Intraoperativno določanje paratiroidnega hormona pri bolnikih s primarnim hiperparatiroidizmom – naše enoletne izkušnje

Intraoperative Parathyroid Hormone Assessment in Patients with Primary Hyperparathyroidism – One–Year Experience

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Izvleček

Namen: *Z analizo dela na področju kirurgije adenoma obščitnic smo želeli ovrednotiti svoje izkušnje z intraoperativnim merjenjem paratiroidnega hormona (PTH) in primerjati rezultate minimalno invazivne paratiroidektomije (MIP) s klasično eksploracijo vratu (KEV).*

Metode: *V obdobju od aprila 2011 do aprila 2012 smo na Oddelku za torakalno kirurgijo UKC Maribor pri 8 bolnikih s primarnim hiperparatiroidizmom (PHP) izvedli paratiroidektomijo, pri kateri smo intraoperativno merili PTH. Paratiroidektomija je bila definirana kot uspešna v primeru padca PTH 10 min po odstranitvi obščitnice za več kot 50 % od izhodiščne meritve, izmerjene po uvodu v anestezijo. Kriterij za uspešno kirurško zdravljenje je bil normalen nivo serumskega kalcija v obdobju šestih mesecev po operaciji.*

Rezultati: *Štirim bolnikom od osmih*

Abstract

Purpose: *We evaluated our one–year experience in the intraoperative measurement of parathyroid hormone (IOPTH) in parathyroid adenoma surgery. We also compared surgical outcome after minimally invasive parathyroidectomy (MIP) and conventional neck exploration (CNE).*

Methods: *Between April 2011 and April 2012, eight consecutive patients with primary hyperparathyroidism (PHP) underwent parathyroidectomy with IOPTH in our institution. Parathyroidectomy was defined as successful when a >50% decrease of IOPTH was observed 10 minutes after resection of the abnormal gland. The second criterion for success was a six month period of postoperative normocalcaemia.*

Results: *We performed four MIPs, two unilateral neck explorations, and two bilateral neck explorations, resulting in a total of seven solitary and one*

smo izvedli MIP in štirim KEV, od tega dve enostranski in dve obojestranski. Odstranili smo sedem solitarnih adenomov in pri enem bolniku dva adenoma. Pri vseh operacijah je po odstranitvi prekomerno delujoče žleze oz. žlez prišlo do >50 % padca PTH. Povprečni čas MIP je bil 31 min, KEV pa 69 min. Pri treh bolnikih s KEV je prišlo do pooperativne hipokalcemije. Vsi bolniki so imeli v 6–mesečnem pooperativnem obdobju normalne vrednosti serumskega kalcija in PTH, tudi ponovitve bolezni po šestih mesecih nismo beležili.

Zaključek: *Pregled našega enoletnega dela potrjuje visoko in klasični eksploraciji vratu primerljivo uspešnost zdravljenja z MIP. Prednosti z intraoperativnim merjenjem PTH usmerjene MIP so: krajši čas operacije, boljši kozmetični rezultat in verjetno nižja pojavnost pooperativne hipokalcemije.*

double adenomas. IOPTH level decrease expectations were met in all cases. The average length of surgery for MIP was 31 minutes, and 69 minutes for CNE. All patients were eucalcaemic with normal PTH levels during the 6 month follow–up period. Three patients had postoperative hypocalcaemia after CNE and there were no recurrences 6 months postoperatively.

Conclusion: *The review of our series of eight consecutive patients with PHP showed a 100% cure rate after employing IOPTH measurement in both surgical approaches. The advantages of MIP are: shorter operating time, better cosmetic results, and a lower incidence of hypocalcaemia.*

INTRODUCTION

Primary hyperparathyroidism (PHP) is defined as autonomous hypersecretion of parathyroid hormone (PTH) by one or more parathyroid glands, resulting in abnormal calcium homeostasis (1). In approximately 85% of cases, PHP is caused by a single adenoma. In 15% of cases, multiple glands are involved (multiple adenomas or hyperplasia) (2). Parathyroid carcinoma is rare and accounts for <1% of the reported cases of PHP (3). Parathyroidectomy is the treatment of choice in all cases of symptomatic PHP and includes excision of all hyperfunctioning parathyroid tissue while preserving normally functioning glands (4,5). In recent years, conventional neck exploration (CNE) has been replaced by minimally invasive parathyroidectomy (MIP) as the surgical approach of choice in patients with PHP (6,7). Due to the relatively short half–life of PTH, a dramatic drop in circulating hormone can be detected once the abnormally secreting gland or glands have been removed (8,9). Thus, preoperative parathyroid adenoma localisation and intraoperative parathyroid hormone (IOPTH) assessment with a curative drop in PTH levels are both associated with the success of focused, unilateral MIP, avoiding additional exploration and thus decreasing the possibility of complications, such as hypocalcaemia and recurrent laryngeal nerve injury and paresis (8,10).

