Original Article

Surgical Management of Primary Hyperparathyroidism: An Institutional Study on Surgical Quality Control

Nepal B, Singh YP, Pokhrel A, Sayami P, Sayami G[1]

Department of Surgery, Tribhuvan University Teaching Hospital, [1]Department of Pathology, Maharajgunj Medical Campus, Tribhuvan University Teaching Hospital, Kathmandu, Nepal

Correspondence to: Dr. Bikash Nepal

E-mail: bikash.nepal3@gmail.com

Abstract

Introduction: Surgery is key treatment of primary hyperparathyroidism. With the inclusion of serum calcium measurement in routine biochemistry panel, majority of primary hyperparathyroidism can be detected in earlier asymptomatic phase. Preoperative localization by Ultrasonography and Sestamibi scan combined together along with CT or MRI in ectopic adenoma enables for focused minimal invasive surgery. Intraoperative intact PTH (iPTH) measurement is used as a surgical quality control in primary hyperparathyroidism surgery. This study was undertaken to look into current status of surgical management of primary hyperparathyroidism in the tertiary care center in Nepal.

Methods: This was a prospective observational study conducted in Department of Surgery, Tribhuvan University Teaching Hospital Kathmandu, Nepal from November 2014 to October 2016. Demography profile, preoperative symptoms, duration of symptoms, preoperative serum calcium, phosphate, immediate preoperative iPTH level and intraoperative iPTH level, post-operative calcium level and localization techniques were recorded. Final pathology report of each of the patients were recorded.

Results: Thirteen patients were operated for primary hyperthyroidism. Mean age of the patients was 36±15 years. None of the patient had multi-glandular disease on preoperative localization.Mean preoperative Calcium level was 12.8±0.9 mg/dl and mean preoperative iPTH level was 998±805 pg/ml. As Intraoperative iPTH measurement was used to ascertain the successful adenoma removal, mean iPTH intraoperative iPTH after the removal of the adenoma was 175±167 pg/ml. Mean difference of iPTH was 823± 725 (p 0.024). There was mean decrease of 81% of iPTH after surgery well above 50% decrease confirmatory of successful adenoma removal.None of patients had reported with recurrent symptoms till date.

Conclusion: Hypercalcemia should be subjected for iPTH scanning to identify more asymptomatic patients and Surgery is key treatment and intraoperative iPTH assay is used for confirmation of adenoma removal.

Keywords: Hypercalcemia- Primary Hyperprathyroidism-Focused Parathyroidectomy- iPTH monitoring

Introduction

With recent incorporation of serum calcium examination in routine biochemical analysis, there is surge in diagnosis and surgical management of hyperparathyroidism. Primarily hyperparathyroidism comes into the notice and patient usually presents with recurrent renal calculi and on evaluation detected with hypercalcemia. Primary hyperparathyroidism is an endocrine disorder found to have increased parathyroid hormone secretion and most of the time it is a parathyroid adenoma[1]. As solitary adenoma is 80% cause for primary hyperparathyroidism, multi-glandular disease account for 15 % of cases and may be one of the failures of parathyroid adenoma excision surgery[2].Rare cause for primary hyperparathyroidism is Parathyroid Carcinoma which accounts for only 1%[3].

The hyperparathyroidism patient is usually being treated by different multi specialties: cardiologist, urologist and gastroenterologist as symptoms are produced in different body system and then patient is usually investigated for hypercalcemia and finally primary hyperparathyroidism diagnosis is made[4]. Majority of the patients are detected while they are asymptomatic in developed countries due to routine use of biochemical assay whereas majority of patients are symptomatic in developing countries due to constraint in health resources[5]. Modern imaging technique like parathyroid sestamibi scintigraphy and high resolution ultrasonography combined together is commonly used to localize the adenoma. Surgery is the treatment of choice for Primary Hyperparathyroidism. Success depends on adequate preoperative imaging localization and the experienced Surgeon. Two types of Surgery:Conventional Bilateral Neck Exploration and Focused Parathyroidectomy/Minimal invasive parathyroidectomy based on preoperative localization are done[6]. Recently rapid assay of iPTH assay to identify more than 50% fall compared to immediate preoperative value is used as confirmatory of removal of the adenoma. Failure to fall more than 50 % may indicate failure to identify the adenoma or may indicate multiglandular disease[7].Intraoperative assay of intact parathyroid hormone (iPTH) measurement immediately after adenoma removal has been the basis of Surgery quality control and has enabled us to perform focused/ minimal invasive parathyroidectomy.

