and new technologies have been proposed and applied such as mini-invasive thyroidectomy, regional anaesthesia and intraoperative neuromonitoring, and new devices like ultrasonic coagulating-dissection and electrothermal bipolar vessel sealing systems for achieving dissection and haemostasis, eventually improving primary and secondary hemostasis rates and the safety of treatment [9, 16].

And as a result of advances in bleeding control, recently, the use of drains in thyroid surgery has decreased considerably. The use of surgical drains in patients undergoing thyroid surgery was standard in surgical teaching. Life-

threatening complications, arising from postoperative hematomas, mandated their utilization [17]. Although several prospective randomized reports regarding the function of drains in thyroid surgery have not justified their use, most surgeons like us give into tradition of leaving a drain following thyroid surgery with the hope that this will obliterate the dead space, evacuate collected blood and serum, and asist in the early detection of postoperative bleeding [1, 28]. However, some surgeons like Bergqvist and Kallero feel that retained blood in the wound bed often clots and blocks the drain, making it ineffective and avoids alerting the surgeon even if major bleeding occurs [10]. Others are concerned that patient discomfort is heightened, infection risks and pain increased, and hospital stays lenghtened [1].

Studying on bleeding control, in 1987 Auvinen et al. [6] examined the effect of the antifibrinolytic drug tranexamic acid on perioperative bleeding and unfortunately stated that tranexamic acid had no measurable effect on perioperative bleeding in connection with thyroid surgery. Consequently, Lachachi et al. [5] used fibrin sealant in 81 patients who underwent thyroid surgery without drainage and concluded that fibrin sealing could be widely used in thyroid surgery as an adjunct to a perfect hemostatic technique.

In 2006, Tonante et al. [13] stated that the use of FloSeal [collagen and thrombin gelatine] to treat bleeding from retroneural arterial vessels, arrested bleeding in 100% of treated patients like the study of Ujam et al. [19] in 2012 which showed reduction in blood loss, hematoma rates, drain usage and hospital stay. In another study, Haas et al. [7] claimed surgical patch coated with human coagulation factors (TachoSil) to be efficacious and safe as a hemostatic treatment in a broad variety of surgical interventions. Dionigi et al. [9] used hydroxylated polyvinyl acetal tampons (HPA) and showed their efficacy for minor bleeding control, fluids removal and tissue dissection during several thyroid procedures. Later on, McNally et al. [20] compared ultrasonic dissection and electronic vessel sealing in patients undergoing thyroidectomy and showed that both were safe and effective.

It is known that adrenalin, added to the local anaesthetic solution, or to saline used to infiltrate the tissues, will minimise capillary and venous bleeding. The use of adrenaline as a hemostatic aid dates back to the end of the nineteenth century with a report of the application of suprarenal gland extract for the treatment of epistaxis [21], and by the turn of the twentieth century, a purified epinephrine chloride (as a 1:1000 solution) was used in ophthalmic and nasal surgery [22]. Also numerous randomized controlled studies and the meta-analysis of Hardwicke et al. [23] have shown a reduction in intraoperative blood loss in reduction mammoplasties and no significant difference in the complication rate related to epinephrine infiltration was reported in any of the reviewed studies. Besides these, the vasoconstrictor effect of adrenaline is also used in various interventions including nasal, urologic, orthopedic operations and endoscopic procedures.

Another advantage of epinephrine infiltration is reduction in postoperative pain when local anesthetic agents are included in the infiltration solution. This can allow the procedure to be performed as a day-case or outpatient procedure. On the other hand, morbidity associated with epinephrine infiltration has also been highlighted with reports of visceral injury, systemic physiologic effects like hypertension, delayed wound healing, skin necrosis, and rebound hemorrhage [24-26]. But we did not experience any complications related with any of these effects, especially rebound hemorrhage. Also none of the patients had any problems about hypertension, maybe owing to the low dose.

As far as we know, there is not a study in the literature about the use of adrenaline after thyroidectomy to reduce bleeding. But, in two studies of long standing, subcutaneous infiltration of adrenaline during surgery was discussed. In 1971, although Brooke [27] considered subcutaneous infiltration of the neck with adrenaline containing solution dangerous, Mair [28] advocated adrenaline stating that introduction of an adequate amount of solution facilitated the approach to the gland and reduced bleeding.

In our study, thyroid volumes were found to be significantly correlated with the drainage amounts and adrenaline spraying over thyroidectomy area significantly reduced bleeding. As a result of these findings, we can conclude that preliminary experience using adrenaline has

been encouraging and it is useful as an adjunct to thyroid surgery in order to prevent hemorrhagia. Besides adrenaline is much more cheaper than the other haemostatic agents. Furthemore, these results can encourage us for not using a drainage after adrenaline spraying. But prospective randomized trials using adequate patient numbers are still needed to validate efficacy and safety.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Yeliz Emine Ersoy or Dr. Erhan Aysan, Department of General Surgery, Faculty of Medicine, Bezmialem Vakif University, Estonsehir KV-28/1, Samlar Koyu, Tatarcik Mevkii, Bahcesehir Yani, Basaksehir 34306/Istanbul, Turkey. Tel: +90 532 610 27 13; Fax: +90 212 6318918; E-mail: yelizemineersoy@yahoo.com (YEE); erhanaysan@hotmail.com (EA)

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