In April 2011, IOPTH measurement was introduced as a new technological adjunct to PHP surgery in our institution in Slovenia. We evaluated our one–year experience in IOPTH measurement and compared surgical outcomes after MIP and CNE.

MATERIAL AND METHODS

Eight consecutive patients with sporadic PHP underwent parathyroidectomy, guided by IOPTH measurement, in the Department of Thoracic Surgery at the University Medical Center Maribor between April 2011 and April 2012. Patients' demographic and biochemical characteristics are shown in Table 1.

The diagnosis of PHP was confirmed biochemically by increased serum calcium and PTH levels. PTH levels were monitored with a Cobas E411 analyzer (Hi-

tachi–Roche, Basel, Switzerland). Serum ionised calcium (mmol/L), total calcium (mmol/L), and intact PTH (pg/mL) levels were measured using standard assays. Indications for parathyroidectomy were assessed according to the National Institutes of Health (NIH) criteria for parathyroidectomy (11). Preoperative localising imaging was performed in all patients to identify abnormal parathyroid gland(s). A technetium–99m sestamibi scan was preferably done in combination with neck ultrasound or computed tomography scan. Selection of surgical approach was based on imaging, thyroid pathology, and surgeon preference. We employed two approaches: neck exploration (bilateral or unilateral) through a 4–cm Kocher's incision and minimally invasive parathyroidectomy through a 2–cm lateral incision. The imaging criteria for a focused minimally invasive parathyroidectomy was a single preoperatively localised parathyroid adenoma.

All patients underwent surgery under general anaesthesia. For IOPTH measurement, peripheral arterial blood samples were collected from an arterial line after induction of anaesthesia, at the time of abnormal gland resection, and 10 minutes after its removal. Resected parathyroid glands were sent for frozen section analysis. PTH measurements were disclosed during surgery.

Parathyroidectomy was defined as successful after a >50% decrease in PTH levels from preincision levels in the peripheral arterial blood sample obtained 10 minutes after the removal of the abnormal gland (12).

In the postoperative follow–up period, serum calcium levels were measured within 2 weeks, as well as 1 and 6 months postoperatively. A normal serum calcium level after surgery, and a serum calcium level within the normal range 6 months after surgery were considered to be indicators of surgical success. Persistent hypercalcaemia and elevated PTH levels within the 6 month follow–up period were considered to be a potential operative failure. Potentially recurrent disease was defined as hypercalcaemia and elevated PTH levels identified greater than 6 months after an initially successful surgery.

Table 1: *Demographic and biochemical characteristics of eight consecutive patients with primary hyperparathyroidism.*

Number of patients	**8**
Gender	
Male	1
Female	7
Median age (range)	56 (35–76)
Mean preoperative value (range)*	
Ionised calcium, (mmol/L)	1.85 (1.56–2.20)
Serum calcium (mmol/L)	2.94 (2.62–3.55)
PTH (pg/mL)	516.2 (86.2–2041)

**Normal ranges: ionised calcium, 1.13–1.32 mmol/L; serum calcium, 2.1–2.6 mmol/L; PTH, 15–65 pg/mL.*

RESULTS

During the one–year study period, eight consecutive patients underwent parathyroidectomy for sporadic PHP in our institution. Preoperative imaging demonstrated solitary adenomas in seven patients and a double adenoma in 1 patient. Technetium–99m sestamibi scanning was performed in all patients; this was combined with neck ultrasound in three patients and computed tomography in one patient. Four of the seven patients with preoperative solitary adenomas were selected for MIP through a 2–cm lateral incision. Three patients were scheduled for unilateral exploration through a 4–cm midline incision, owing to concomitant thyroid pathology necessitating unilateral thyroidectomy (one patient) and surgeon preference (two patients). One patient was selected for bilateral exploration through a midline incision secondary to double adenoma. In the series, there were no intraoperative conversions of MIP to unilateral exploration, whereas one unilateral exploration was converted to bilateral because the intraoperative findings were not consistent with preoperative imaging. Therefore, two unilateral and two bilateral neck explorations were performed. There was an additional negative imaging result in a patient with double adenoma, necessitating a more extended exploration. The criterion of a >50% drop in IOPTH was met in all cases. Regarding duration of surgery, we observed a shorter average op-

erating time in MIP (31 minutes) in comparison with neck exploration (69 minutes).