This study was done to review the current status of surgical management of hyperparathyroidism in one tertiary center Hospital in Nepal.

Methods

This is a prospective observational study conducted in Department of Surgery Tribhuvan University Teaching Hospital Kathmandu, Nepal from November 2014 to October 2016 over a period of two years. Consecutive patients with primary hyperparathyroidism who underwent surgery were included in the study. Demography profile, preoperative symptoms, duration of symptoms, preoperative serum calcium, phosphate, immediate preoperative iPTH level and intraoperative iPTH level, post-operative calcium level were also recorded. Localization method primarily used were high resolution ultrasonography, parathyroid sestamibi scintigraphy both combined together (Figure 1). CT scan of neck and chest were used in two patients were used who had ectopic parathyroid adenoma located in mediastinum (Figure 2). Focused Parathyroidectomy was done in all patients based on image guided localization finding. Preoperative iPTH and intraoperative iPTH assay were compared to measure the success of Surgery. Similarly Preoperative Calcium and postoperative Calcium level was also compared to see the effect of surgery.

Results

Over two years there were thirteen patients operated for primary hyperthyroidism. Mean age of the patients were 36±15 years (ranging from 11-65 years). There were five male patient and eight female patients

Table 1: Clinico-pathologic features of 13 patients with parathyroid adenoma

S. No.	Age (years)	Sex (M/F)	Presentation	Parathyroid scan (pole of thyroid)	Preop- Calcium level (mg/dl)	Preop Phosphorous Level (mg/dl)	Preop iPTH level (pg/ml)	Intraop iPTH level (pg/ml)	Parathyroid adenoma size (cmxcm)
1	20	M	Renal calculi	Left lower	13.7	2.3	544	112.2	1.5x1
2	32	F	Flank pain with nephrocalcinosis	Right lower	12.5	2.1	168	34.2	2x1
3	22	F	Recurrent renal calculi with history of B/L PCNL	Right lower	12.6	2.4	659	66.8	1.5x1
4	65	F	Acute Renal Failure with Pneumonia	Left Lower	12.5	2.3	3458	220	2x1
5	48	F	Neck Nodule	Left Lower	13.5	2.2	456	540	2x1.5
6	39	F	Renal calculi & Nephrocalcinosis	Left Lower	12.6	2.1	1570	120	1x1
7	21	M	Bony Deformity	Mediastinum	12.6	2.3	1450	240	1.5x1
8	46	M	Intertochanteric Fracture	Left Lower	13.2	2.1	1640	340	2x1
9	29	F	Renal Calculi	Left Lower	11.5	2.3	167	43	1x1
10	42	M	Neck Nodule	Right Lower	12.2	2.3	325	89	2x1
11	36	M	Renal Calculi	Mediastinum	12.3	2.2	435	120	1x1
12	11	F	Renal calculi	Left inferior	12.4	2.1	165	30	1x1
13	58	F	Bone fracture	Left Inferior	12.6	2.2	1990	135	3x3

None of the patient had multi-glandular disease on preoperative localization. Majority of the patients presented with renal stone disease, seven presented with renal symptoms whereas three presented with bony symptoms, other two presented with neck nodule and one patient presented with pneumonia with acute renal failure. Two patients had ectopic parathyroid adenoma located in mediastinum. Eight patients had parathyroid adenoma located in left inferior pole whereas other three had location in right inferior pole. So all patients underwent focused parathyroidectomy. (Table 1)

Mean preoperative Calcium level was 12.8±0.9 mg/dl and mean preoperative iPTH level was 998±805 pg/ml. As Intraoperative iPTH measurement was used to ascertain the successful adenoma removal, mean iPTH intraoperative iPTH after the removal of the adenoma was 175±167 pg/ml. Mean difference of iPTH was 823± 725 (p 0.024). There was mean decrease of 81% of iPTH after surgery well above 50% decrease confirmatory of successful adenoma removal. Additionally post operative calcium level was also reduced mean postoperative calcium level was 9.2±1.1 mg/dl despite calcium and vitamin D supplementation suggesting the evidence of hungry bone syndrome indicating successful parathyroid surgery. (Table 2)

As two patients had mediastinal adenoma underwent successful minimal invasive surgery, video assisted thoracoscopic removal of parathyroid adenoma. All patients had parathyroid adenoma on final histopathology examination (Figure 3 & 4). None of patients had reported with recurrent symptoms till date.

