

Efficacy of fibrin sealant in thyroid surgery. Is drainage still necessary?



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Efficacy of fibrin sealant in thyroid surgery. Is drainage still necessary?

INTRODUCTION: The routinely use of drains in thyroid surgery is a traditional and well-defined method, even if there is no clear evidence of significant improvement in patients outcomes. Aim of our study is to define the feasibility, safety and cost-effectiveness of fibrin sealant in total thyroidectomy in order to overcome the use of drains.

MATERIALS AND METHODS: We enrolled 262 patients (45 men and 217 women, mean age 54.7 yrs) undergone total thyroidectomy in University Hospital of Palermo (Italy), between July 2015 and October 2017. We randomized patients into group A (drain) and group B (no drain, fibrin sealant application).

RESULTS: We registered statistical difference between the two groups in mean operative time, visual analogue scale of pain, post-operative stay, incidence of seromas and/or deep and superficial hematomas, re-operation and wound infection (reduced in the fibrin sealant group). No significant difference have been found in intraoperative blood loss, postoperative cough, post-operative use of analgesic and in incidence of hypoparathyroidism or recurrent palsy.

CONCLUSIONS: Our study demonstrates that there is no evidence that the use of suction drains improves patients outcome and that routinely use of fibrin sealant can be advocated in thyroid surgery as an adjunct to a good surgical procedure.

KEY WORDS: Complication, Drainage, Fibrin Sealant, Thyroidectomy

Introduction

The routinely use of drains in thyroid surgery, natural free fall (using only gravitative forces) better than negative pressure or aspirative ¹, is a traditional and well-defined method, even if there is no clear evidence of significant improvement in patients outcomes. As a matter of fact, drains could lead to an increased length of hospital stay and post-surgical infection rate; so that they

should only be used in complicated surgery or in case of huge dead space such as in retrosternal goiter ^{2,3}.

On the other hand fibrin sealants could be considered today as a modern opportunity to improve the aesthetic outcome of post-thyroidectomy wound and to prevent the outbreak of seroma and hematoma by sealing the residual cavity, without any change on safety or cost of thyroid surgery ^{4,5}.

Therefore our study aims to define the feasibility, safety and cost-effectiveness of fibrin sealant in total thyroidectomy in order to overcome the use of drains.

Materials and Methods

PATIENTS

We enrolled 262 patients (45 men and 217 women, male-female ratio 1:4.8, mean age 54.7 yrs, range 20-88 yrs) (Table I) undergone total thyroidectomy at the

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TABLE I - Demographics and diagnosis

	Group A (drain) n = 128	Group B (no drain + fibrin sealant) n = 134
Mean age (range)	54.1 (20-79) yrs	55.3 (22-88) yrs
M:F ratio	1:4.3	1:5.3
ASA score I (%)	5/128 (4%)	4/134 (3%)
ASA score II (%)	48/128 (37.5%)	55/134 (41%)
ASA score III (%)	75/128 (58.5%)	75/134 (56%)
Diabetes (%)	18/128 (14%)	21/134 (15%)
Previous coagulopathy (%)	22/128 (17%)	29/134 (21%)
Allergy (%)	12/128 (9%)	10/134 (7%)
COPD (%)	21/128 (16%)	28/134 (21%)
Multinodular goiter (%)*	72/128 (56%)	81/134 (60%)
Toxic goiter (%)*	68/128 (53%)	71/134 (63%)
Graves' disease (%)	21/128 (16%)	30/134 (22%)

* Also in the same time in the same patients

Section of General and Thoracic Surgery of University Hospital of Palermo (Italy), between July 2015 and October 2017. We excluded from the study patients who underwent lateral compartment neck dissection or surgery for extracapsular lesions.

SURGERY

We randomized patients into group A (drain, n = 128, 24 men and 104 women, mean age 54.1, range 20-79) and group B (no drain, fibrin sealant application, n = 134, 21 men and 113 women, mean age 55.3 yrs, range 22-88 yrs).

Total thyroidectomy has been performed by a high volume surgeon through extracapsular dissection. Before wound closure, an accurate washing of both thyroid residual cavities with warm saline solution has been required in order to remove fibrinogen degradation

