

Is it possible to identify a risk factor condition of hypocalcemia in patients candidates to thyroidectomy for benign disease?



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It is possible to identify a risk factor condition of hypocalcemia in patients candidates to thyroidectomy for benign disease?

AIM: Hypocalcaemia is the most frequent complication after total thyroidectomy. The incidence of postoperative hypocalcaemia is reported with different percentages in literature.

METHODS: We report 227 patients undergoing surgery for benign thyroid disease. After obtaining patient's informed consent, we collected and analyzed prospectively the following data: calcium serum levels pre and postoperative in the first 24 hours after surgery according to sex, age, duration of surgery, number of parathyroids identified by the surgeon, surgical technique (open and minimally invasive video-assisted thyroidectomy i.e. MIVAT). We have considered cases treated consecutively from the same two experienced endocrine surgeons. Hypocalcaemia is assumed when the value of serum calcium is below 7.5 mg / dL.

RESULTS: Pre-and post-operative mean serum calcium, with confidence intervals at 99% divided by sex, revealed a statistically significant difference in the ANOVA test ($p < 0.01$) in terms of incidence. Female sex has higher incidence of hypocalcemia. The evaluation of the mean serum calcium in pre-and post-operative period, with confidence intervals at 95%, depending on the number of identified parathyroid glands by surgeon, showed that the result is not correlated with values of postoperative serum calcium. Age and pre-and postoperative serum calcium values with confidence intervals at 99% based on sex of patients, didn't show statistically significant differences. We haven't highlighted a significant difference in postoperative hypocalcemia in patients treated with conventional thyroidectomy versus MIVAT.

CONCLUSION: A difference in pre- and postoperative mean serum calcium occurs in all patients surgically treated. The only statistical meaningful risk factor for hypocalcemia has been the female sex.

KEY WORDS: Hypocalcaemia MIVAT, Thyroidectomy, Thyroid disease.

Introduction

Hypocalcemia is the most frequent complication after total thyroidectomy. Many causes are associated with this

clinical condition. The perfect knowledge of thyroidal anatomy regarding the embryological origin of the parathyroid glands is the most concrete element to decrease incidence of postoperative hypocalcemia.

The incidence of postoperative hypocalcemia is reported with different percentages in literature and this diversity depends on the type of surgery performed. In case of subtotal thyroidectomy (small amounts of thyroid tissue is left to protect the recurrent nerves) and total thyroidectomy an incidence of hypocalcemia of 0.33 - 65% is respectively reported¹⁻⁵.

The challenge of hypocalcemia is not in its clinical control due to the fact that it can be easily treated with

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supportive calcium and vitamin D therapy. The challenge lies in the ability to predict its onset in thyroid surgery.

Several studies have attempted to use preoperative, intraoperative, postoperative values of PTH, as well as the plasma concentration of ionized calcium and the serum calcium values as early markers of postoperative hypocalcemia, although no operative guidelines have been proposed yet⁶⁻¹⁸. The only marker that seems to have a good predictive value of early onset of postoperative hypocalcemia is the intraoperative measurement of PTH, obtained from the internal jugular vein¹⁹.

However, until now no one can claim to have identified a real, safe and early predictor of postoperative hypocalcemia.

The inability to predict hypocalcemia affects the cost of the management of patients following total thyroidectomy in a short stay unit. For a safe discharge in fact, every patient should be given an appropriate supportive calcium therapy, but this increases costs for public health service and above all patient's management over time could become difficult and expensive.

Because of this, we chose to conduct a prospective observational study on patients of our division treated with thyroidectomy with the aim of identify situations of risk or clinical factors relating to the possible development of postoperative hypocalcaemia, independent of serum calcium levels, and to develop a potential risk score that could be easily calculated in every endocrine unit.

Materials and methods

From October 2008 to June 2009 we prospectively analyzed 227 patients undergoing thyroid surgery (hemi-thyroidectomy, subtotal thyroidectomy, total thyroidectomy) for non-malignant disease. All patients were operated by two experienced endocrine surgeons. Patients with proven or suspected primary or secondary hyperparathyroidism were excluded from the study as well as patients affected by recurrent goiter, cancer or suspected cancer, with or without lymph nodes dissection. Our protocol provides the measurement of preoperative PTH values²⁰.

