The use of intraoperative parathyroid hormone monitoring in minimally invasive parathyroid surgery

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ABSTRACT

INTRODUCTION Surgery is the first-line management option for patients with primary hyperparathyroidism (pHPT). Minimally invasive parathyroidectomy (MIP) is now preferable but few centres offer this service, mainly because of lack of intraoperative parathyroid hormone (IOPTH) testing. The aim of this study was to identify whether the measurement of IOPTH in patients having minimally invasive parathyroidectomy for pHPT alters their management.

METHODS A retrospective review was carried out of 78 consecutive patients who underwent parathyroid surgery by a single surgeon with a special interest in parathyroid surgery. The clinical impact of IOPTH monitoring was recorded postoperatively in a timely manner. Serum adjusted calcium levels were checked preoperatively (on admission) and one month postoperatively; normalisation was considered a cure.

RESULTS In the setting of curative MIP, IOPTH measurement did not influence the management in any of the patients but it could have led to bilateral parathyroid exploration (BPE) in three instances. Similarly, in cases that required lengthening of the MIP incision, IOPTH results did not influence patient management although it could have led to BPE in one case.

CONCLUSIONS MIP offers an effective cure for patients with hyperparathyroidism. The addition of IOPTH testing adds increased expense, operating time and risk to patients otherwise suitable for MIP.

KEYWORDS

Parathyroid hormone – Minimally invasive – Parathyroid adenoma – Endocrine disorder

Accepted 16 April 2016

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The most common cause of primary hyperparathyroidism (pHPT) is a solitary parathyroid adenoma.¹ Surgical removal remains the only curative option for these symptoms. Even for patients who are asymptomatic, this treatment can offer improved cardiovascular function and diabetic control.^{2,3} Both standard parathyroidectomy and minimally invasive parathyroidectomy (MIP) are considered acceptable approaches. MIP involves a smaller lateral incision guided by preoperative radiology, which is now largely replacing the traditional method of bilateral parathyroid exploration (BPE) of all four parathyroid glands because of superior cosmesis, shorter postoperative stay and comparable cure rates. This move to a less invasive procedure is mostly due to the advances in preoperative radiological localisation studies.

Although single adenomas remain the most common cause of pHPT, multiple adenomas occur in up to 15% of patients and can lead to continuing hyperparathyroidism following resection of the primary adenoma.^{4–6} Intraoperative parathyroid hormone (IOPTH) is currently measured prior to and following adenoma resection during MIP to confirm the success of the parathyroidectomy given that not all four parathyroid glands can be visualised. On the

day of surgery, before resection, a baseline parathyroid hormone (PTH) assay is obtained. Once the abnormal parathyroid gland is removed, a PTH sample is taken at ten minutes after resection. A decline in PTH of 50% from baseline is considered a cure.⁷

In the UK, the number of centres offering MIP remains suboptimal, mainly as a result of costs and limited availability of IOPTH testing.⁸ In the presence of concordant radiology (ultrasonography and sestamibi imaging), intraoperative frozen section and expert clinical opinion, some surgeons argue that IOPTH monitoring is unnecessary.

The aim of this study was to identify whether the measurement of IOPTH in patients having MIP for pHPT alters their management. Clinically, it has been hypothesised that IOPTH testing does not alter the management plan in most patients, and results in a longer operating time and increased economic costs.

Methods

Prospectively collected data from 78 consecutive patients with pHPT managed by a single consultant surgeon with a

specialist interest in parathyroid surgery at Gloucestershire Royal Hospital between July 2009 and October 2012 were reviewed retrospectively. Patients underwent preoperative technetium sestamibi imaging and (if indicated) localising ultrasonography shortly prior to the planned procedure. If a single adenoma was visualised successfully on ultrasonography, the location was marked by the performing radiologist as appropriate. Imaging was considered concordant if the parathyroid lesion was identified in the same location by both sestamibi imaging and ultrasonography. However, imaging was considered non-concordant if there was failure to identify a parathyroid lesion by either the ultrasonography or the sestamibi imaging, or if a parathyroid lesion was identified by both modalities but in different locations.

In the absence of concordant radiology or if clinically indicated, BPE was performed. In the presence of concordant radiology or in the setting of non-concordant radiology but confident ultrasonography visualisation and marking of a parathyroid adenoma, MIP was attempted. In cases of technical difficulty, poor radiological localisation or clinical indication, the minimally invasive incision was extended to allow BPE.

IOPTH levels were measured at baseline and then at least once no less than ten minutes after excision of the suspected adenoma. A reduction of >50% was considered sufficient to exclude multiglandular disease. Intraoperative frozen section was performed on the excised tissue to confirm histology. The clinical impact of IOPTH levels was recorded postoperatively in a timely manner. Serum adjusted calcium was checked preoperatively (on admission) and one month postoperatively; normalisation was considered a cure.

