

# Intraoperative parathormone measurement in patients with primary hyperparathyroidism

## A prospective clinical study

Thomas M. Beck<sup>a</sup>, Peter R. Huber<sup>b</sup>, Daniel Oertli<sup>a</sup>

<sup>a</sup> General Surgical Service, Department of Surgery, University Hospital Basel, Switzerland

<sup>b</sup> Clinical Chemistry and Hormone Laboratory, Department of Central Laboratories, University Hospital Basel, Switzerland

## Summary

**Background:** The objective of this pilot study was to evaluate the use of intraoperative iPTH measurement in combination with bilateral neck exploration in patients with primary hyperparathyroidism.

**Methods:** A prospective study was conducted in a single centre university hospital in Switzerland comprising 33 patients with primary hyperparathyroidism undergoing neck surgery. No routine preoperative localisation studies were conducted. Intraoperative iPTH measurement was performed at defined times. Exploration was discontinued when iPTH fell below 15% of baseline.

**Results:** For all patients with adenoma the median serum iPTH decreased to 11.9% (standard

deviation 5.5%) of baseline concentrations. All patients with hyperplasia achieved normocalcaemia. At median follow-up of 17.7 weeks neither recurrent nor persistent hypercalcaemia was observed. Eleven patients were explored unilaterally.

**Conclusion:** Measurement of intraoperative serum iPTH is a helpful tool in the differentiation of single adenoma from hyperplastic glands. When we call for a strict 78% decrease in serum iPTH from base levels after 10 minutes, measurement of this marker protein even allows differentiation of single- from multi-glandular disease.

**Key words:** parathyroidectomy; hyperparathyroidism; parathormone; iPTH measurement

## Introduction

Parathyroid surgery is routine at specialised centres with a high success rate, low morbidity and a mortality rate near zero. The basic goal of parathyroidectomy in primary hyperparathyroidism is postoperative normocalcaemia by removal of all abnormal parathyroid tissue. The standard surgical therapy for primary hyperparathyroidism is bilateral neck exploration and exposure of four parathyroid glands as described for the first time by Felix Mandl in 1926 [1]. With new, improved preoperative localisation techniques and the availability of intraoperative intact parathormone (iPTH) monitoring, a switch to less

invasive procedures has occurred. These advances have even resulted in a change in anaesthesia from general to local procedures, and parathyroidectomy of an enlarged gland may be performed under videoassistance, with minimal incisions and/or complete endoscopic techniques. Hitherto our standard care has been bilateral neck exploration and exposure of all four parathyroid glands. The purpose of this pilot study was to evaluate the efficacy of rapid PTH assay in combination with standard bilateral neck exploration, as well as its potential for limited explorations.

## Methods

From March 2000 to April 2002, 33 patients with primary hyperparathyroidism were included in this prospective study. The median age of the patients (25 female and 8 male) was 64 (range 18 to 88 years). Clinical symptoms

were fatigue and depression in 69% of patients, concurrent hypertension in 39%, nephrolithiasis in 33%, bone disease (elevated alkaline phosphatase) in 27%, pain in the extremities in 7% and peptic ulcer in 3%. Only 9% of the

patients were asymptomatic. The median preoperative calcium level was 2.82 mmol/l (range 2.54–3.36 mmol/l). The normal laboratory range in our institution is 2.10–2.65 mmol/l. Only one patient had undergone prior thyroid surgery. Preoperative localisation studies were not routinely requested prior to the primary neck exploration, but had already been carried out by the referring physicians in 18 cases: Tc-Sesta-MIBI scintigraphy was therefore done in four cases, ultrasound diagnosis in 10 patients and MR diagnosis in two. One patient underwent scintigraphy and ultrasound or MRI and ultrasound respectively.

Surgery was always performed under general anaesthesia and exploration was started on the side suggested by pathological imaging. For quantification of the intact parathormone (iPTH) we used a commercially available immunochemiluminometric assay (IMMULITE Turbo intact PTH, Diagnostic Products Corporation [DPC], Los Angeles USA). This assay uses two polyclonal anti-

bodies against intact PTH, one coated on a polystyrene bead and another conjugated to alkaline phosphatase. Results were obtained after 15 minutes and were transmitted by phone to the operating theatre.

Two samples were drawn at 5 and 10 minutes before skin incision and were averaged to define a base level of PTH. After a Kocher incision, neck exploration for enlarged parathyroid glands was done. Enlarged glands were removed and blood was drawn at intervals of 2, 4, 10, 15 and 20 minutes for quantification of iPTH after the removal of each suspicious gland.

