

REVIEW ARTICLE

Role of Intraoperative Parathormone monitoring in Parathyroidectomy for Primary Hyperparathyroidism: A narrative review

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ABSTRACT

Introduction: Intraoperative parathyroid hormone (ioPTH) has emerged as a valuable tool in improving the success of minimal invasive parathyroidectomy which has become the standard management in Primary Hyperparathyroidism. It appears a very attractive tool with a significant academic advantage to confirm the removal of parathyroid adenoma during surgery. Despite having such an advantage no direct Randomized studies comparing MIP (minimal invasive parathyroidectomy) with ioPTH and MIP without ioPTH have been performed nor much detailed systematic reviews and meta-analyses are available in the literature on this topic.

Objective: we performed this review to evaluate the role of ioPTH in surgeries for Primary Hyperparathyroidism due to parathyroid adenoma.

Data Source: A systematic search of databases PubMed, Scopus, Embase and Google Scholar using keywords Intraoperative Parathormone monitoring, primary Hyperparathyroidism was performed to identify all studies assessing the role of ioPTH during parathyroidectomy. All studies including randomized clinical trials and observational studies with a retrospective or prospective design from 2019 to 2024 were analysed.

Results: A total of 15 studies involving more than 1500 patients with Primary Hyperparathyroidism were included for analysis. All studies demonstrated the effectiveness of ioPTH in improving the success rate of focused Parathyroidectomy to around 99% compared to 97% without the use of ioPTH. The benefit was however more in cases with discordant preoperative imaging studies Ultrasonography and Sestamibi scan and in cases where the preoperative localization of parathyroid adenoma was equivocal (66%). The benefit of ioPTH comes with an increased duration of surgery noted in many studies with a statistically significant difference (0.0001).

Conclusion: The use of ioPTH is associated with higher cure rates for patients with primary hyperparathyroidism undergoing MIP. However, ioPTH monitoring is most useful as an adjunct to preoperative imaging when imaging results are equivocal allowing for more focused/unilateral operations to be performed. When ultrasonography and MIBI are used for preoperative localisation and the results are concordant, the additional benefit of ioPTH is marginal, especially given the longer duration of surgery.

Keywords: Parathormone, Hyperparathyroidism, ioPTH

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INTRODUCTION

Primary hyperparathyroidism (PHP) is a common condition with an estimated incidence of 28 out of 100 000 individuals in the general population.¹ The nature of the disease in 70% to 95% of cases is an aberrant adenoma oversecreting parathyroid hormone (PTH); however, the cause also includes multi gland hyperplasia (up to 15%) and carcinoma (1%).² Surgical excision remains the only means of cure. The use of ioPTH was first

reported by Nussbaum et al³ in 1988. It is based on the principle that the half-life of PTH is 3 minutes, and thus results can be obtained while surgery is ongoing.⁴ An adequate reduction in PTH measured intraoperatively provides the surgeon with the confidence to terminate the procedure on successful excision of the pathologic gland.⁴ The main proposed advantage of ioPTH is an

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improved cure rate in patients undergoing MIP.^{5, 6} Advocates of ioPTH maintain that regardless of the advances made in imaging modalities, ioPTH assists the surgeon in confirming that the pathologic gland has been appropriately excised and is “essential to avoid a surgical failure,”⁷ and that ioPTH should be used routinely by all surgeons when performing surgery for PHP.⁸ Despite its increasing and widespread use, controversy regarding the utility of ioPTH remains.^{5,9} Some authors maintain that the benefits of ioPTH are marginal in cases where a pathologic gland has been localized by concordant dual imaging preoperatively.^{9,10,11} It is argued that in these cases, the use of ioPTH unnecessarily uses hospital resources and equipment for an intraoperative adjunct that is unlikely to save operative time or diagnostic yield.¹²

There is also concern regarding potential false-negative and false-positive results in the analysis of ioPTH that may lead to unnecessary exploration or premature termination of surgery when the pathologic gland(s) has not yet been excised.^{9,11,13} Given this uncertainty, we performed this systematic review to evaluate the utility and benefit of ioPTH in the surgical treatment of primary Hyperparathyroidism.

MATERIAL AND METHODS

The objective of this systematic review and meta-analysis was to assess if ioPTH monitoring can reduce the incidence of persistent or recurrent PHPT. A systematic literature search was performed using PubMed, Scopus, Embase and Google Scholar Database. Prospective and retrospective studies addressing the efficacy of ioPTH monitoring were included in the

systematic review.

