POSTOPERATIVE PTH MEASUREMENT AS A PREDICTOR OF HYPOCALCAEMIA AFTER THYROIDECTOMY

MONIKA PROCZKO-MARKUSZEWSKA, JAROSŁAW KOBIELA, TOMASZ STEFANIAK, ANDRZEJ J. ŁACHIŃSKI, ZBIGNIEW ŚLEDZIŃSKI

Department of General, Endocrine and Transplant Surgery, Medical University in Gdańsk
Kierownik: prof. dr hab. Z. Śledziński

Hypocalcemia after thyroidectomy is the most common postoperative complication with reported incidence from 0.5% to even half of the operated patients. Hypoparathyroidism could be a result of careless or inadequate preparation during the surgical procedure. There is a variety of proposed options for prediction of the incidence of hypocalcemia. The most effective of them are the perioperative and intraoperative measurements of PTH level.

The aim of the study was to assess the potential correlation between the iPTH levels after the operation and development of hypocalcaemia. The possible prediction value of postoperative iPTH levels was to be evaluated.

Material and methods. A prospective study was performed on 100 patients who underwent total thyroidectomy from January 2007 to June 2009. The total calcium level and intact human PTH (iPTH) levels were measured 24 hours before, 1 and 24 hours after the surgery.

Results. We have presented a significant correlation between early iPTH measurement and risk of hypocalcaemia. Moreover a significant correlation between the iPTH level 1 hour after operation with the calcium level 24 hours after the operation was demonstrated.

Conclusions. Early postoperative assessment of iPTH levels can be used to identify the group of patients at risk of hypocalcaemia after thyroidectomy. Pre-emptive calcium supplementation can lead to avoidance of complications causing prolonged hospital stay and most importantly to prevent severe hypocalcemia.

Key words: hypocalcaemia, postoperative parathyroid hormone measurement, thyroidectomy, calcium supplementation
There are two modalities of iPTH measurement. Intraoperative measurement, is a very valuable method which allows for autotransplantation of the unintentionally resected parathyroid gland during the same procedure before the skin closure, but it still remains an expensive and not widely accessible method. Selective intraoperative PTH measurement guided parathyroid autotransplantation reduces a risk of permanent and transient postoperative hypoparathyroidism (7, 8). The alternative solution is the early post-operative measurement of iPTH based on standard laboratory assessments of this hormone.

**MATERIAL AND METHODS**

A group of 100 patients, who underwent total thyroidectomy in Department of General, Endocrine and Transplant Surgery between January 2007 and June 2009 was prospectively analysed. Six of the patients from this group were excluded because of accidentally diagnosed concurrent hyperparathyroidism (two patients) or already taking calcium supplementation due to osteoporosis (four patients).

Hypocalcemia was symptomatic in 9 patients. The symptoms onset were observed between second and forth postoperative day.

Total calcium level before the operation, 1 and 24 hours after the surgery were assessed. The iPTH level was assessed before, 1 and 24 hours after thyroidectomy. Specificity and sensitivity of iPTH level assessments 1 and 24 hours after surgery was calculated aiming to evaluate its potential usage as a predictor of postoperative hypocalcaemia.

Serum calcium levels were measured in mg/dl with reference ranges 8.5-10.5 mg/dl. Hypocalcaemia symptoms are rather uncommon unless serum level is below 8.0 mg/dl and thus we considered hypocalcaemia when the level was below 8.2 mg/dl. Typical hypocalcaemia-related symptoms such: paresthesia in the face or upper and lower limbs, nervousness and anxiety were observed in different severity from asymptomatic cases to severe tetany.

The reference values for iPTH in our laboratory were 10-62 pg/mL, with the analytical sensitivity of 2-3 pg/mL. The relationships between development of hypocalcaemia and iPTH levels were analyzed using Pearson not-parametric correlation test. For every parametric evaluation ANOVA was used, p level was considered significant when it was over 0.05, correlation was considered strong above 0.70.

**RESULTS**

Hypocalcaemia was observed in 24 patients out of 100 operated cases. Out of these patients in 14 cases total calcium level was lower then 7.5 mg/dl.