products and any colloid residues. Underflap suction drains have been placed and brought out through a separate incision before wound closure in group A patients while in group B no drain was used. In group B patients, after total thyroidectomy, 4 to 10 ml fibrin sealant (Tisseel® Baxter, Italy) have been sprayed on to the surgical site and under the flap using a dedicated double-barrel syringe and spray tip applicator next, platysma layer of absorbable sutures were placed approaching the two surfaces to close the dead space; the wound has been immediately closed, allowing the fibrin sealant to seal the apposed tissues (Fig. 1). In the 2 groups of patients we take into consideration operating time, postoperative pain, total amount of intramuscular analgesic administration, hospital stay, early and late complications (such as wound infection, seroma, bleeding, hematoma, recurrent laryngeal nerve palsy or hypoparathyroidism), aesthetic and functional results at one year follow-UP. ASA scores and clinical data, were recorded from our surgical electronic database. The operating time was defined as the time from the first incision to the last suture placement. Postoperative pain was assessed according to visual analogue scale (VAS) from 0 (no pain) to 10 (worst pain imaginable) on postoperative day (POD) 0 and POD 1, if the patient was not discharged. A standard analgesic protocol has been used according to VAS scores, psychometric response scale for subjective characteristics or attitudes that cannot be directly measured ⁶.

The patients has been discharged at first post-operative day when there were no complication or when they were not anymore in need of intramuscular analgesics. In the drain group, the volume of fluid collected has been measured and the drains were removed after drainage was reduced to less than 20 ml. The patients have been examined by a standard physical examination after one week, after one month, every three months and after one year thereafter; we classified the aesthetic result of scar according to Mustoe scar classification in (1) mature scar, (2) immature scar, (3) linear hypertrophic, (4) widespread hypertrophic, (5) minor and (6) major keloid ⁷.

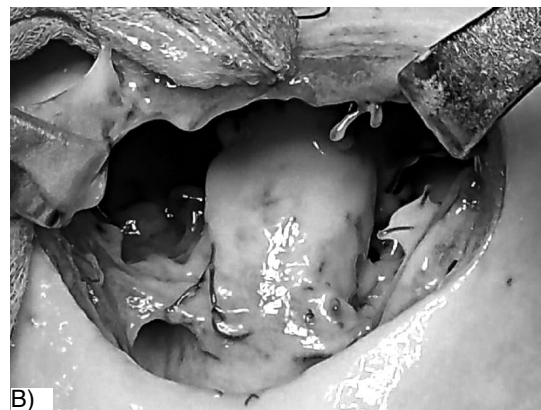
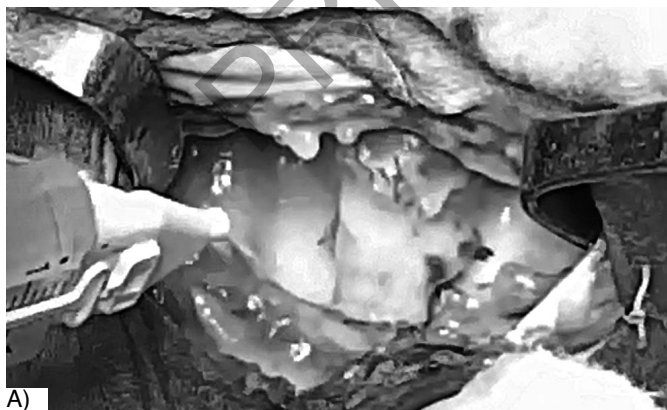


Fig. 1: beginning (A) and end (B) of application of fibrin spay sealant on the surgical site.

TABLE II - Operative data

	Group A (drain)n = 128	Group B (no drain + fibrin sealant)n = 134	p
Operative time	101 ± 19 minutes	89 ± 20 minutes	< 0.05
Intraoperative blood loss	25 ± 40 ml	25 ± 35 ml	n.s.
Bipolar cauthery	100%	100%	n.s.
Ultrasonic scissors	15/128 (11%)	12/134 (9%)	n.s.
Drainage diameter	10 Ch	n.a.	-

