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Betamethasone to prevent hypocalcemia and other complications after total thyroidectomy: A retrospective case-control study

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ABSTRACT

Objective: Hypocalcemia (HC) is a common complication after thyroid surgery. This retrospective case-control study aimed to evaluate the efficacy of postoperative betamethasone infusion in reducing the incidence of HC following thyroid surgery, with recurrent laryngeal nerve palsy and other complications as secondary outcomes.

Material and Methods: A total of 196 patients who underwent total or completion thyroidectomy were retrospectively analyzed. Patients were divided into groups receiving postoperative betamethasone infusion or no glucocorticoid treatment. Postoperative data on HC incidence (at least one serum calcium measurement below 8.0 mg/dL), symptomatic HC (HC associate with numbness of the extremities, facial paresthesia, muscular spasms, and Chvostek's or Trousseau's signs), pain, recurrent laryngeal nerve palsy, voice dysfunction, sore-throat and dysphagia were collected and analyzed. Additionally, demographic and clinical characteristics were assessed, including preoperative assessments, intraoperative techniques, and postoperative recovery parameters.

Results: The study found a significantly lower incidence of HC and symptomatic HC in the betamethasone group compared to the control (32.0% vs. 49.5%, p=0.013; 11.3% vs. 25.3%, p=0.012, respectively). Betamethasone-treated patients also reported lower postoperative pain scores (p=0.002).

Conclusion: Betamethasone infusion post-thyroidectomy demonstrated efficacy in reducing HC and symptomatic hypoparathyroidism, with minimal impact on other complications. The findings suggest the potential of glucocorticoids as a therapeutic option in thyroid surgery to enhance postoperative outcomes and patient recovery.

Keywords: Endocrine surgery, parathyroid, thyroid surgery

INTRODUCTION

Total thyroidectomy is an effective therapy for both benign and malignant diseases of the thyroid gland. Although thyroid surgery is considered a safe procedure, it can cause serious postoperative complications.

Hypocalcemia (HC) and recurrent laryngeal nerve (RLN) palsy are serious complications after thyroidectomy. Biochemical HC represents the most frequent complication with rates ranging from 15.7% to 76.7% in a recent systematic review (1). HC can often cause a prolonged postoperative recovery with increased hospital care cost, so that preventing this complication is very important (2). Even when the procedure is expertly performed, surgical trauma remains a recognized cause of HC because the parathyroid glands may be unintentionally traumatized or devascularized. This damage triggers an inflammatory reaction that compromises parathyroid physiology (3).

Glucocorticoids are anti-inflammatory drugs that may improve surgical outcomes and reduce complications by modifying perioperative inflammatory responses (4). However, the literature reports limited and conflicting information regarding the optimal timing of their use in thyroid surgery. Some studies suggest that a single preoperative dose of dexamethasone may reduce the occurrence of postoperative HC, although results are often conflicting in different studies (5-7). One recent meta-

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analysis found no effect on the incidence of permanent HC, although transient biochemical HC reduction with or without related symptoms was observed in the early recovery (8). Similarly, another meta-analysis found no significant impact of intraoperative glucocorticoid administration on reducing RLN palsy, while evidence of effect on subjective voice impairment was insufficient (9).

Our research group previously published a study demonstrating that postoperative infusion of betamethasone at the end of thyroidectomy reduces the risk of postoperative HC (10). The present study further explores this issue by analysing the same database but with a significantly larger group of patients. It also assesses RLN palsy and other common complications as secondary outcomes.

MATERIAL and METHODS

This was a retrospective case-control study that used data from a prospective database. It included adult patients who underwent total or completion thyroidectomy consecutively between January 2018 and December 2023. The surgeries were performed in the Surgical Department of the University La Sapienza of Rome, Polo Pontino at the "A. Fiorini" Hospital in Terracina. The study was approved by the local bioethics committees, and preoperative informed consent was obtained from all patients upon hospital admission. Ethics committee approval for the study was obtained from the Lazio 2 Ethics Committee of ASL Roma 2 on February 9, 2022, under protocol no: 0031401/2022. This research was conducted without specific funding from any public, private, or non-profit organizations. It enrolled patients regardless of whether they had a malignant or benign condition requiring surgery. A diagnosis of thyroid cancer was confirmed if the final pathology report showed cancer of any size.

