

Limited role for intraoperative intact PTH measurement in parathyroid surgery

P Tan FRCS

Senior House Officer in General Surgery

S H Leveson MD FRCS

Consultant Surgeon

York District Hospital, York

H Wilkinson FRCPath

Consultant Chemical Pathologist

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Primary hyperparathyroidism may be cured surgically by complete excision of abnormal parathyroid tissue.

Reoperation for persistent hypercalcaemia due to residual abnormal parathyroid tissue may be associated with a high complication rate. It is possible to assay intact parathormone (iPTH) intraoperatively and as iPTH has a relatively short half-life, its measurement intraoperatively may be used to predict successful parathyroidectomy. We have studied intraoperative iPTH levels in a consecutive series of 33 patients undergoing surgery for primary hyperparathyroidism. We found that iPTH levels fell significantly ($P < 0.05$) from a median pre-excision level of 122 pg/ml to a median level of 36 pg/ml 20 min after excision. However, in 3/31 successful parathyroidectomies, the intraoperative iPTH levels either remained unchanged or had risen. Reliance on intraoperative iPTH levels in these patients may have resulted in unnecessary re-exploration. We conclude that intraoperative iPTH measurement has limited usefulness as a predictor of successful parathyroidectomy for primary hyperparathyroidism.

Primary hyperparathyroidism is a common cause of hypercalcaemia (1) and may be cured by complete surgical excision of abnormal hyperfunctioning parathyroid tissue. For an experienced surgeon, the cure rate after first operation is at least 95% (2). However, in the event of persistent hypercalcaemia, reoperation can be difficult and may be attended by a complication rate of up to 35% (3). Assuming a correct diagnosis of primary hyperparathyroidism has been made, persistent hypercal-

caemia implies that there remains residual hyperfunctioning parathyroid tissue owing to a missed adenoma or insufficient excision of hyperplastic tissue at the first operation.

Intraoperative monitoring of intact parathormone (iPTH) has been advocated to improve the success rate of parathyroidectomy (4-6). Its rationale being that:

- 1 The parathyroid glands are the only site of secretion of iPTH and that biologically active iPTH has a short half-life of 3-4 min.
- 2 iPTH levels may be measured intraoperatively by a two-site immunoradiometric assay with a 15 min incubation period.
- 3 Complete removal of abnormal parathyroid tissue should result in a rapid fall in iPTH levels.

Therefore, iPTH levels which have fallen within 20-30 min of excision should, in theory, predict successful parathyroidectomy.

This study aims to examine the usefulness of intraoperative iPTH measurement as a predictor of successful parathyroidectomy for primary hyperparathyroidism.

Patients and methods

A consecutive series of 33 patients undergoing cervical exploration for primary hyperparathyroidism were studied. All patients were undergoing parathyroidectomy for the first time and no preoperative localisation techniques were employed. All parathyroidectomies were performed by one operator (SHL) whose routine practice was four gland identification and excision of abnormal parathyroid tissue without the use of histological frozen section for primary explorations.

A pre-excision blood sample was taken by peripheral

Table I. Histological findings (n = 33)

	Successful	Failed
Adenoma	28	1
Hyperplasia	3	1

venepuncture when the patient was anaesthetised and sent immediately for separation and frozen storage of the plasma in the laboratory. Two further samples were taken at 5 min and 20 min after completion of excision of abnormal parathyroid tissue. All plasma samples were assayed for iPTH by a two-site immunoradiometric method (Allegro PTH, Nicholls Institute, Saffron Walden, Essex, UK) using an overnight incubation at room temperature.

The Wilcoxon signed rank test for matched pairs was employed with $P < 0.05$ reported as significant.

Results

The 33 patients had a mean pre-excision total calcium level (adjusted for albumin) of 2.83 mmol/l, SD 0.17 mmol/l (normal range 2.10–2.60 mmol/l) and a median pre-excision iPTH level of 122 pg/ml (range 55–1550 pg/ml). The normal iPTH value being < 10 pg/ml in the presence of hypercalcaemia (total serum calcium > 2.60 mmol/l).