n.s. = not significant

n.a. = not applicable

TABLE III - Post-operative data Post-

	Group A (drain)n = 128	Group B (no drain + fibrin sealant)n = 134	p
Post-operative cough	39/128 (30%)	42/134 (31%)	n.s.
Post-operative analgesic	15/128 (12%)	23/134 (17%)	n.s.
VAS score > 0-2 (POD 0)	10/128	3/134	< 0.05
VAS score > 0-2 (POD 1)	6/128	0/134	< 0.05
VAS score > 0-2 (POD 2)	6/128	0/134	< 0.05
Hospital post-op stay (days)	3 ± 2	2 ± 1	< 0.01
Deep hematoma	11/128 (8%)	0/134	< 0.001
Subcutaneous hematoma	13/128 (10%)	3/134 (2%)	< 0.05
Bleeding from drain orifice	16/128 (12%)	Not applicable	< 0.01
Seroma	6/128 (5%)	0/134	< 0.001
Re-operation	10/128 (8%)	0/134	< 0.001
Wound infection	7/128 (5%)	0/134	< 0.001
Transient hypoparathyroidism	5/128 (4%)	6/134 (4%)	n.s.
Transient bilateral recurrent palsy	1/128 (1%)	1/134 (1%)	n.s.
Transient unilateral recurrent palsy	4/128 (3%)	6/134 (4%)	n.s.
Gas embolism	n.a.	0	-
Cosmetic result at one week	Class 1 25%	Class 1 20%	n.s.
	Class 2 75%	Class 2 80%	n.s.
	Class 3 -	Class 3 -	-
	Class 4 -	Class 4 -	-
Cosmetic result at one month	Class 1 85%	Class 1 100%	< 0.01
	Class 2 15%	Class 2 -	n.s.
	Class 3 -	Class 3 -	-
	Class 4 -	Class 4 -	-
Cosmetic result at three months	Class 1 95%	Class 1 100%	n.s.
	Class 2 5%	Class 2 -	-
	Class 3 -	Class 3 -	-
	Class 4 -	Class 4 -	-
Cosmetic result at one year	Class 1 100%	Class 1 100%	n.s.
	Class 2 -	Class 2 -	-
	Class 3 -	Class 3 -	-
	Class 4 -	Class 4 -	-

For scar classification, see in the text ⁶

n.s. = not significant;n.a. = not applicable

Results

Results are summarized in table 2 and 3: the mean operative time in the two groups was respectively 101 ± 19 minutes in the drain group and 89 ± 20 minutes in the

fibrin sealant group, with a statistical difference between the two groups ($p < 0.05$), while no significant difference were found in intraoperative blood loss (Table II), post-operative cough and post-operative analgesic (Table III). Moreover, probably due to the absence of drainage, visu-

al analogue scale of pain was better in no drain group, as the post-operative stay (Table III).

Because of the early obliteration with fibrin sealant of residual space post-thyroidectomy, the difference in terms of incidence of deep and superficial hematomas has been statistically reduced in the fibrin sealant glue, with consequent reduction of seromas, re-operation, wound infection, post-operative stay and with better aesthetic results and patients' satisfaction.

No significant differences in terms of transient hypoparathyroidism or recurrent palsy were registered in the two groups, even if our attention has been attracted by a singular case of temporary bilateral recurrent stupor, resolved after 32 days, probably due to the spray application too close to the surgical site (<10 cm), with consequent barotrauma on laryngeal nerve.

From the aesthetic point of view, we found, in a statistically significant way, a notable reduction of the late edema of the cervicotomy.

Discussions

Thyroid is a vascular gland placed in a high-vascularized district as the neck and total thyroidectomy leaves a huge dead space. Any small postoperative bleeding or excessive fluid accumulation may lead to serious life-threatening complications such as venous oedema of the airway, which if detected early enough requires emergency decompression, otherwise it may lead to fatal consequences¹⁻³.

Experimental studies on pigs suggest that pressure due to post-operative hematomas of the neck would not be sufficient to cause airway obstruction by direct compression on the trachea. Therefore, the most likely cause of airway obstruction would be supraglottic oedema secondary to venous obstruction; at pressures of 257 mmHg, equivalent to the maximum possible pressure in the neck (i.e. systolic blood pressure), there was an average compression of 21% of the original anterior-posterior tracheal diameter⁸.

Moreover, the incidence of significant post-thyroidectomy bleeding varies in literature between 0.3 and 1.3% but it has proposed that clotted blood blocking up the drain may cause more harms than benefits, as the surgeon may not be aware of a major bleeding^{9,10}; patient factors that increase the risk of postoperative bleeding have not been clearly defined although the authors found a tendency toward increased bleeding risk in patients on anticoagulants or with arterial hypertension^{10,11}.

Nevertheless, surgeons keep on considering that under-flap suction drains placed after total thyroidectomy can act as an 'early indicator' of significant postoperative haemorrhage and provide a safeguard against compressive effects³, even if their use may augment scarring in a cosmetically sensitive area, add discomfort to the patient¹² and have the theoretical potential to disturb hemostasis at the time of drain removal¹³.

Coughing and straining are to be avoided during extubation at the end of surgery as nausea and vomiting in the early postoperative recovery¹³.

As an alternative to surgical drainage, fibrin glue has been proposed in early 2001's. It is a biological adhesive material that is made of human fibrinogen and its multiple components. Fibrin glue promotes wound healing by enhancing homeostasis and angiogenesis, and stimulating macrophages, which have a role in fibroblast proliferation and collagen production in the wound site¹⁴. It has been successfully used to reduce wound drainage and to improve other short-term post-operative results¹⁵. It has been shown that fibrin glues, firstly in breast surgery, are effective in reducing seroma formation in animal models and in reducing drainage¹⁶. They offer a comparative advantage over under-flap suction drains in thyroid surgery, resulting in decreasing the drain output after total thyroidectomy by reducing wound drainage⁴ and the length of hospital stay in a statistically significant way¹⁷.