Hemithyroidectomy is performed removing one thyroid lobe together with the isthmus without manual surgical exploration of the contralateral lobe; in case of subtotal thyroidectomy the surgeon left in place a small amount of thyroid tissue to protect the recurrent laryngeal nerve.

In total thyroidectomy the whole gland is removed without leaving macroscopic parenchyma. Bilateral recurrent laryngeal nerves were identified during surgery. We have collected and analyzed prospec-

tively on a dedicated data base the following data:

1. pre-and postoperative (24 hours after surgery) serum calcium levels;
2. serum calcium levels according to sex, age, number of parathyroids identified by the surgeon;
3. pre and-postoperative serum calcium levels according to type of surgery performed (conventional thyroidectomy or mini invasive video assisted thyroidectomy (MIVAT))²¹⁻²³.

Hypocalcemia was defined as value of serum calcium below 7.5 mg / dL. In patients with mild to moderate symptoms of hypocalcemia, supplemental calcium therapy was administered at the dose of 1 gr every 12 hours of calcium carbonate and 0.5 mcg every 12 hours of calcitriol.

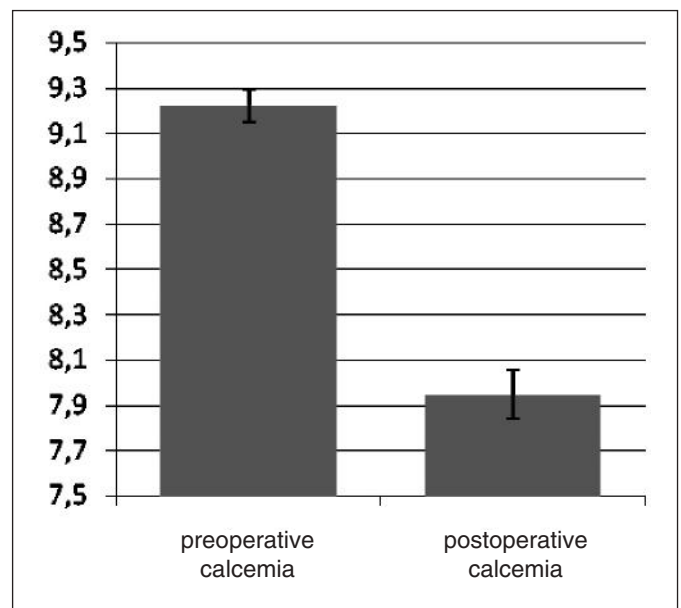
STATISTICAL ANALYSIS

Collected data were analyzed using SPSS 17.0. We used Student's T test for independent samples, ANOVA and Pearson's correlation coefficient; Chi-square test and the Mann-Whitney test for non-parametric data.

Results

Preoperative serum calcium levels were significantly higher, as shown in Table I (p <0.0001, 99% confidence interval). Anova identified sex as a risk factor for postoperative hypocalcemia (Table II); in fact females were more likely to have lower postoperative

TABLE I - Pre and postoperative mean serum calcium.



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TABLE II - Pre and postoperative mean serum calcium levels according to sex.

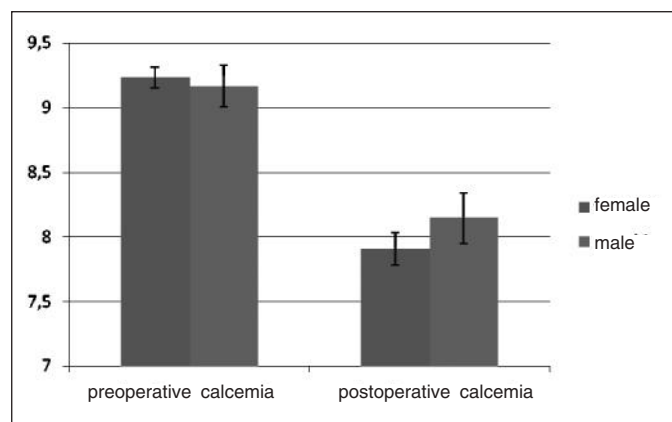


TABLE III - Patients undergoing total thyroidectomy.