RESULTS

The initial literature search yielded more than 50 studies for full-text review, of which 15 studies including more than 1500 patients with PHP were included for review. 35 articles were excluded as they did not fulfil the requisite criteria.

DISCUSSION

Recent advances in imaging technology and surgical adjuncts have increased the use of the MIP approach for parathyroid surgery. This approach aims to achieve similar or higher success rates with minimal morbidity.¹⁴ The introduction of ioPTH is deemed by some authors to have been a critical part of this movement.^{6,8} Despite its increasing use as a component of the management of a common disorder, controversy regarding the utility of ioPTH for PHP remains about operative success, operative time, cost, and other considerations.^{9,10,11}

Although PHP is a common disorder, it can have serious consequences. The associated hypercalcemia may result in renal complications, skeletal involvement, cognitive impairment, and potentially fatal cardiac events.¹⁵ Prompt management is necessary to avoid sometimes irreversible morbidity. For this reason, the primary endpoint when evaluating MIP for PHP should ultimately be the cure of the disease with a return to normocalcemia. Patients who undergo unsuccessful surgery remain persistently hypercalcemic and are at increased risk of morbidity.¹⁶ There may be increased patient anxiety regarding the need for reoperation and the potential loss of faith by the patient or the surgeon in the surgical process.¹⁷

To Improve the outcome of Parathyroid surgeries for Correct identification and complete excision of the abnormal parathyroid glands with minimal complications and to reduce the morbidity associated with reoperations many studies have focused on the effective preoperative localizations of adenoma with focussed ultrasonography of neck and sestamibi (MIBI) scan with the use of ioPTH as an adjunct to confirm the intraoperative complete excision of the pathology.

A number of studies state that ioPTH is not required when imaging is concordant on 2 separate imaging modalities, namely focused ultrasonography scan of the neck and MIBI scan,^{11,18,19} owing to the costs and time associated with its use and the likelihood that it will not add anything to an already straightforward procedure.^{11,18,19} However, ultrasonography is operator dependent and, although MIBI scan has a sensitivity of 68% to 95% and specificity of 90%, it has a high false negative rate, with rates as high as 20% reported.^{20,21} Several old studies by Lew and Irvin after examining the long-term outcome of focussed parathyroidectomy found that ioPTH use is successful with regards to limited scarring and it does not increase the recurrence rate when normal parathyroid glands are left intact with no failure in detecting multi-gland disease (MGD).²²

One of the main issues that has been raised regarding the use of ioPTH surrounds the interpretation of the biochemical results.^{23,24}

Miami and Vienna criteria have the highest rate of false positives (0.4%), wherein patients are deemed cured but are persistently hypercalcemic postoperatively, due to a second adenoma or undetected multi-gland disease. Halle and Rome's

criteria have a significantly higher false negative rate (35% vs 16.2%), defined as incorrect prediction of incomplete excision.^{11,24} Unfortunately no comparison of the relative performance of the available techniques was possible due to scant reporting of the requisite data, and at present there is no recommendation regarding which criterion to use.¹¹ Another proposed drawback of ioPTH is the perceived increased procedural cost.^{13,25} It is argued that ioPTH may be associated with an increase in the length of the operation while the surgeon awaits the laboratory result^{12, 18} and that there is significant expense associated with the infrastructure and the biochemical expertise required to rapidly process ioPTH.⁹

Patients are more likely to undergo focused operations if the preoperative images are strongly positive in both ioPTH and non-ioPTH groups of the use of ioPTH. This was previously demonstrated by Sebag et al.²⁵ - patients who had two concordant images had a single gland disease and ioPTH did not add anything to the surgical management for these patients. Those patients with negative imaging are more likely to undergo bilateral operations. These results suggest imaging has a significant role in the type of surgical approach used. It can therefore be argued that the use of ioPTH has a less important role in those with strongly positive or negative imaging with regards to the surgical approach used.

CONCLUSION

In conclusion, this analysis demonstrates that ioPTH monitoring is most useful as an adjunct to preoperative imaging when imaging results are equivocal allowing for more focused operations to be performed. However, some authors

advocate that MIP should only be undertaken with the availability of ioPTH as an adjunct. However, when ultrasonography and MIBI are used, the additional benefit of ioPTH is marginal, especially given the longer duration of surgery.

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