Results

The median age of the patients included in the study was 64 years (range: 26–89 years) and 54 patients (69%) were female. The median preoperative adjusted calcium level was 2.8mmol/l (range: 2.51–3.39mmol/l). One patient had normal preoperative adjusted calcium with an inappropriately raised PTH level and concordant radiology.

Preoperative radiology

Preoperative sestamibi imaging and ultrasonography were performed in 75 out of the 78 patients. A summary of these cases is shown in Table 1.

Procedures performed

The procedures performed are summarised in Table 2. Forty-one patients underwent an uncomplicated and curative MIP. Thirty-six of these had concordant radiology and five had non-concordant radiology but confident ultrasonography visualisation and marking of a parathyroid adenoma.

In a further 13 patients for whom MIP was planned, it was necessary for the incision to be extended. For seven, radiological localisation was inaccurate. For five, MIP was technically difficult; two patients had venous anomalies

Table 1 Breakdown of radiology concordance

	<i>n</i>
Concordant radiology	51 (68%)
Non-concordant radiology	24 (32%)
Negative ultrasonography	9 (12%)
Negative sestamibi imaging	3 (4%)
Negative ultrasonography and sestamibi imaging	3 (4%)
Indicative of parathyroid carcinoma	1 (1%)
Ultrasonography and sestamibi imaging showed different locations for the lesion	8 (11%)

obstructing access, two had adenomas that were unextractable via MIP owing to size and/or location, and one had an adenoma that was adherent to the inferior pole of the ipsilateral thyroid gland. For the 13th patient, the adenoma was localised incorrectly and then also too large to remove via a MIP incision. Normal serum adjusted calcaemia levels were achieved in 12 patients postoperatively. In one patient, despite BPE, calcium remained elevated following surgery; she later underwent a hemithyroidectomy for an intrathyroid parathyroid adenoma.

One patient (81 years, male) underwent MIP concurrently with a hemicolectomy for perforated diverticular disease. Preoperative radiology was concordant and conclusive, suggesting a right lower parathyroid adenoma. Despite an incomplete reduction in IOPTH (23mmol/l to 19.3mmol/l), the decision was made not to proceed to BPE as the patient was becoming unstable owing to the duration of anaesthetic. Postoperative calcium failed to normalise. Histological examination indicated gland hyperplasia.

In another patient (69 years, female), preoperative sestamibi imaging demonstrated high uptake throughout the left lobe of the thyroid and ultrasonography identified what

Table 2 Breakdown of procedures performed (*n*=78)

Procedure	<i>n</i>
Uncomplicated, curative MIP	41
with concordant radiology	36
with non-concordant radiology	5
Planned MIP converted to BPE	13
owing to inaccurate radiological localisation	7
owing to technical difficulty	5
owing to inaccurate localisation and technical difficulty	1
Failed MIP	2
(with concordant radiology)	2
Planned BPE	22
due to poor radiological localisation	18
due to clinical indication	4
MIP = minimally invasive parathyroidectomy; BPE = bilateral parathyroid exploration	

Table 3 Complete reduction rates for intraoperative parathyroid hormone in relation to procedure performed

Procedure	Outcome	n	Complete reduction observed?		
			Yes	No	Not available
MIP	Curative	41	35	3	3
	Non-curative	2	0	2	0
Planned MIP converted to BPE	Curative	12	10	1	1
	Non-curative	1	0	1	0

MIP = minimally invasive parathyroidectomy; BPE = bilateral parathyroid exploration

appeared to be a left lower parathyroid adenoma. She underwent MIP but no reduction in IOPTH was observed (13.7mmol/l to 17.9mmol/l). Postoperatively, calcium failed to normalise. On bilateral neck re-exploration, a fifth intra-thyroid parathyroid adenoma was found and excised.

Planned BPE was performed in 22 patients. This was owing to inconclusive radiology in 18 cases and clinical indication in 4.

Intraoperative parathyroid hormone monitoring

The results from the IOPTH testing are described in Table 3. In the setting of curative MIP, IOPTH results did not influence the management of any of the patients but it could have led to BPE in three instances. Similarly, in cases that required lengthening of the MIP incision, IOPTH measurement did not influence patient management although it could have led to BPE in one case. Three patients did not have IOPTH monitoring but postoperative PTH normalised.

Where MIP was non-curative, proceeding to BPE was not clinically appropriate regardless of the IOPTH result in one case (colectomy patient). Arguably, IOPTH testing may have prevented the need for repeat surgery in the 69-year-old female patient described above.

Discussion

MIP remains a highly successful treatment for pHPT. The benefits of a less invasive surgical approach have led to decreased morbidity and fewer complications. Patients can go home within a few hours of surgery and the success rates are equal to those of BPE.^{9,10}

The success of a minimally invasive technique relies heavily not only on the expertise of the surgeon but also on the quality of the preoperative imaging and intraoperative techniques to avoid unnecessary conversion to BPE.¹¹ With experienced centres and preoperative imaging, a minimally invasive approach can be employed without measuring IOPTH, with equal success rates to those centres that do use IOPTH monitoring.