From January 2018 to June 2019, patients received 4 mg of intravenous betamethasone (Bentelan, Alfasigma SpA) 2 hours after surgery and 1.5 mg of intravenous betamethasone on postoperative days 1, 2, and 3 (beta group); from July 2019 to June 2020, no glucocorticoids were injected (no-beta group). From July 2020 to December 2023, betamethasone was administered using an alternating method, i.e., injection in one patient and no infusion in the subsequent patient.

We collected the following prospective data: Gender, age, body mass index (BMI), presence of co-morbidities, indication to surgery, American Society of Anesthesiology (ASA) score, type of operation, operating time, recovery after surgery, pathologic examination, presence of any parathyroid gland in the specimen; moreover, the number of parathyroid glands remaining *in situ* (PGRIS) score was calculated using the formula: 4 minus parathyroid glands found in the specimen. All subjects underwent flexible laryngoscopic examinations of the vocal cords preoperatively.

All surgeries were carried out under general anesthesia with orotracheal intubation and were completed by an experienced surgeon with more than 50 certified thyroidectomies. A standard open procedure was used to perform a total thyroidectomy. Surgeons identified and exposed the RLN and its branches, meticulously following its course to its point of entry into the larynx. They also located the parathyroid glands when feasible; no autotransplantation of damaged glands were performed. Additionally, two suction drains were inserted in each patient.

Plasma levels of parathyroid hormone (PTH) (reference range: 15-65 pg/mL), total calcium (reference range: 8.4-10.4 mg/dL), serum albumin, and C-reactive protein (CRP) (reference range: 0-0.5 mg/dL) were measured preoperatively and on the first, second, and third postoperative days.

The primary outcome was HC, defined as at least one serum calcium measurement below 8.0 mg/dL.

Secondary outcomes were as follows:

1. Symptomatic HC (SHC), defined as the presence of the following signs and symptoms, along with HC: numbness of the extremities, facial paresthesia, muscular spasms, and Chvostek's or Trousseau's signs.

2. Biochemical hypoparathyroidism (hPT) defined as a low intact PTH level, below the lower limit of the reference range, accompanied by HC.

3. Biochemical hPT with symptoms, defined as biochemical hPT amidst symptoms and/or signs of HC.

4. Differences in serum calcium levels.

5. Differences in serum PTH.

6. Differences in serum CRP.

7. Differences in pain 24 hours after surgery, assessed with a numeric rating scale (NRS), ranging from 0 (no pain) to 10 (worst imaginable pain).

8. Differences in common postoperative complications, such as voice dysfunction, sore-throat and dysphagia.

9. Difference in postoperative hospital stay (days).

Patients who developed HC were given oral calcium supplements along with a vitamin D analogue. For those with severe HC symptoms or when oral treatment was ineffective, 10% calcium gluconate was administered intravenously. All patients received an intravenous infusion of 1g of paracetamol three times a day after surgery.

Patients were discharged from the hospital once their serum calcium level was above 8.0 mg/dL. A 30-day follow-up was conducted for all patients to monitor for any morbidity.

Statistical Analysis

MedCalc® Release 14.8.1 was used for the statistical analysis of the data. The characteristics of the patients were reported as mean and 95% confidence interval (CI) for continuous parametric variables, as median and interquartile range (IQR) for continuous non-parametric variables, and as number (percentage) of patients for categorical variables. Student's t-test test was used to compare continuous parametric variables and Mann-Whitney U test was used to compare continuous non-parametric variables; for categorical variables, the two-sided chi-square and Fisher's exact test were used as appropriate. The association between HC and dichotomic variables was analysed by means of both univariate and multivariate analysis. An odds ratio (OR) greater than one, reported with 95% CI and p-values indicates a higher chance of the event occurring in one study group compared with the other. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 196 patients were analysed, divided into a betamethasone group (97 pts) and a control group (99 pts).