In the group of patients with hypocalcaemia the average level of iPTH 1 h after surgery was below 7.76 and after 24 h 9.91 pg/mL (p<0.001). Average level of total calcium level 1 h after operation was 8.39 mg/dl, after 24 h 7.89 mg/dl (p<0.001) (fig. 1).

In all hypocalcaemic patients levels of iPTH measured at 1 h after the operation ranged between 7 and 20 pg/mL. All patients with iPTH levels at 1 h after surgery higher then 20pg/mL remained eucalcaemic.

The measurements of Ca^{2+} levels after 1 and 24 hours post-operatively were not significantly different between the groups that later developed hypocalcaemia vs normocalcemic patients (fig. 2).

A strong correlation between iPTH measured 1 h after subtotal thyroidectomy and the risk of developing hypocalcaemia was found (Pearson coefficient r=0.73, p<0.05), similar correlation was found between the level of iPTH assessed after 24 hours (Pearson coefficient r=0.68, p<0.05) (tab. 1). Diagnostic specificity of iPTH assessment 1 hour after operation equalled 83.87% and sensitivity equalled 92.89% (tab. 2).
DISCUSSION

The number of patients with postoperative transient hypoparathyroidism is still significant with most series reporting an incidence around 20-30% (the rate of permanent hypoparathyroidism varies between 0.4-1.7%) (9, 10, 11). There are also many different definitions of persistent and transient hypocalcemia (12, 13). In our study, the percentage of hypocalcemia reached 24% and the percentage of symptomatic hypocalcemia was 9% (what represents 37.5% of the hypocalcemic patients). The prospective analysis of perioperative iPTH-kinetics could help to explain the mechanism of postoperative hypoparathyroidism and calculate the cut-off iPTH level prognostic for postoperative hypocalcaemia. It is obvious that the most important factor determining the presentation of hypocalcaemia is the success rate of preserving parathyroid function. There have been several studies that evaluated the risk factors of postoperative hypocalcemia after subtotal thyroidectomy and also some studies on patients after total thyroidectomy for cancer or benign thyroid diseases. Some reports suggest that early postoperative total or ionized calcium level predicts hypoparathyroidism after both total and subtotal thyroidectomy (14, 15). Intraoperative iPTH levels are thought to be an accurate predictor of symptomatic hypocalcemia (16), but this method can not be used in many surgical centres due to financial conditions.

It has also been postulated that the biochemical and symptomatic hypocalcemia can be prevented by routine administration of calcium accompanied or not by vitamin D. In a study by Roh the patients undergoing large neck dissections were randomised to receive calcium plus vitamin D vs calcium alone vs no supplementation. Although the results clearly pointed to the benefits of calcium and vitamin D supplementation, it should be mentioned that even that extensive strategy did not entirely prevent hypocalcemia, with 2% of symptomatic and 8.2% of biochemical hypocalcemia. Moreover in a group of calcium supplementation alone corresponding percentages were as high as 12.2 and 24.5 (17).

In even more radical strategy, proposed by Abboud et al. the patients were treated with routine parathyroid autotransplantation and calcium plus vitamin D supplementation after total thyroidectomy. Surprisingly, in this study the frequency of biochemical hypocalcemia reached 17% and minor symptoms were noted in 1.6% of patients (18). These results might suggest that in some patients standard supplementation alone may not be sufficient. We believe that in those cases extra supplementation should be proposed basing on the results of intraoperative or early postoperative PTH level assessment.