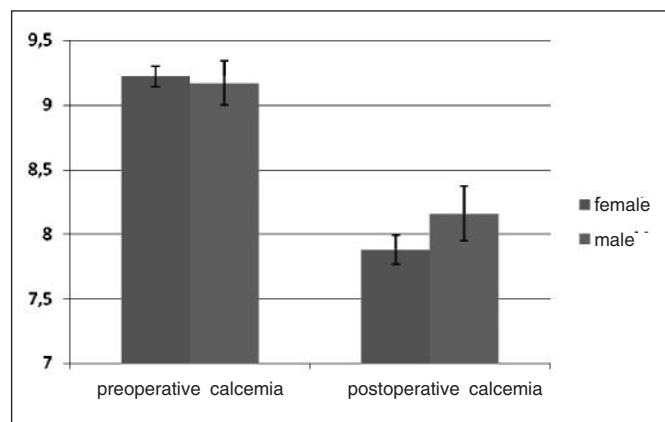
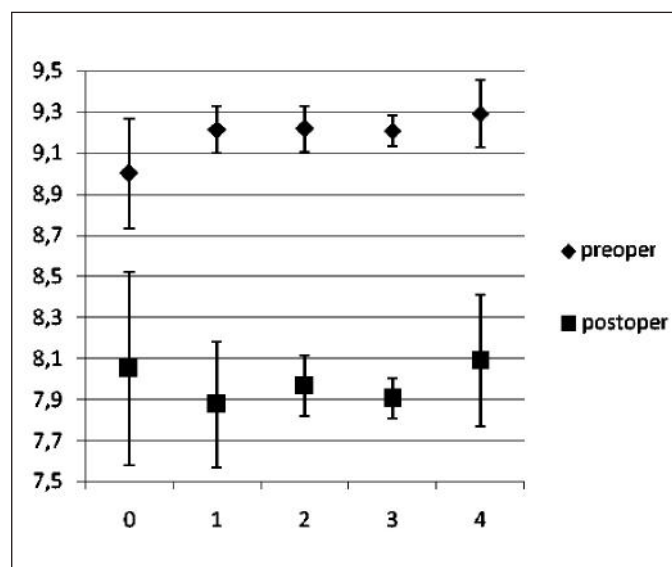


TABLE IV - Data related to surgical procedures.

| Surgical procedures | Preoperative calcium mg/dL | Postoperative calcium mg/dL | Ratio pre/post-calcemia | Difference pre/post-calcemia | Number of parathyroid glands identified from surgeon |
|--------------------------------------|----------------------------|-----------------------------|-------------------------|------------------------------|--|
| Hemithyroidectomy 16 cases | 9.22 ± 0.20 | 8.21 ± 0.50 | 0.89 ± 0.05 | 1.04 ± 0.48 | 1.33 ± 0.31 |
| Near total thyroidectomy 16 cases | 9.37 ± 0.26 | 7.71 ± 0.19 | 0.83 ± 0.03 | 1.66 ± 0.38 | 2.50 ± 0.36 |
| Total thyroidectomy 195 cases | 9.21 ± 0.06 | 7.96 ± 0.09 | 0.86 ± 0.01 | 1.28 ± 0.10 | 2.75 ± 0.12 |

TABLE V - Evaluation of mean serum calcium depending on the number of identified parathyroid glands. Confidence intervals at 95%.



serum calcium levels than men (confidence intervals 99%, $p < 0.001$). Although, if we stratify the patients according to the type of surgery performed (total thyroidectomy vs hemithyroidectomy or subtotal thyroidectomy), sex remains a risk factor only for patients undergoing total thyroidectomy ($p < 0.02$) (Table III). The paucity of data in the hemithyroidectomy and sub-total thyroidectomy groups is likely responsible for this result, as reflected by differences in the confidence intervals (Table IV).

The number of identified parathyroid glands during surgery was not significantly related to postoperative serum calcium levels (confidence interval 95%, $p = ns$) (Table V). This result is in contradiction with our recent report, although that series was limited by the small cohort of patients²⁴.

If we observe within the gender groups, age is not significantly related to pre and postoperative calcium levels (Table VI). The type of surgery performed (open vs MIVAT) was also not significantly related to hypocalcemia (Table VII).