In all, 31/33 cervical explorations resulted in successful parathyroidectomies with a mean postoperative total calcium level of 2.34 mmol/l, SD 0.12 mmol/l. The histological findings are given in Table I. In the 2/33 patients who had failed surgery, one subsequently went on to have another adenoma excised and the other had further hyperplastic parathyroid tissue removed.

The iPTH levels obtained are illustrated in Fig. 1 and Fig. 2. In the 31/33 successful parathyroidectomies, the iPTH level had fallen to a median of 100 pg/ml (range 18–720 pg/ml) 5 min after excision, which was not significant. By 20 min after excision it had fallen significantly ($P < 0.05$) to a median level of 36 pg/ml (range 11–246 pg/ml). However, in three patients the intraoperative iPTH levels either remained relatively unchanged or had risen, despite successful operation (Table II). The iPTH levels remained relatively unchanged in the 2/33 unsuccessful parathyroidectomies.

Table II. Intraoperative iPTH levels (pg/ml) in three patients who had successful surgery

Preop.	5 min postop.	20 min postop.
234	672	246
73	533	117
133	125	126

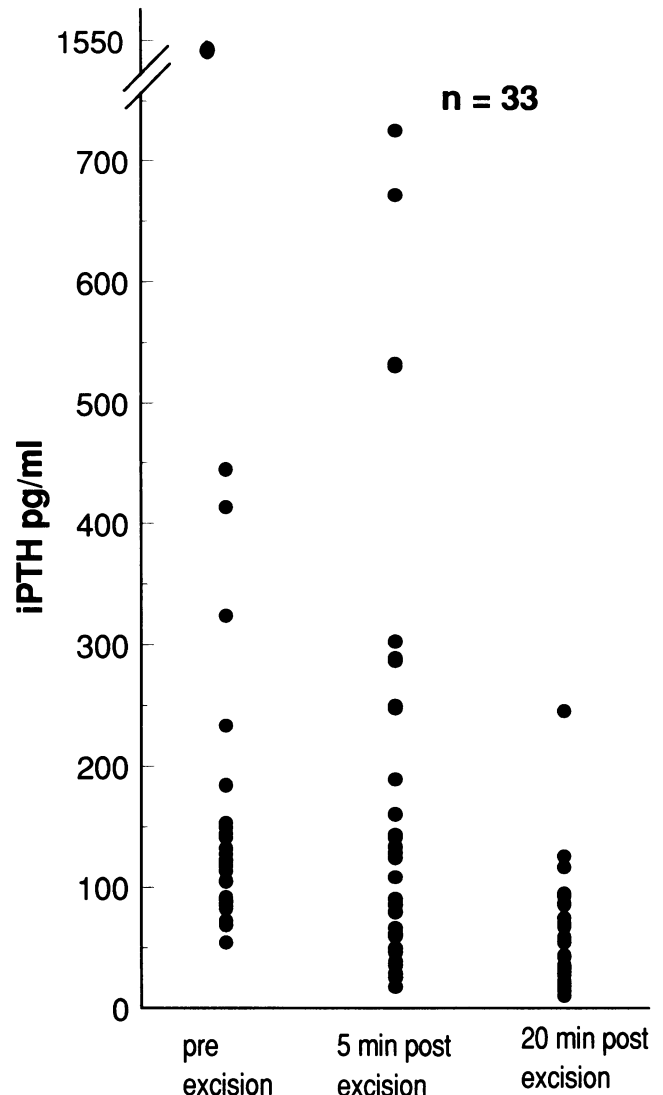


Figure 1. Intraoperative PTH levels.