The two groups were similar with respect to their demographic and clinical characteristics, although the no-beta group had a higher prevalence of PIGRIS scores 1 and 2, which was not statistically significant. None of the patients were on calcium or vitamin D supplementation before surgery (Table 1).

HC

HC occurred in 80 pts (40.8%), and symptoms were reported in 36 pts (18.4%). The occurrence of HC was significantly lower in the beta group compared with the no-beta group [31 pts (32.0%) vs. 49 pts (49.5%); p=0.013]. The difference was confirmed when SHC was considered: 11 pts (11.3%) in the beta group and 25 pts (25.3%) in the no-beta group (p=0.012). HC required intravenous administration of 10% calcium gluconate in 62 (31.6%) patients: 20 (20.6%) in the beta group and in 42 (42.4%) in the no-beta group (p=0.001). At discharge, the persistence of HC was similar between the two study groups [19 pts (19.6%) vs. 27 pts (27.3%); p=0.205]. Median (IQR) postoperative hospital stay was 3 (3-5) overall and 3 (3-5) in both the beta and no-beta groups (p=0.568).

Biochemical hPT was present in 51 pts (26.0%) of the entire series and occurred together with symptoms in 30 cases (15.3%). The two study groups were similar with respect to biochemical hPT alone [21 pts (21.6%) vs. 30 pts (30.3%); p=0.168]. In contrast, a significant difference was found when considering the percentage of patients with biochemical hPT associated with symptoms and/or signs of HC in the beta group vs. the no-beta group [9 pts (9.3%) vs. 21 pts (21.2%), respectively; p=0.021].

Serum calcium, PTH, and CRP levels during recovery in the two study groups are reported in Figures 1-3, respectively. In the beta group, serum calcium levels were significantly higher on the first postoperative day [8.5 (8.4-8.6) mg/dL vs. 8.2 (8.1-8.3) mg/dL in the no-beta group; p<0.000] and on postoperative day 2 [8.5 (8.4-8.7) mg/dL vs. 8.2 (8.1-8.3) mg/dL in the no-beta group; p<0.000]. Serum PTH was similar in the two groups. In the beta group, serum CRP levels were significantly lower on postoperative day 2 [0.7 (0.5-1.0) mg/dL vs. 2.0 (1.5-2.6) mg/dL in the no-beta group; p=0.002] and postoperative day 3 [0.5 (0.3-0.6) mg/dL vs. 2.3 (1.3-3.2) mg/dL in the no-beta group; p=0.039]. One day after surgery, serum albumin levels were 3.9 (3.8-4.0) g/dL; they were 3.9 (3.8-4.0) g/dL in the beta group and 3.8 (3.7-4.0) g/dL in the no-beta group (p=0.067).

Predictors of HC Symptoms

Both univariate and multivariate analyses assessing predictors of SHC are reported in Table 2. In univariate analysis, betamethasone treatment significantly decreased the risk of SHC occurrence [OR=0.38 (0.17 to 0.82); p=0.014], while a PIGRIS score <3 was associated with an increased risk of SHC occurrence [OR=3.17 (1.51 to 6.67); p=0.002]. In multivariate analysis, the only factor that significantly decreased the risk of developing SHC was betamethasone treatment [OR=0.23 (0.07 to 0.78); p=0.019], whereas a PIGRIS score <3 was significantly associated with SHC occurrence [OR=5.01 (1.42 to 17.65); p=0.012].

The same evaluation was performed to assess the predictors of hPT (Table 3). A PIGRIS score <3 was the only independent factor significantly associated with a higher incidence of hPT [OR=2.53 (1.23 to 5.18); p=0.011].