The vast majority of parathyroid adenomas are single lesions. The frequency of double adenomas varies in the literature but is approximately up to 15% and they are currently the most common reason for failure of MIP.⁴⁻⁶ The difficulty lies in the fact that the second adenoma can remain dormant or functionally suppressed until after the

first excision of the primary adenoma with no evidence of a second adenoma on preoperative imaging. In this study, IOPTH measurement did not provide any additional information to alter the management for patients in the setting of concordant radiology, intraoperative frozen section and expert clinical opinion. It may also have led to conversion from MIP to BPE in around 10% of the patients. Furthermore, IOPTH testing could have caused increased operating and anaesthetic time as well as potential complications and morbidity owing to the more extensive operation.

Previous studies have endorsed the use of IOPTH monitoring. One of the main arguments for this is that a significant proportion of patients with pHPT will have multiglandular disease and will not be cured unless all four glands are visualised during the procedure. It is claimed that IOPTH testing has avoided failure during MIP from missed multiglandular disease.^{8,12} A prospective study with a cohort of 350 patients who underwent MIP based on concordant neck ultrasonography and sestamibi imaging observed that only 79% of patients were identified correctly as having single gland disease without IOPTH monitoring.¹² Further exploration showed that 15% of patients had multiglandular disease.

Similar results were found in another study where two groups of patients were compared: those in whom IOPTH testing was used and those in whom only preoperative imaging was used.¹³ IOPTH monitoring in 188 patients resulted in a 100% cure rate whereas among the 157 patients relying on imaging, 10% had persistent hyperparathyroidism due to multiglandular disease that was missed at the time of surgery.

This is contested by many authors suggesting equally high cure rates with concordant imaging alone, without IOPTH measurement.¹⁴⁻¹⁸ In a study of 500 patients who underwent MIP without IOPTH monitoring, PTH levels were measured postoperatively to inform discharge only; a 97.5% cure rate was reported.¹⁵ This is in keeping with the British Association of Endocrine Surgeons guidelines, which suggest that 95% of patients should be normocalcaemic following the first neck exploration.¹⁹ Eleven patients in the aforementioned study subsequently underwent re-exploration but analysis of the results showed that IOPTH testing would have increased the cure rate by only 1%.¹⁵

Another study of 100 patients reported a cure rate of 98% with concordant preoperative radiology only.¹⁶ With IOPTH

monitoring, the cure rate would have been increased by 1% but it would also have led to unnecessary conversion to BPE based on the 9% false negative rate for 10-minute samples and the 4% rate for samples at 30 minutes.

However, IOPTH levels do not always demonstrate the presence of multiglandular disease.²⁰ In a study of 423 patients, IOPTH testing did not identify multiglandular disease in 11 patients.²¹ This has also occurred with a more traditional BPE approach. One study of 69 patients reported that 75% of cases had missed multiglandular disease despite IOPTH monitoring.¹⁸

Failure of PTH levels to fall significantly after excision of a single abnormal parathyroid gland leading to bilateral conversion has been also been reported in a number of other studies.^{22–24} A study of 119 patients collected PTH results without disclosing these at the time of surgery.¹⁴ In four of the cured patients, IOPTH failed to decrease sufficiently, which would have led to unnecessary BPE. Although it cannot be proved that these patients would have been harmed by false negative results, this would have led to prolonged anaesthetic and surgical time, and extended surgical treatment. Comparatively, in the same study, only two of the reoperations would have been prevented through IOPTH monitoring.

IOPTH tests add additional cost and increased operative time while waiting for the assay of the ten-minute sample. Operative times vary but one study reported a mean duration of 41 minutes (range: 19–120 minutes) for MIP without IOPTH monitoring.²⁵ The addition of IOPTH monitoring to this is therefore clearly considerable.

Currently, in the UK, the number of centres offering MIP remains suboptimal; this is mainly because of the costs and the limited availability of IOPTH testing.⁸ Elimination of IOPTH measurement from the management of patients with pHPT could help increase the use of the MIP and the range of benefits it provides.

Study limitations

This study is not without its limitations. First, this study was retrospective. Second, the patients in this series were managed by a single experienced endocrine surgeon with a specialist interest in minimally invasive parathyroid surgery. The results of this study might therefore not be applicable to all centres.

Conclusions

MIP offers an effective cure for patients with hyperparathyroidism. The addition of IOPTH testing adds increased expense, time and risk to the operation without significant benefit. These patients would have a similar outcome with the use of clinical expertise, preoperative radiology and intraoperative frozen section only. The use of IOPTH monitoring for MIP is unnecessary in patients with concordant radiology.

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