Table 2: Base line characteristics of 13 patients

Pre-operative mean values	Post-operative
Age in years	36±15
Sex Male/Female	5/8
Pre-operative PTH level pg/ml	998±805
Preoperative Ca level mg/dl	12.8±0.9
Preoperative P level mg/dl	2.3±0.6
Post operative Ca level mg/dl	9.2±1.1
Post operative P level mg/dl	3.2±0.8
Intra operative PTH level pg/ml	175±167

Discussion

Surgical management of primary hyperparathyroidism is poorly reportedentity in Nepal. This study of two years period with thirteenpatients is an attempt to reflect the work on parathyroid surgery in a tertiary care center of the country. Primary hyperthyroidism is more common in elderly patient (age more than 55 years with male:female ratio being 2-3:1[8]. Having small sample size we donot have the same report as mean age of the patient was 36 years and more of the patients were female. Over the years there has been paradigm shift of presentation of primary hyperparathyroidism. In older days patient was diagnosed after having florid disease presentation whereas more of the patients are detected during asymptomatic phase in developed world because of frequent biochemical examination for most of the population[9]. In developing country still many patients are diagnosed only when they are symptomatic as in our study all patients were diagnosed only when they were symptomatic as most of the patients had renal calculi and were being treated for multiple calculi. Several report suggest that nephrocalcinosis with nephrolithiasis is most common symptom in symptomatic hyperparathyroidism[10].

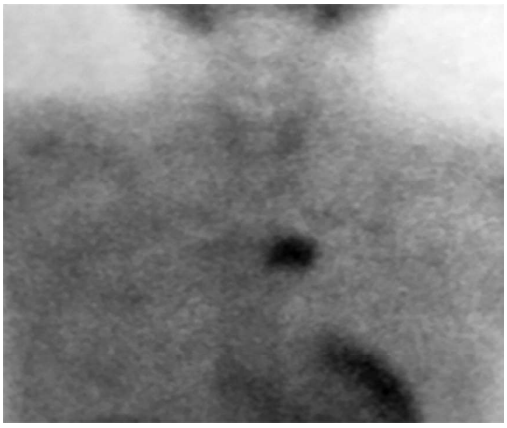

Figure 1 Mediastinal Parathyroid Adenoma on Sestamibi Scan

Hypercalcemia with symptomatic patient is generally initial lead point for the diagnosis of primary hyperparathyroidism. Intact Parathyroid adenoma is measured to confirm hyperparathyroidism exclusively[11]. The mean iPTH in our study was 998 and all patients had high iPTH. Localization is an important management issue in primary hyperthyroidism which enables us to perform focused parahtyroidectomy. Preoperative localization by imaging techniques Ultrasonography and Parathyroid adenoma scan, both combined has been very effective tool to identify whether the patient has single adenoma or multiglandular disease[12]. Ultrasonography was used in all cases to localize the adenoma which became successful to localize the adenoma, eight in left lower thyroid pole and three in right inferior thyroid pole. But, Ultrasonography could not visualize the adenoma in two cases. Subsequently Parathyroid Sestamibi scan was performed in all cases, which localized the adenoma of remaining two cases in superior mediastinum and confirmed the same location in previous eleven cases. Subsequently Mediastinal Parathyroid adenomas were further confirmed by CT Scan. So,two combined techniques were used in this study to confirm the parathyroid adenoma location.

Figure 2 Mediastinal adenoma on CT scan

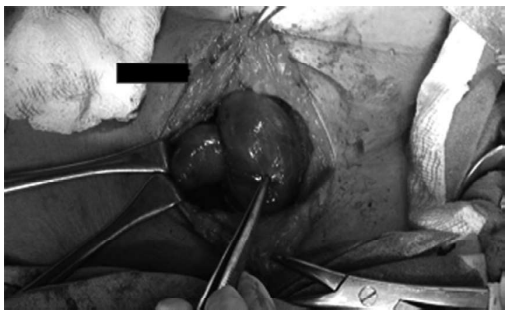

Figure 3 Parathyroid adenoma

Focused Parathyroid adenoma excision was performed on all cases based upon preoperative localization. Video assisted thoracoscopic removal was performed in two cases of mediastinal parathyroid adenoma. Median half-life of iPTH is known to be 3 minute 9 seconds[13]. This

short half-life of iPTH has allowed the intra operative quality control of parathyroid adenoma excision surgery. Intraoperative iPTH measurement after 10 minutes of adenoma excision with more than 50% drop in iPTH compared to immediate preoperative value is confirmatory of curative surgery. This has provided a strong foot hold on minimal invasive surgery in parathyroid adenoma with the benefit of small cosmetic scar with no risk of permanent hypoparathyroidism and early ambulation and earlier discharge[14]. In this study there was mean drop of 84% iPTH after adenoma removal quite suggestive of successful surgery.