The alternative method could be the early post-operative measurement of intact PTH to identify the patients at risk of developing hypocalcaemia. In our study, iPTH levels were assessed 1 h and 24 h after surgical procedure, and strong correlation was found between iPTH level measured 1 h after surgery and the development of hypocalcaemia (Pearson coefficient r=0.73, p<0.05) with measurement correlation at the level of r=0.68, p<0.05. Intrest-
ingly Ca\textsuperscript{2+} level was not correlated significantly with later presentation of hypocalcaemia either after 1 or 24 hours (respectively 0.21, p<0.05 and 0.46, p<0.05). We presume that early post-operative measurement of PTH might be as accurate as results obtained several hours after surgery, because the half-life of PTH is 2-5 min. In other trials different combinations of PTH and calcium measurements were also used. Payene et al. published results of PTH measurements at 6, 12, 20 hours after thyroidectomy, concluding that PTH and calcium level at 6 h accurately identified patients at risk for developing hypocalcaemia (18). Therefore, it seems crucial to set optimal timing for measurement of PTH levels after surgical procedure (19). In other studies compared PTH levels assessed 1-12 h postoperatively with those at 24 h, finding that early results are equally accurate. Vescan et al. in a study on two hundred patients after thyroidectomy compared the results of PTH measured 1 h after surgery with level diagnosed next morning after surgery. The levels did not differ significantly. Similar timing of blood sampling and PTH measurements was used by Roh & Park. They assessed quick PTH (qPTH) levels preoperatively and 10 min, 1 h, 24 h – postoperatively. Hypocalcaemic patients had significantly lower level of PTH measured 10 min after surgery than the normocalcemic group. It was suggested that PTH measured 10 after surgery could be predictive for hypocalcaemia. Ghaheri et al. in a group of 80 patients after total thyroidectomy obtained less definitive results (20, 21, 22). PTH was measured immediately after surgical procedure and it was concluded that low PTH level correlated with postoperative hypocalcaemia but could not predict it.

Even more disappointing results were obtained by Lombardi et al. (24). In large series of 523 consecutive patients undergoing thyroidectomy, 199 developed hypocalcaemia. PTH level measured 4 h after surgery was normal in 70 hypocalcaemic cases, and among them 11 patients were clinically symptomatic. Ultimately it was concluded that PTH level alone did not accurately predict relevant postoperative hypocalcaemia. The guidelines of The Society of Australian Endocrine Surgeons has published a review of 458 patients after thyroidectomy revealing that 7% of the patients despite with normal PTH level developed a mild self-limiting hypocalcaemia that did not require calcium supplementation (24). Del Rio et al. studied a group of 1000 thyroidectomised patients, checking the accuracy of the 24 h PTH measurement in the prediction of hypocalcaemia. 253 patients developed hypocalcaemia, 152 were symptomatic by 24 h and 101 presented delayed (>24 h) hypocalcaemia. However only 49 patients had low PTH level at 24 h. Therefore authors suggested that PTH at 24 h after thyroidectomy was not a predictive factor of postoperative hypocalcaemia (25, 26, 27).

As a conclusion of our study we suggest PTH levels 1 and 24 hours postoperatively as good predictors of postoperative hypocalcaemia with sensitivity of 93%. There were no cases in our study with hypocalcaemia and reference PTH level. We also suggest that PTH measurement obtained during the first hour after the surgical procedure or even 24 hours after is still predictive one. Decreased prediction value could be connected with undertaken lower limit of PTH level or highest PTH level before the surgery.

Thanks to early diagnosis of potential hypocalcaemia, it is possible to institute calcium supplementation and avoid progress of it’s symptoms. This would lead to further reduction in hospital stay, costs and risk for postthyroidectomy patients.

**SUMMARY**

Summarizing, hypoparathyroidism after thyroidectomy is still significant source of morbidity and expenses. To prevent severe hypocalcaemia or even tetany it is critical to identify the group of patients at risk, what enables early supplementation of calcium. With such policy normocalcemic patients with normal iPTH level could be safely discharged early after surgery. On the other hand we should realize that the accuracy of early iPTH measurement is about 93%. This is relieved by the fact that in some patients who developed symptomatic hypocalcaemia with normal PTH level, hypocalcaemia was mild and self-limiting. They could be safely early discharged and treated by oral calcium supplementation.

**CONCLUSION**

iPTH level at 1h after surgery is a strong early predictor of hypocalcaemia after subtotal
thyroidectomy. iPTH level at 1h after surgery could therefore differentiate between patients at risk of hypocalcaemia and patients that that could be safely discharged early.

REFERENCES