An 85% fall from baseline 20 minutes after the last tissue resection indicated adequate resection of enlarged glands. On the first postoperative day we assessed the serum calcium level and documented all surgical and metabolic complications. All suture material was removed on the third postoperative day. The wound remained protected by sterile strips.

## Results

Overall, 85% of the patients operated on proved to have uniglandular disease. One patient had a double adenoma and another a microinvasive carcinoma (3%). Three patients (9%) had multiglandular hyperplasia. 87% of the glands removed were at their normal anatomical localisation. In four patients (12%) the enlarged glands were at an ectopic location (once mediastinal, once paraoesophageal, twice tongue of the thymus gland). None of the patients had supernumerary glands.

Seven patients had combined thyroid surgery during the same exploration.

A significant decrease in the iPTH-level below 85% from baseline after a unilateral approach made it possible to limit 11 interventions to unilateral exploration.

### Accuracy of imaging techniques

Comparing the intraoperative findings with the preoperative localisation studies, 2 of 4 scintigraphies proved accurate. Six out of 11 ultrasound searches matched and the two MRI explorations performed revealed a correct localisation. In addition, their combination with ultrasound procedures was successful. However, the combination of

ultrasound and scintigraphy was misleading in the single case.

### Postoperative iPTH concentrations

For all patients with single gland disease the median serum iPTH levels decreased to 10.8% (standard deviation 5.5%) from the base level 20 minutes after the last tissue resection (Fig. 1). The 95% confidence interval at this time was 10–14%. The 95% confidence interval 10 minutes after the last resection was 16–21%.

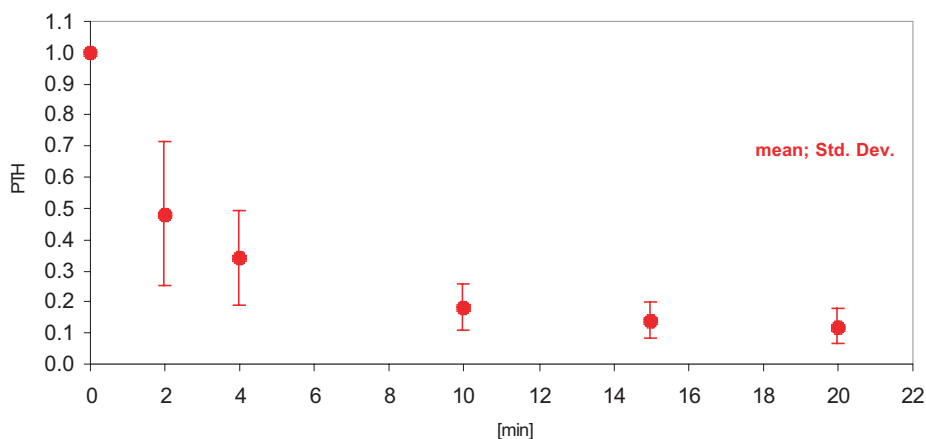
In the single case with double adenoma the 20-minute iPTH level decreased to 33% after removal of the first adenoma. After further exploration and removal of a second adenoma, a final iPTH level of under 15% from baseline average was achieved.

In 3 cases with multiglandular hyperplasia we performed total parathyroidectomy. We thus reached the requested 15% limit and then partially retransplanted parathyroid tissue (twice forearm, once close to the sternocleidomastoid muscle). The median operation time was 100 min. (range 25–205 min).

The median postoperative serum calcium level was 2.28 mmol/l (range 1.93–2.68 mmol/l), a re-

**Figure 1**

Overall mean and standard deviation. 30 cases (3 cases with multiglandular hyperplasia not included).



duction from 2.82 mmol/l. No surgical complications occurred. In one patient who suffered from hoarseness vocal cord function was checked by endoscopy and was considered normal. Five patients had postoperative asymptomatic hypocalcaemia. Four patients with postoperative normocalcaemia, however, had paraesthesia of the fingers. These nine patients were substituted with oral calcium.

Most of the follow-up data were collected by the referring physicians. After median follow-up of

17.7 weeks (range 2–91 weeks), 29 of the 30 patients with single gland disease had a median serum calcium level of 2.27 mmol/l (range 2.03–2.53 mmol/l). One single patient had asymptomatic hypocalcaemia.

All the patients with previous general hyperplasia had normocalcaemia at a median follow-up of 28 weeks (range 21–67 weeks). No patient had hypercalcaemia. No cosmetic-related complaints were documented.