Other Common Complications

Other common complications occurring within the 30-day postoperative follow-up period are reported in Table 4. The NRS score for pain was 2 (2-3), with a significant decrease in the beta group [2 (1-3) in the beta group vs. 3 (2-4) in the no-beta group; p=0.002]. After surgery, dysphonia was present in 85 pts (43.4%) and persisted in 65 pts (33.2%) during follow-up; RLN palsy was documented in 9 pts (4.6%) by laryngoscopy; sore throat was present in 49 pts (25.0%); and dysphagia occurred in 12 pts (6.1%). No statistically significant difference was observed between the two study groups. No surgical site infections occurred during follow-up.

Table 1. Demographic and clinical characteristics of the study group				
Characteristics	**Total (n=196)**	**Beta group (n=97)**	**No beta group (n=99)**	**p**
Gender, female	42 (21.4)	27 (27.8)	15 (15.2)	**0.031**
Age, years	56.6 (54.77 to 58.52)	58.8 (56.13 to 61.57)	54.5 (51.91 to 57.19)	**0.021**
Age >50 years	130 (66.3)	68 (70.1)	62 (62.6)	0.269
BMI, kg/m^2	27.4 (26.61 to 28.12)	27.2 (26.21 to 28.29)	27.5 (26.36 to 28.59)	0.768
BMI >30	49 (25.0)	25 (25.8)	24 (24.2)	0.805
Co-morbidities	151 (80.4)	78 (77.5)	73 (73.7)	0.268
Preoperative diagnosis				
Multinodular goitre	161 (82.1)	76 (78.4)	85 (85.9)	
Toxic multinodular goitre	17 (8.7)	7 (7.2)	10 (10.1)	0.445
Grave's disease	4 (2.0)	1 (1.0)	3 (3.0)	
Other*	14 (7.1)	9 (9.3)	5 (5.0)	
Hyperthyroidism	25 (12.7)	11 (11.3)	14 (14.1)	0.557
PTH, pg/mL	79.1 (75.01 to 83.24)	76.6 (70.45 to 82.72)	81.4 (75.84 to 87.03)	0.246
Serum calcium, mg/dL	9.3 (9.24 to 9.45)	9.4 (9.22 to 9.58)	9.3 (9.18 to 9.41)	0.351
C-reactive protein, mg/dL	0.3 (0.20 to 0.37)	0.3 (0.20-0.41)	0.3 (0.24-0.39)	0.847
ASA				**0.030**
I	32 (16.3)	12 (12.4)	20 (20.2)	
II	142 (72.4)	70 (72.2)	72 (72.7)	
III	22 (11.2)	15 (15.5)	7 (7.1)	
Operation				
Total thyroidectomy	188 (95.9)	93 (95.9)	95 (95.9)	0.998
Completion thyroidectomy	8 (4.1)	4 (4.1)	4 (4.1)	
Duration of surgery, min.	75.0 (72.78 to 77.24)	76.9 (73.85 to 79.98)	73.1 (69.9 to 76.38)	0.0946
Postoperative recovery, days	3 (3-3)	3 (3-3)	3 (3-3)	0.568
Final pathology				
Benign	193 (98.7)	95 (97.9)	98 (100)	0.196
Malignant	3 (1.3)	2 (2.1)	1 (1.0)	
Thyroid tissue weight, gr	49 (35-89)	47 (35-91)	51 (36-87)	0.749
PIGRIS score				0.458
1	2 (1.0)	-	2 (2.0)	
2	16 (8.2)	6 (6.2)	10 (10.1)	
3	52 (26.5)	27 (27.8)	30 (30.3)	
4	126 (64.3)	64 (66.0)	57 (57.6)	

Data are presented as number (percentage) or mean (95% confidence interval). Beta: Betamethasone, *: Indeterminate or suspicious nodule 11 pts, PIGRIS: Parathyroid glands remaining *in situ*, BMI: Body mass index, ASA: American Society of Anesthesiologists, PTH: Parathyroid hormone.