Discussion

Various methods of identifying parathyroid tissue intraoperatively have been described and these include:

- 1 The use of preoperative intravenous infusion of methylene blue which is taken up selectively by parathyroid tissue and in particular abnormal stimulated glands (7).
- 2 Histological frozen section.
- 3 The density test advocated by Wang and Reider (8) where parathyroid tissue is said to float in a mannitol solution of specific gravity 1.055.

These methods are based on identifying parathyroid tissue removed, but provide no information of tissue left behind and so cannot assess the completeness of excision of abnormal parathyroid tissue. Changes in serum calcium can take more than 24 h to occur and so cannot be of help intraoperatively.

iPTH would, in theory, seem to be the ideal predictor of successful parathyroidectomy but this study has identified some of its limitations. In three patients who

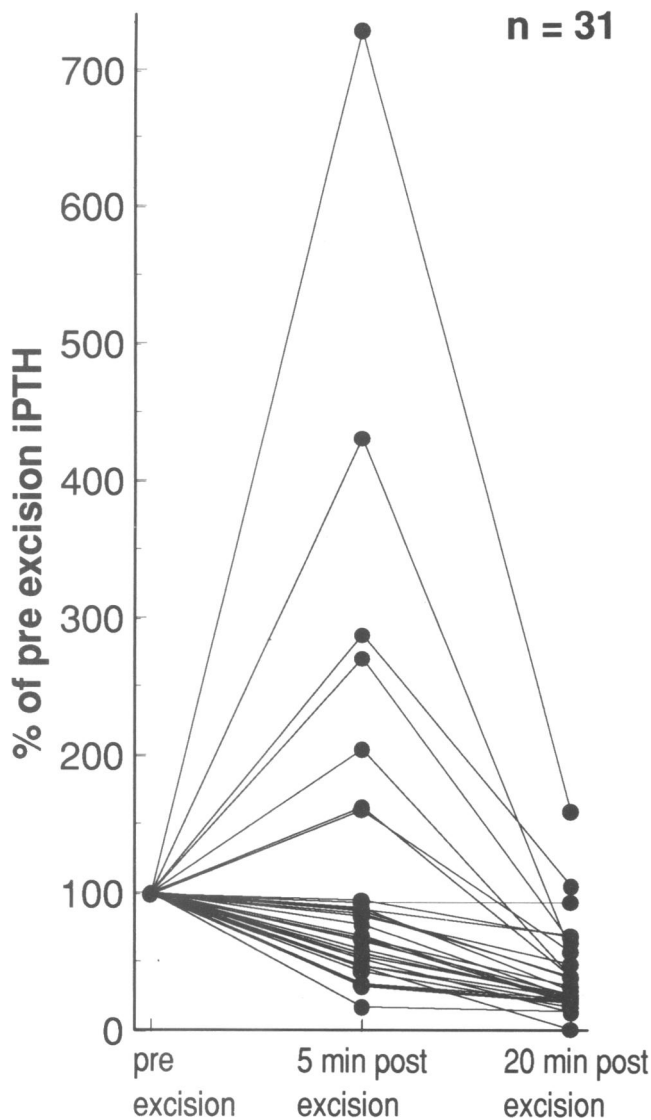


Figure 2. Change in iPTH levels in 31 patients who underwent successful parathyroidectomy.

had successful parathyroidectomies, as indicated by normocalcaemia and eventually normal iPTH levels up to 3 months postoperatively, intraoperative iPTH levels either remained unchanged or had risen after excision. This may be attributed to the effects of surgical

manipulation. Reliance on iPTH levels in these patients may have resulted in unnecessary re-exploration. A recent study which compared histological frozen section and intraoperative iPTH monitoring found that despite truncated incubation times for the iPTH assay the results were not available on a truly intraoperative basis (9).

In the rare event of a double adenoma, removal of just one adenoma may result in a fall in iPTH levels giving a false impression of adequate excision (6).

Therefore, we conclude that intraoperative iPTH measurement has limited usefulness as a predictor of successful parathyroidectomy.

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