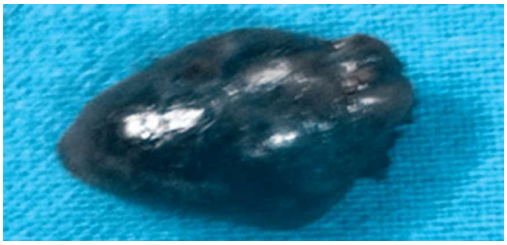

Figure 4 Parathyroid adenoma specimen

Mediastinal Parathyroid adenoma is due to aberrant migration of inferior parathyroid. Mediastinal parathyroid adenoma incidence ranges from 6-20% in several reported series[15]. Incidence of mediastinal parathyroid adenoma was 18% (2/11). Unlike Parathyroid adenoma ultrasonography is useless in identifying mediastinal parathyroid. Technitium sestamibi scan usually localize the mediastinal adenoma; CT or MRI is required to visualize the exact anatomical location[16]. In this study Technetium Sestamibi scan was able to localize after ultrasonography failed to localize and further CT scan neck and chest was used to visualize the anatomy. Minimal invasive surgery, video assisted thoracoscopy was done to remove the mediastinal adenoma. All patients had successful removal of adenoma documented by histopathology report as all reports showed parathyroid adenoma. None of the patients had recurrence till date.

Conclusion

Hypercalcemia should be subjected for iPTH scanning to identify more asymptomatic patients and Surgery is key treatment and intraoperative iPTH assay is used for confirmation of adenoma removal.

Conflict of interest: None declared

Reference

1. Morks AN, Van Ginhoven TM, Pekelharing JM et al. Intra-operative parathyroid hormone measurements Experience of a non-academic hospital. S Afr J Surg 2011; 49: 123–127.
2. Molinari AS, Irvin GL, Deriso GT, Bott L. Incidence of multiglandular disease in primary hyperparathyroidism determined by parathyroid hormone secretion. Surgery 1996; 120: 934–936
3. Sharretts JM, Kebebew E, Simonds WF. Parathyroid cancer. Semin Oncol 2010;37:580-90.
4. Pyram R, Mahajan G and Gliwa A. Primary hyperparathyroidism: Skeletal and non-skeletal effects, diagnosis and management. Maturitas 2011; 70: 246-255
5. Bilezikian JP, Silverberg SJ. Clinical practice. Asymptomatic primary hyperparathyroidism. N Engl J Med 2004; 350: 1746-51.
6. Fraker DL, Harsono H, Lewis R. Minimally invasive parathyroidectomy: benefits and requirements of localization, diagnosis, and intraoperative PTH monitoring.Long-term results. World J Surg 2009; 33: 2,256–2,265
7. Ypsilantis E, Charfare H, Wassif WS.Intraoperative PTH assay during minimally invasive parathyroidectomy May Be helpful in the detection of double adenomas and May minimise the risk of recurrent surgery. Int J Endocrinol 2010,2010:178671
8. Bilezikian JP, Silverberg SJ. Clinical Practice Asymptomatic Primary Hyperthyroidism. N Engl J Med. 2004; 350: 1746-1751.
9. Pallan S, Rahman MO, Khan AA. Diagnosis and management of hyperthyroidism BMJ; 2012; 344 e 1013.
10. Silverberg SJ, Clarke BL, Peacock M, Current issue in the presentation of asymptomatic hyperparathyroidism. J Clin Endocrinol Metab. 2014; 380-94.
11. Bandeira F,Griz L et al. Diagnosis and Management of Primary Hyperparathyroidism. Arq Bras Endocrnol Metab. 2013; 57: 406-24
12. Agcagiu O. Aliyev S,Heiden K, Neumann D, Milas M, Mitchell J,et al. A new classification of positive sestamibi and ultrasound scans in parathyroid localization. World J Surg. 2012;36:2516-21
13. Vieira JGH, Kunil IS, Nishnida SR. Evolution of PTH assays. Bras Endocrinol Metab. 2006;50:621-27
14. Udelsman R. Six hundred fifty-six consecutive explorations for primary hyperparathyroidism. Ann Surg 2002;235:665-70
15. Moran CA, Suster S. Primary parathyroid tumors of the mediastinum. Am J Clin Pathol 2005; 124: 749-754.
16. Moka D, Voth E, Dietlein M et al. Tecnetium 99m-MIB: a higly sensitive diagnostic tool for localization of parathyroid adenomas. Surgery 2000; 128: 29-35.