DISCUSSION

The use of glucocorticoids during the perioperative period is common due to their various benefits, including reduction of postoperative nausea and vomiting, analgesic effects and a significant improvement of the quality of recovery (11). However, concerns regarding their side effects, such as potential immunosuppression that could lead to complications, including infections and impaired wound healing, limit their use. Two recent meta-analyses reported the safety of glucocorticoids in patients submitted to surgery, though they also highlighted biases that warrant caution (12,13). While most studies describe the administration of a single preoperative dose of the glucocorticoid dexamethasone, we chose to prescribe betamethasone postoperatively. Our decision stems from studies indicating that glucocorticoids taper the

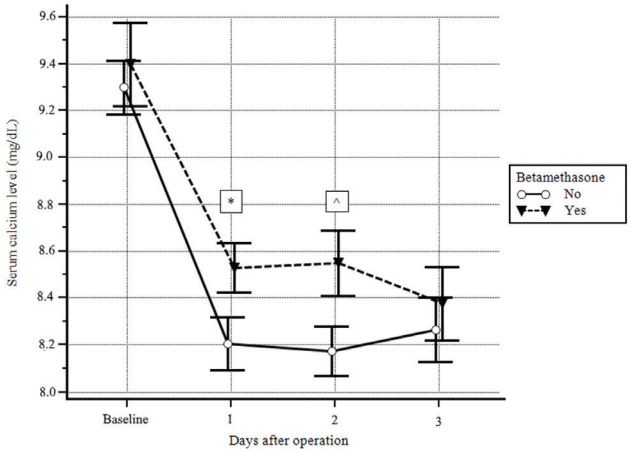

Figure 1. Differences in serum calcium levels between patients who received or did not receive betamethasone. In the betamethasone group, serum calcium levels were significantly higher on post-operative day 1 (*p<0.000) and on day 2 (^p<0.001).

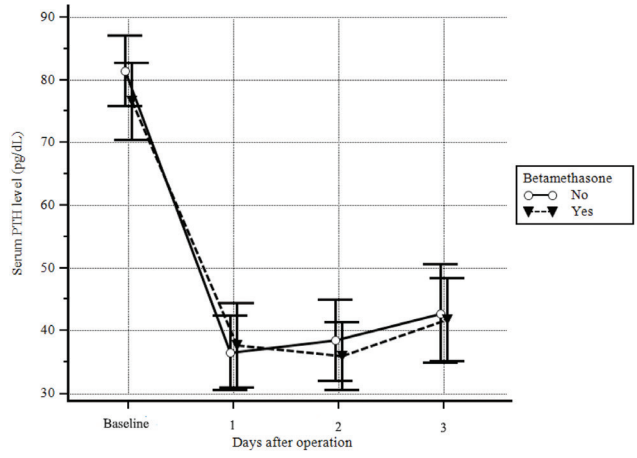

Figure 2. Differences in serum parathyroid hormone (PTH) levels between patients who received or did not receive betamethasone. No significant difference was observed between the two study groups.

immune response, when inflammation is absent, but stimulate immunological response when inflammation occurs (4). The anti-inflammatory effect of glucocorticoids in the postoperative phase is confirmed by our results, which show a significant decrease in CRP levels in the beta group after thyroidectomy. The intraoperative administration of glucocorticoids does not impact the incidence of surgical site infection, as reported in two large randomized trials (14,15). Thyroid surgery is considered a clean procedure with a very low rate of surgical site infection, and the lack of surgical site infections in our study support the safety of glucocorticoids, in spite of their anti-inflammatory properties.

After thyroidectomy HC may stem from various events, including the accidental removal or trauma of the parathyroid glands,

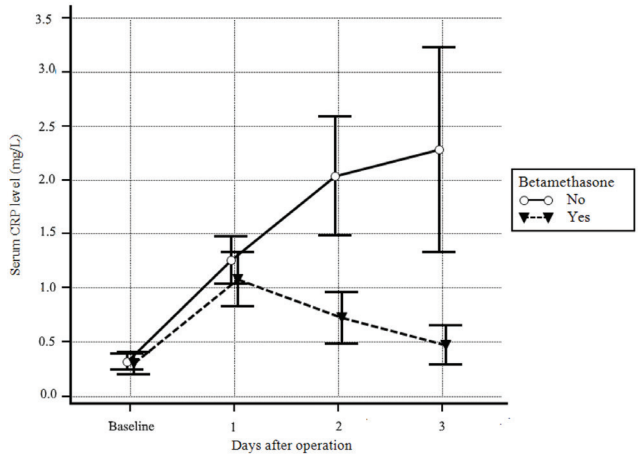

Figure 3. Differences in serum C-reactive protein (CRP) levels were assessed between patients who received betamethasone and those who did not. In the betamethasone group, CRP levels were significantly lower on post-operative day 2 (*≤0.002) and on day 3 (^p<0.039).