The active ingredients of Tisseel® are formulated as two sterile, deep-frozen solutions; the sealer protein solution (synthetic aprotinin 3000KIU/mL, factor XIII 1.2IU/mL and fibrinogen 72mg/mL) and thrombin solution (human Thrombin 400IU/mL and Calcium chloride 36 micromole/mL). Each solution is presented in a separate preloaded chamber of one double-chamber syringe. The active ingredients are fractionated from pooled human plasma¹⁸.

To reduce the risk of a gas embolism, while applying Tisseel® using a spray device, the pressure should be within the pressure range recommended by the spray device manufacturer (1.4 - 1.7 bars or 20 - 25psi). Do not spray if the distance is closer than 10 - 15cm from the surface of the tissue. By the way, when spraying Tisseel®, changes in blood pressure, pulse, oxygen saturation and end tidal CO₂ should be monitored because of the possibility of occurrence of air or gas embolism¹⁸.

In our experience, the routinely use of fibrin spray glue leads apparently to an initial increase in costs of the surgical tools (4 ml prefilled set = € 179.58, 10 ml prefilled set = € 457.35, 1 Easyspray kit = € 3.00 vs 1 aspiration drainage = € 5.00, 1 non-absorbable suture = € 2.50), but it also brings to a statistically significant reduction of hospitalization rates (on average, 20 hours less), post operative pain, medication costs (€ 205.00/day in group B vs € 250.00 / day in group A) and meals (€ 35.00 / day).

In addition reduction of operative time allowed by the use of Tisseel®, although not statistically significant, allowed to insert 3 additional surgical interventions in a typical 36-hour week.

The routinary use of haemostatic agent may improve the comfort of patients' postoperative hospital stay, as well as reduce their length of stay, and allow for more rapid resumption of normal daily activities, facilitating the option of one-day surgery¹⁹.

As far as complications are concerned, it is not possible to state that the use of fibrin glue has statistically reduced the incidence of postoperative bleeding, even if, in line with what has been reported in literature, we have observed a satisfactory improvement.

The only case of temporary bilateral recurrent stupor, however treated conservatively and resolved with functional *restitutio ad integrum* after 32 days, is probably due to the spray application too close to the surgical site (<10 cm), resulting in tracheo-esophageal barotrauma and therefore of the inferior laryngeal nerve in its normal course.

Conclusions

Obviously, the use of drain or fibrin sealant do not obviate the mandatory need for intraoperative meticulous haemostasis.

Nevertheless, our results demonstrate that there is no evidence that the use of suction drains improves patients outcome and that routinely use of fibrin sealant can be advocated in thyroid surgery as an adjunct to a good surgical procedure, perhaps making unnecessary prophylactic drainage, except in selected cases.

Moreover, a more great number of validated clinical studies are need to certificate real and effective reduction of hemorrhagic complication.

Riassunto

INTRODUZIONE: L'uso routinario dei drenaggi in chirurgia tiroidea è un metodo tradizionale e ben definito, anche se non vi è una chiara evidenza di un miglioramento significativo nei risultati dei pazienti. Scopo del nostro studio è definire la fattibilità, la sicurezza e l'economicità della colla di fibrina nella tiroidectomia totale al fine di superare l'uso di drenaggi.

MATERIALI E METODI: Sono stati arruolati 262 pazienti (45 uomini e 217 donne, età media 54.7 anni) sottoposti a tiroidectomia totale presso l'Ospedale Universitario di Palermo, tra luglio 2015 e ottobre 2017. Abbiamo randomizzato i pazienti nel gruppo A (drenaggio) e nel gruppo B (nessun drenaggio, applicazione di sigillante di fibrina).

RISULTATI: Abbiamo registrato la differenza statistica tra i due gruppi in tempo operatorio medio, scala analogica visiva del dolore, degenza post-operatoria, incidenza di sieromi e / o ematomi profondi e superficiali, reinterventi e infezione della ferita (ridotta nel gruppo con sigillante di fibrina). Nessuna differenza significativa è stata trovata nella incidenza di emorragia intraoperatoria, nella tosse postoperatoria, nell'uso post-operatorio di analgesici e nell'incidenza di ipoparatiroidismo o paralisi del nervo ricorrente.

CONCLUSIONI: Il nostro studio dimostra che non vi è alcuna prova che l'uso di drenaggi in aspirazione miglio-

ri l'esito dei pazienti e che l'uso routinario del sigillante fibrinoso possa essere sostenuto nella chirurgia della tiroide in aggiunta ad una ottimale procedura chirurgica.

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