TABLE VI - Age and pre-postoperative serum calcium values. Confidence Interval 99%.

| | Age years | Preoperative hypocalcemia mg/dL | post-operative hypocalcemia mg/dL |
|-------------------|--------------|------------------------------------|--------------------------------------|
| Female - 188 casi | 55.4 ± 14.3 | 923 ± 0.40 | 7.90 ± 0.63 |
| Male - 39 casi | 58.3 ± 12.6 | 9.16 ± 0.39 | 8.17 ± 0.46 |
| Total - 227 casi | 55.9 ± 14.1 | 9.22 ± 0.41 | 7.95 ± 0.6 |

TABLE VII - Values of postoperative calcemia in pts treated with conventional or videoassisted total thyroidectomy (MIVAT) for benign disease.

| | | Number | Mean (mg/dL) | Standard deviation. | Error std. Mean |
|---|------------------------|--------|--------------|---------------------|-----------------|
| Calcemia | Surgical procedures | | | | |
| Post-operative calcemia | traditional | 170 | 7,967 | ,6089 | ,0441 |
| | video | 25 | 7,804 | ,6471 | ,1294 |
| Post-operative variation of calcemia | traditional | 170 | 1,5832 | 2,14551 | ,15096 |
| | video | 25 | 1,5200 | ,71239 | ,14248 |

Discussion and conclusions

Hypocalcemia after thyroidectomy is a complication that might increase the costs of management of patients and undermine the safety and feasibility of thyroidectomy in short stay units. In our study we have identified that there are no significant differences in the incidence of hypocalcemia after surgery according to type of procedure performed (hemithyroidectomy, total thyroidectomy and subtotal thyroidectomy). However, the small number of hemithyroidectomies in this series may account for this result. The only statistically significant risk factor for hypocalcemia appears to be sex, in fact female seemed to be more prone to develop this complication. Larger series are necessary to confirm these preliminary results and to propose a risk score for patient undergoing thyroid surgery.

Riassunto

SCOPO: L'ipocalcemia è la complicanza più frequente associata alla tiroidectomia totale. L'incidenza di ipocalcemia postoperatoria è riportata con percentuali differenti in letteratura.

MATERIALI E METODO: Riportiamo 227 casi di pazienti sottoposti ad intervento di tiroidectomia per patologia benigna. Dopo aver ottenuto da tutti il consenso informato, abbiamo raccolto ed analizzato prospetticamente i seguenti parametri: livello pre e post operatorio nelle prime 24 ore dall'intervento chirurgico del calcio sierico rapportando tale dato al sesso, età, numero di paratiroidi identificate dal chirurgo, tecnica chirurgica (tiroidec-

tomia tradizionale o videoassistita - MIVAT). Abbiamo analizzato i casi trattati consecutivamente da due chirurghi senior esperti in chirurgia tiroidea. Abbiamo considerato ipocalcemia la presenza di valori di calcio sierico inferiori a 7,5 mg/dl.

RISULTATI: Il valore medio di calcio sierico pre e postoperatorio rapportato al sesso dei pazienti ha dimostrato una differenza statisticamente significativa all'ANOVA test ($p < 0.01$) in termini di incidenza postoperatoria. Il sesso femminile presenta la più alta incidenza di ipocalcemia. La valutazione del valore medio di calcio sierico nel periodo pre e postoperatorio, con intervallo di confidenza al 95%, rapportato con il numero paratiroidi identificate dal chirurgo non è risultato statisticamente significativo. L'età dei pazienti trattati, con intervallo di confidenza pari al 99%, rapportata al sesso dei casi esaminati non ha dimostrato differenze statisticamente significative. Non abbiamo registrato una differenza statisticamente significativa nell'incidenza di ipocalcemia postoperatoria tra i pazienti operati con chirurgia tradizionale ed i casi trattati con tecnica MIVAT.

CONCLUSIONI: Abbiamo registrato una differenza nel valore medio di calcio sierico nel periodo pre e postoperatorio in tutti i casi trattati. Il solo fattore di rischio statisticamente significativo per l'ipocalcemia è risultato il sesso femminile.

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