which can lead to devascularization and damage (1); another potential cause includes postoperative alkalosis-induced HC from hyperventilation due to pain, and dilution HC (16).

Surgical trauma is a major cause of HC after thyroidectomy; therefore, reducing trauma-related inflammation is a potentially effective way to manage it. However, there is a lack of studies confirming this relationship. There are only three randomized studies that compare patients treated with preoperative dexamethasone injection vs. placebo before thyroidectomy (5-7). The trial of Kolahdouzan et al. (5), showed a lower rate of postoperative symptomatic HC in patients treated with dexamethasone before total thyroidectomy, although there was no statistical significance. In the study of Dhahri et al. (6), a single preoperative dose of dexamethasone significantly reduced postoperative HC and symptomatic HC. In the trial of Latif et al. (7), dexamethasone prophylaxis before sub-total thyroidectomy was effective in reducing postoperative HC. A Chinese retrospective study on patients, who underwent thyroid surgery for papillary carcinoma, showed that the incidence of hPT after surgery was lower in subjects submitted not only to intraoperative but also to postoperative administration of glucocorticoids (17). The present study demonstrated that both biochemical HC and SHC levels were significantly reduced when betamethasone was administered postoperatively. Biochemical hPT was similar in the two study groups, with a significant decrease in the beta group when it was associated with symptoms and/or signs of HC, suggesting that parathyroid gland function was potentially unaffected and that the finding may reflect the subjective nature of symptoms. Although postoperative hospital stay was similar in the two study groups, there was a a significantly increased need to administer an intravenous infusion of calcium to correct HC

Table 2. Predictors of SHC

Characteristics	SHC (n=36)	No SHC (n=160)	Univariate OR (95% CI)	p	Multivariate OR (95% CI)	p
Gender, male	8 (22.2)	28 (77.8)	1.06 (0.44 to 2.53)	0.898	0.979 (0.23 to 3.98)	0.967
BMI >30	6 (16.7)	43 (26.9)	0.54 (0.21 to 1.39)	0.206	0.72 (0.15 to 3.34)	0.676
Age >50 years	21 (58.3)	109 (68.1)	0.65 (0.31 to 1.37)	0.263	2.07 (0.30 to 14.12)	0.458
Co-morbidities	25 (77.8)	126 (80.7)	0.61 (0.27 to 1.37)	0.233	0.36 (0.06 to 2.06)	0.254
Preoperative diagnosis						
Multinodular goitre	28 (77.8)	133 (83.1)	Reference		Reference	
Other	8 (22.2)	27 (16.9)	1.40 (0.58 to 3.42)	0.451	1.32 (0.26 to 6.78)	0.741
ASA						
I-II	19 (11.9)	141 (88.1)	Reference		Reference	
III	3 (8.3)	33 (91.7)	0.67 (0.19 to 2.41)	0.545	0.97 (0.26 to 3.62)	0.961
Betamethasone	11 (30.6)	86 (53.7)	0.38 (0.17 to 0.82)	**0.014**	0.23 (0.07 to 0.78)	**0.019**
Final pathology						
Benign	34 (94.4)	150 (93.7)	Reference		Reference	
Malignant	2 (5.6)	10 (6.2)	0.88 (0.18 to 4.21)	0.875	1.66 (0.24 to 11.45)	0.605
PIGRIS						
≥3	15 (41.7)	111 (69.4)	Reference		Reference	
<3	21 (58.3)	49 (30.6)	3.17 (1.51 to 6.67)	**0.002**	5.01 (1.42 to 17.65)	**0.012**

Data are presented as number (percentage), unless otherwise specified. SHC: Symptomatic hypocalcemia, OR: Odds ratios, PIGRIS: Parathyroid glands remaining *in situ*, BMI: Body mass index, ASA: American Society of Anesthesiologists.