---

## Discussion

In our study intraoperative iPTH monitoring proved to be a very helpful tool. It shows a clear correlation between intraoperative iPTH decrease and postoperative normalisation of serum calcium levels. Unfortunately we have no information on the correlation between intraoperative iPTH level and postoperative parathormone levels [2].

We agree with Westerdahl [3] that measurement of intraoperative PTH during surgery of primary hyperparathyroidism accurately distinguishes between single- and multiple-gland disease and provides good long-term results.

In the light of the results of the 95% confidence interval at 10 and at 20 minutes, we intend to change our future time schedule to one sample 10 minutes after resection of the adenoma. This further reduces the intraoperative waiting time. We still call for an iPTH decrease to below 22% of the averaged baseline level. We believe that such a stringent level for iPTH reduction is necessary in order to distinguish between single- and multiple-gland disease. If we demanded only a 50% reduction as proposed by Irvin [4], a clear-cut distinction is impossible and we could miss additional adenomas.

We found that iPTH measurement usefully guides the surgical approach to patients with hyperplasia.

If we compare our series with older data from our institution, our age and sex distribution is identical and our histological findings are similar [5]. Thus far this new series has shown no recurrence or persistent hyperparathyroidism and no need for a second intervention, compared with the older series with 3.5% recurrence and 1.2% persistent hyperparathyroidism. Comparison of the median operation times in both of our series reveals a differ-

ence of 10 minutes in favour of the older study. It is notable that in our study surgery is beset by two time-consuming factors: first, the interval between resection and the blood samples, and second, the interval between the last sample and the laboratory result. The first interval will be modified in future in view of the reduction in the number of blood samples taken, as described above. The second interval can be shortened only if the iPTH measurement is performed in the operating theatre.

The major advantage of intraoperative parathormone measurement is the possibility of reducing the scope of exploration in selected cases, even without preoperative localisation studies.

The accuracy of the available preoperative localisation studies in our series is fairly low. Other authors report similar sensitivities [6]. In one case we attempted to localise enlarged glands by intraoperative radioguidance using a handheld navigator, but the attempt failed and we abandoned the procedure [7].

Minimal invasive, video-assisted or even fully endoscopic parathyroidectomy is based on reliable, highly sensitive preoperative localisation studies. These studies, such as  $^{99m}\text{Tc}$ -Sesta-MIBI scans imaged using SPECT, are not currently available in our institution [8]. On the other hand, more than 20% of our parathyroidectomies are combined with thyroidectomies where minimally invasive procedures are not usually feasible. In iodine-rich areas this proportion of patients requiring simultaneous thyroidectomy is lower (10%) [8].

In our experience the cosmetic outcome after regular cervicotomy is not a problem if the incisions are strictly confined to skin creases and the suture material is removed as described above.

## Conclusions

Intraoperative iPTH measurement allows differentiation of single- from multiple-gland disease and limited unilateral exploration in selected cases after a significant decrease in intraoperative iPTH. Unilateral exploration is thus the major advantage of this method.

In combination with high quality localisation techniques, successful exploration of a less invasive kind will be possible.

---

### Correspondence:

Thomas M. Beck, M. D.  
General Surgical Service  
Department of Surgery  
University Hospital Basel  
Spitalstrasse 21  
CH-4031 Basel  
E-Mail: tbeck@ubbs.ch

---

## References

- 1 Mandl F. Richtlinien für die Praxis: Die Behandlung der lokalisierten und generalisierten Ostitis fibrosa. Wiener Klinische Wochenschrift 1926;39(37):1046-1048.
- 2 Starr FL, DeCresce R and Prinz RA. Normalization of intraoperative parathyroid hormone does not predict normal postoperative parathyroid hormone levels. Surgery 2000;128 6:930-5; discussion 935-6.
- 3 Westerdahl J, Lindblom P and Bergenfelz A. Measurement of intraoperative parathyroid hormone predicts long-term operative success. Arch Surg 2002;137 2:186-90.
- 4 Irvin G, Sfakianakis G, Yeung L, Deriso G, Fishman L, Molinari A et al. Ambulatory parathyroidectomy for primary hyperparathyroidism. Arch Surg 1996;131 10:1074-8.
- 5 Oertli D, Richter M, Kraenzlin M, Staub JJ, Oberholzer M, Haas HG et al. Parathyroidectomy in primary hyperparathyroidism: preoperative localization and routine biopsy of unaltered glands are not necessary. Surgery 1995;117 4:392-6.
- 6 Lowney JK, Weber B, Johnson S and Doherty GM. Minimal incision parathyroidectomy: cure, cosmesis, and cost. World J Surg 2000;24 11:1442-5.
- 7 Goldstein RE, Blevins L, Delbeke D and Martin WH. Effect of minimally invasive radioguided parathyroidectomy on efficacy, length of stay, and costs in the management of primary hyperparathyroidism. Ann Surg 2000;231 5:732-42.
- 8 Udelsman R, Donovan PI and Sokoll L J One hundred consecutive minimally invasive parathyroid explorations. Ann Surg 2000;232 3:331-9.