In this series of eight patients, seven solitary (one cystic) and one double adenoma were histologically confirmed. All patients were eucalcaemic with normal PTH levels in the 6 month follow–up period, translating to a surgical success rate of 100%. We observed and treated three cases of symptomatic postoperative hypocalcaemia. Two were transient (lasting from one to four days postoperatively) and occurred after the classic surgical approach with neck exploration. One patient who underwent cystic adenoma resection with unilateral thyroidectomy had prolonged hypocalcaemia (lasting more than 1 month) due to hungry bone syndrome. To date, there have been no recurrences, taking into account that all patients have already completed the 6 month postoperative period. Comparison of the two surgical approaches with treatment success rates is shown in Table 2.

Table 2: *Comparison of the two surgical approaches in patients with primary hyperparathyroidism.*

Surgical approach	MIP*	CNE*
Number of cases	4	4
Mean operating time, min (range)	31 (25–40)	69 (44–112)
Treatment success rate (%)	4 (100%)	4 (100%)
Postoperative hypocalcaemia	0	3 (37.5%)
Recurrence rate	0	0

**MIP, minimally invasive parathyroidectomy; CNE, conventional neck exploration.*

DISCUSSION

In the past two decades, MIP has become the surgical procedure of choice in patients with PHP. This significant change is largely due to improved preoperative localising imaging with both scintigraphy and ultrasound assessment of parathyroid adenomas. The central role of the procedure has the IOPTH measurement that provides biochemical confirmation of hyperfunctioning gland removal (6–8). This is based on the short half–life of PTH, which is approximately 4–8 minutes (13). Regarding these recommendations and trends, we were the first in Slovenia to introduce the method of MIP with IOPTH measurement. Although our patient cohort is small, we thought it prudent to analyse our work during this one–year period in order to evaluate the success of introducing this new approach. We aimed to compare the results of this newly introduced method with the classic method with the results published in the scientific literature.

The surgical approach, techniques, and the protocol for sampling IOPTH levels have been adopted from literature that has been applied in the state–of–the–art medical centres worldwide (2,3,7,8). Our results are comparable and in accordance with global guidelines in the management of hyperparathyroidism.

Our review of our series of eight consecutive patients demonstrated a 100% cure rate in both surgical approaches. This is comparable to data showing that the surgical cure rate after MIP is comparable with CNE (14,15) Our results demonstrate the advantages of IOPTH–guided minimally invasive parathyroidectomy (8).

Compared to CNE, this new surgical technique is safer since surgical trauma is significantly reduced to avoid extensive postoperative scarring of vital neck structures. Subsequent procedures that may be required later (due to conditions involving the thyroid, larynx, oropharyngeal structures, and carotid arteries) become safer.

During MIP, the recurrent laryngeal nerve is not exposed. After performing this technique, there were no signs of laryngeal nerve damage, including temporary hoarseness. Moreover, by using this goal–oriented procedure, injury to the healthy parathyroid glands can be avoided and hormone synthesis continues from the normal glands, as PTH production from adenomas ceases and no microvascular damage is present. Finally, MIP has a superior aesthetic effect, with the majority of our patients being young women.

The main limitations of our intention–to–treat study included a lack of patient randomisation and small sample size, which decreases its relevance. We emphasise that this is a presentation of our initial experience after introducing the new method, which is important for continuing the development of MIP in our country. Our selection of patients was subjective, in order to decrease or avoid altogether the possibility of complications during the introduction of the new method. The presented results and their comparability with those from the scientific literature are an encouragement to continue our work.

Our next challenge is to treat patients with multiple adenomas and parathyroid hyperplasia, which represents approximately 10% of the overall patient population with hyperparathyroidism (16). Improvements in our technique and the future introduction of intraoperative localisation of the hyperfunctional parathyroid using the gamma camera (17) will enable us to preserve our good results. Our next goal is to incorporate this surgical method for the treatment of different parathyroid pathologies.

CONCLUSION

IOPTH measurement proved to be an important technological adjunct avoiding unnecessary additional exploration and potential harm to vital structures, therefore leading us to further develop minimally invasive parathyroid surgery at our institution.

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