Table 3. Predictors of hPT

Characteristics	hPT (n=51)	No hPT (n=145)	Univariate OR (95% CI)	p	Multivariate OR (95% CI)	p
Gender, male	9 (17.6)	33 (22.8)	0.72 (0.32 to 1.65)	0.445	0.86 (0.36 to 2.06)	0.742
BMI >30	8 (15.7)	41 (28.3)	0.47 (0.20 to 1.09)	0.079	0.48 (0.19 to 1.16)	0.102
Age >50 years	28 (54.9)	102 (70.3)	0.51 (0.27 to 0.99)	**0.047**	0.73 (0.32 to 1.62)	0.440
Co-morbidities	33 (64.7)	118 (81.4)	0.42 (0.21 to 0.85)	**0.017**	0.45 (0.19 to 1.09)	0.078
Preoperative diagnosis						
Multinodular goitre	42 (82.3)	119 (82.1)	Reference		Reference	
Other	9 (17.7)	26 (17.9)	0.98 (0.42 to 2.26)	0.964	0.85 (0.35 to 2.08)	0.720
ASA						
I-II	48 (94.1)	126 (86.9)	Reference		Reference	
III	3 (5.9)	19 (13.1)	0.41 (0.12 to 1.46)	0.171	0.55 (0.14 to 2.09)	0.380
Betamethasone	21 (41.2)	76 (52.4)	0.64 (0.33 to 1.21)	0.169	0.84 (0.42 to 1.68)	0.617
Final pathology						
Benign	50 (98.0)	137 (94.5)	Reference		Reference	
Malignant	1 (2.0)	8 (5.5)	0.34 (0.04 to 2.81)	0.318	0.38 (0.04 to 3.28)	0.377
PIGRIS						
≥3	26 (51.0)	100 (69.0)	Reference		Reference	
<3	25 (49.0)	45 (31.0)	2.14 (1.11 to 4.10)	**0.023**	2.53 (1.23 to 5.18)	**0.011**

Data are presented as number (percentage), unless otherwise specified. OR: Odds ratios, PIGRIS: Parathyroid glands remaining *in situ*, hPT: Hypoparathyroidism, CI: Confidence interval, ASA: American Society of Anesthesiologists, BMI: Body mass index.

Table 4. Complications in the study groups				
Variable	**Total** (n=196)	**Beta group** (n=97)	**No beta group** (n=99)	**p**
Dysphonia				
At hospital discharge	85 (43.4)	44 (45.3)	41 (41.4)	0.788
At 30-day follow-up	65 (33.2)	30 (30.1)	35 (35.3)	0.439
RLN palsy	9 (4.6)	3 (3.1)	6 (6.1)	0.318
Sore throat	49 (25.0)	25 (25.8)	24 (24.2)	0.619
Dysphagia	12 (6.1)	7 (7.2)	5 (5.1)	0.541
Pain, NSR score	2 (2 to 3)	2 (1 to 3)	3 (2 to 4)	**0.002**
Data are presented as number (percentage) or mean (95% confidence interval). Beta: Betamethasone, RLN: Recurrent laryngeal nerve, NRS: Numeric rating scale.				

during recovery in the no-beta group. Moreover, treatment with betamethasone was significantly associated with a reduction in SHC after surgery in both univariate and multivariate analyses.

Our study confirms that PIGRIS score is a factor significantly related to postoperative SHC and hPT, as it is well documented in the literature (18). Due to the quite large number of patients, the higher but not significant prevalence of PIGRIS score 1 and 2 in the no-beta group does not affect the validity of the results.