## The many reasons why you should choose SMW to publish your research

### What Swiss Medical Weekly has to offer:

- SMW's impact factor has been steadily rising, to the current 1.537
- Open access to the publication via the Internet, therefore wide audience and impact
- Rapid listing in Medline
- LinkOut-button from PubMed with link to the full text website <http://www.smw.ch> (direct link from each SMW record in PubMed)
- No-nonsense submission – you submit a single copy of your manuscript by e-mail attachment
- Peer review based on a broad spectrum of international academic referees
- Assistance of our professional statistician for every article with statistical analyses
- Fast peer review, by e-mail exchange with the referees
- Prompt decisions based on weekly conferences of the Editorial Board
- Prompt notification on the status of your manuscript by e-mail
- Professional English copy editing
- No page charges and attractive colour offprints at no extra cost

### Editorial Board

Prof. Jean-Michel Dayer, Geneva  
 Prof. Peter Gehr, Berne  
 Prof. André P. Perruchoud, Basel  
 Prof. Andreas Schaffner, Zurich  
 (Editor in chief)  
 Prof. Werner Straub, Berne  
 Prof. Ludwig von Segesser, Lausanne

### International Advisory Committee

Prof. K. E. Juhani Airaksinen, Turku, Finland  
 Prof. Anthony Bayes de Luna, Barcelona, Spain  
 Prof. Hubert E. Blum, Freiburg, Germany  
 Prof. Walter E. Haefeli, Heidelberg, Germany  
 Prof. Nino Kuenzli, Los Angeles, USA  
 Prof. René Lutter, Amsterdam,  
 The Netherlands  
 Prof. Claude Martin, Marseille, France  
 Prof. Josef Patsch, Innsbruck, Austria  
 Prof. Luigi Tavazzi, Pavia, Italy

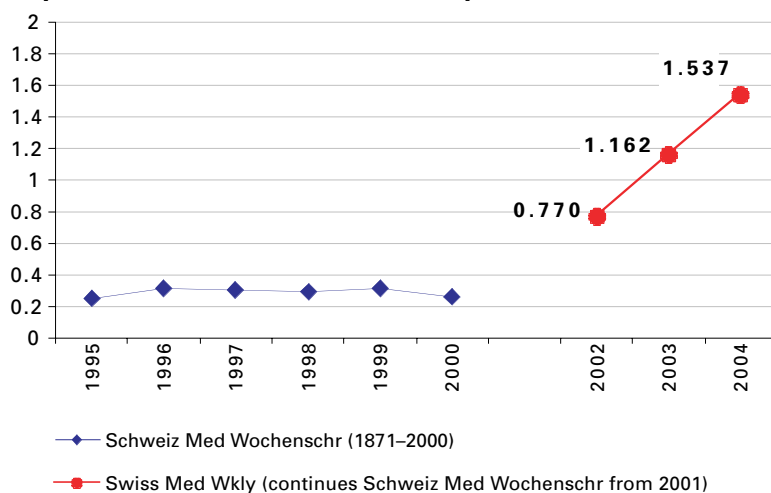
We evaluate manuscripts of broad clinical interest from all specialities, including experimental medicine and clinical investigation.

We look forward to receiving your paper!

Guidelines for authors:

[http://www.smw.ch/set\\_authors.html](http://www.smw.ch/set_authors.html)

### Impact factor Swiss Medical Weekly



All manuscripts should be sent in electronic form, to:

EMH Swiss Medical Publishers Ltd.  
 SMW Editorial Secretariat  
 Farnsburgerstrasse 8  
 CH-4132 Muttenz

Manuscripts: [submission@smw.ch](mailto:submission@smw.ch)  
 Letters to the editor: [letters@smw.ch](mailto:letters@smw.ch)  
 Editorial Board: [red@smw.ch](mailto:red@smw.ch)  
 Internet: <http://www.smw.ch>