

Predictors of early post –operative
hypocalcemia after total parathyroidectomy in
renal failure patients with secondary
hyperparathyroidism

By

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MD (USM)

Dissertation Submitted In
Partial Fulfillment Of The Requirement For
The Degree Of Master Of Medicine
(General Surgery)



UNIVERSITI SAINS MALAYSIA

2017

II. ACKNOWLEDGEMENTS

I would like to take this opportunity to extend my upmost appreciations and gratitude to those who have helped me in many ways throughout the process of my dissertation.

- My dissertation supervisor, Dr Andee Dzulkarnaen Bin Zakaria, Department of Surgery, School of Medical Science, UNIVERSITI SAINS MALAYSIA for his continuous feedbacks and advices in this study.
- My co-supervisor, Dato Dr Imisairi A. Hadi, consultant and surgeon of Breast and Endocrine Unit, Department of Surgery, Hospital Raja Perempuan Zainab II (HRPZII) for his suggestion of this topic and his guidance and supervision for my research.
- To all the staff nurses in surgical outpatient department, Hospital Raja Perempuan Zainab II, especially staff nurse Ong Guat Yen for her dedicated support in record tracing and data handling.
- To Miss Nazmi Liana from Clinical research center Hospital Raja Perempuan Zainab II for helping me in constructing an appropriate study design and performing data analysis.
- My lovely wife, Chan Li Shih for her endless support and continuous encouragement in ensuring the completion of this study
- To my adorable Son, Armstrong Tan Berlin for the joy he bring to my family and as the driving force for completion of this study.

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IV. ABSTRACT IN BAHASA MALAYSIA

Pengenalan

Hiperparatiroidisme sekunder merupakan satu penyakit yang sentiasa berlaku di kalangan pesakit buah pinggang dan ianya mempunyai simptom klinik yang berlainan. ‘Total parathyroidectomy’ merupakan pembedahan terbaik untuk keadaan sebegini. Di antara komplikasi-komplikasi yang sentiasa berlaku selepas pembedahan ini ialah hipokalsiumia di kalangan pesakit yang menjalani pembedahan tersebut.

Objektif

Kajian ini untuk mengenalpasti faktor-faktor ramalan untuk meramal golongan pesakit yang akan menghadapi masalah hipokalsiumia selepas pembedahan. Objektif kedua adalah untuk mengenalpasti tanda-tanda hyperparathyroidism sekunder di kalangan pesakit buah pinggang.

Kaedah

Rekod pesakit buah pinggang yang menghadapi masalah hiperparatiroidisme sekunder yang menjalani pembedahan ‘total parathyroidectomy’ dari 1st Januari 2007 sehingga 31st Desember 2014 akan dikaji. Pesakit yang terlibat akan dibahagikan kepada 2 kumpulan berdasarkan tahap kalsium dalam darah didalam 24 jam pertama selepas pembedahan. Kumpulan hipokalsiumia (25 pesakit) dengan tahap kalsium 2mmol/L dan kurang daripada 2mmol/L: Kumpulan kalsium normal (43 pesakit) dengan tahap kalsium lebih dari 2mmol/L. Faktor-faktor berkaitan seperti umur, jantina, tempoh buah pinggang rosak, keputusan darah sebelum operation seperti tahap kalsium,

tahap fosfat, tahap 'alkaline phosphatase', tahap 'albumin', tahap 'creatinine' dan tahap paratiroid hormone akan dikaji dan dianalisis untuk mengenalpasti faktor ramalan bagi golongan pesakit yang berkecenderungan menghadapi komplikasi hipokalsiumia selepas pembedahan. Tanda-tanda hiperparatiroidisme sekunder di kalangan pesakit akan direkodkan.

Keputusan

Analisis logistik regresi pelbagai menunjukkan tahap 'alkaline phosphatase' sebelum pembedahan ialah faktor ramalan berlakunya hipokalsiumia selepas pembedahan 'total parathyroidectomy' dengan nisbah ganjil 1.004. Kebanyakan pesakit yang menjalani pembedahan adalah golongan yang mempunyai tanda-tanda hiperparatiroidisme dengan 73% pesakit menghadapi masalah sakit tulang and 21% pesakit menghadapi masalah lemah tubuh. Dua puluh lima pesakit (37%) menghadapi masalah hipokalsiumia selepas pembedahan "total parathyroidectomy".

Kesimpulan

Tahap alkaline phosphatase sebelum pembedahan berkaitan rapat dengan kebarangkalian berlakunya komplikasi hipokalsiumia selepas pembedahan di kalangan pesakit hipertiroidisme sekunder. Pesakit yang mempunyai tahap alkaline phosphatase yang tinggi sebelum pembedahan seharusnya dipantau dengan lebih teliti dan menerima rawatan rapi pada fasa awal selepas pembedahan .