It is common for patients to experience voice dysfunction after thyroidectomy. While RLN palsy is a known cause of dysphonia, a complete transection of the RLN is rare. Instead, the primary cause of functional impairment of the RLN is typically the trauma consequent to the manipulation of the nerve during the operation (19). Another possible cause, not related to surgery, is the trauma caused by the tracheal intubation (20). Based on these observations, glucocorticoids were proposed during the perioperative period to decrease inflammation caused by surgical trauma and thereby preserve RLN function. Six randomized studies have been published that examine the effect of preoperative injection of dexamethasone before surgery on voice outcomes (6,7,21-24). Temporary improvement of the voice after preoperative dexamethasone infusion was described in four trials (6,21,23,24). The studies by Latif et al. (7) and Feroci et al. (22) found no effect of dexamethasone on this complication. Similarly, the present study showed that glucocorticoids do not influence voice outcomes when administered postoperatively.

Glucocorticoids are also effective in minimizing sore throat after tracheal intubation (25). The occurrence of sore throat is particularly frequent in thyroid surgeries performed under general anesthesia (26). A randomized trial indicated that dexamethasone, administered preoperatively could reduce this complication (27). However, our results do not confirm the effectiveness of glucocorticoids infused postoperatively in preventing this common side effect after thyroidectomy.

Dysphagia is also a frequent occurrence (28,29). When there is no RLN transection, swallowing difficulties seem to be primarily linked to surgical trauma (30). One retrospective study showed that perioperative dexamethasone could influence dysphagia in the early postoperative phase (31). Our study found a tendency toward reduced swallowing complaints in the beta group, although this difference was not statistically significant when compared with the no-beta group.

Perioperative glucocorticoids have been extensively used to alleviate postoperative pain across various surgical procedures, offering considerable benefits (32). In the context of thyroid surgery, some trials showed that glucocorticoids significantly reduce pain after the operation, even when pain was not the primary outcome of the study (22,23,33). One trial, that specifically had postoperative pain as its primary outcome, found that two different preoperative doses of dexamethasone were not effective to reduce pain or to spare opioids with respect to placebo (34). Our results support the efficacy of glucocorticoids in reducing postoperative pain following thyroidectomy.

Study Limitations

The main limitation of this study is the retrospective analysis of the data. Moreover, the administration or non-administration of betamethasone was performed without any previously defined protocol. However, because a single experienced surgeon performed all operations, two potential biases were avoided: Variation in expertise (the surgeon was already experienced at the beginning of the study) and variation in surgical technique (he did not change it during the study period). Furthermore, all postoperative symptoms were reported subjectively by patients, without objective measurements. Serum calcium levels after surgery may be affected by several factors such fluid administration, alkalosis, and serum albumin levels: Another limitation of our study is that we only assessed albumin levels after surgery. Although we suggested that betamethasone after thyroid surgery may preserve parathyroid function due to its anti-inflammatory effect, the conflicting results of our study, showing that biochemical hPT was unaffected, with only a reduction in hPT with symptoms, do not clearly support this mechanism.

CONCLUSION

The present study supports the use of betamethasone at the end of thyroidectomy to decrease the incidence of both biochemical HC and SHC. Postoperatively, pain is significantly reduced, while voice dysfunction, sore-throat and dysphagia are unaffected after betamethasone infusion. Further prospective, randomized trials are needed to assess the effectiveness of glucocorticoids in reducing complications after total thyroidectomy.

Ethics

Ethics Committee Approval: Ethics committee approval for the study was obtained from the Lazio 2 Ethics Committee of ASL Roma 2 on February 9, 2022, under protocol no: 0031401/2022.

Informed Consent: The study was approved by the local bioethics committees, and preoperative informed consent was obtained from all patients upon hospital admission.

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Footnotes

Author Contributions

Surgical and Medical Practices - R.M., A.D.C., E.S.; Concept - M.P., A.D.C., E.S.; Design - M.P., E.S.; Data Collection or Processing - M.P., R.M., A.R.D.F.; Analysis or Interpretation - M.P., R.M., A.S.D.U.; Literature Search - M.P., A.R.D.F., M.S.; Writing - M.P., A.S.D.U.

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