V. ABSTRACT IN ENGLISH

Background:

Secondary Hyperparathyroidism (SHPT) in renal failure patients are common and had different clinical presentations. Total parathyroidectomy is the surgery of choice in this group of patient. Hypocalcaemia or even hungry bone syndrome are well known and is one of the serious complication in post-parathyroidectomy patient. The objectives of this study are to identify the predictors of early post-operative hypocalcaemia after total parathyroidectomy as well as the clinical presentations of secondary hyperparathyroidism in renal failure patient.

Methods:

Renal failure patient with secondary hyperparathyroidism who had underwent total parathyroidectomy in between 1st January 2007 till 31st December 2014 were retrospectively reviewed. The patients were divided into 2 groups according to their serum calcium level within 24 hours post surgery: the Hypocalcaemia group (25 patients) with post-operative serum calcium level of 2mmol/L or less, and the normocalcaemia group (43 patients), with the post-operative serum calcium level more than 2mmol/L. Patient details (age, gender and duration of renal failure) and pre-operative blood investigations (preoperative serum calcium level , phosphorus level, alkaline phosphatase level ,serum albumin, serum intact parathyroid hormone and creatinine level) were analyzed in order to identify the predictor for early post-operative hypocalcaemia. The clinical presentations of secondary hyperparathyroidism in renal failure patient have also recorded.

Results:

By using multiple logistic regression analysis, alkaline phosphatase (ALP) has predictive value for early post operative hypocalcaemia with adjusted Odd ratio 1.004. Most of the patient who underwent surgery is symptomatic pre-operatively and the common presentations were bone pain (73%) and muscle weakness (21%). Hypocalcaemia is common in renal hyperparathyroidism patient post total parathyroidectomy. Up to 37% of our patient suffered from this post op complication.

Conclusion:

In conclusion, preoperative serum alkaline phosphatase correlate positively with the development of early post-operative hypocalcaemia so patient with high pre-operative alkaline phosphatase should be monitored more closely in the early post operative period.

Keywords: *Renal failure, secondary hyperparathyroidism, parathyroidectomy, hypocalcaemia, hungry bone syndrome*

1-INTRODUCTION

1.1- INTRODUCTION

Hyperparathyroidism is a disease characterized by elevated serum calcium and inappropriate elevated parathyroid hormone (PTH) level. Prevalence for hyperparathyroidism is around 0.3% in general population.(1)

There are 3 type of hyperparathyroidism -primary, secondary and tertiary. Secondary hyperparathyroidism (SHPT) refers to excessive secretion of parathyroid hormone in response to hypocalcaemia and associated hyperplasia of the parathyroid glands. SHPT will enhance vascular calcification with increased cardiovascular mortality.

Chronic renal failure, hypermagnesiumia, osteoporosis and osteomalacia/ ricket can cause SHPT. By far the most common cause of SHPT is chronic renal failure but its clinical effects were not well elucidated until recently. Chronic renal failure or stage 5 chronic kidney disease is defined as glomerular filtration rate (GFR) less then 15ml/min/1.73m² or requiring dialysis. Chronic renal failure patient with SHPT have variant presentation, range from completely asymptomatic to severe bone pain and pruritus. Patient also may present with osseous lesion such as fracture, growth retardation and osteitis cystica.

Pathogenesis of secondary hyperparathyroidism is complex, involving every aspect of renal failure from the decreased synthesis function to metabolic abnormalities to even treatment of renal failure that can contribute to it. Factors that lead to hypertrophy and hyperplasia transformation of the parathyroid gland with subsequent elevation of PTH in an attempt to normalized serum calcium level are:

- Hyperphosphatemia and hypocalcemia
- Reduce renal 1-alpha hydroxylase and calcitriol
- Bony resistance to PTH (if excessive PTH)
- Change in PTH set point (rise in set point)
- Aluminium intoxication

Initial treatment for SHPT is medical treatment with the aim to bringing the serum calcium and phosphate to a physiological level to prevent overstimulation of parathyroid glands and hence over production of parathyroid hormone. Medical therapy includes calcium supplement, vitamin D supplement, phosphate-poor diets, aluminium-binding agents, haemodialysis with calcium enriched dialysate and calcimimetic agent eg, Cinacalcet. Surgical therapy for secondary hyperparathyroidism includes renal transplant (definite therapy) and operative parathyroidectomy.

Despite the advent of the new therapeutic agents, patient with long term SHPT secondary to renal failure often require parathyroidectomy. Rate of parathyroidectomy has not changed significantly for the past 20 years despite the introduction of new medical therapy agents. Parathyroidectomy is indicated in patients who failed medical treatment, patients with intractable bone pain/pruritus, fracture and patients with symptomatic ectopic calcification

Hypocalcaemia or even hungry bone syndrome are well known and serious complication post-parathyroidectomy, but not all patient will develop this complication. So it will be very helpful and clinically significant if we can identify which patient is more prone to develop post operative hypocalcaemia/hungry bone syndrome in order to monitor them more closely during the early post-operative period. In this study, we

sought to identify the risk factors for developing early post-operative hypocalcaemia after total parathyroidectomy for secondary hyperparathyroidism.

1.2- LITERATURE REVIEW

According to *21st REPORT OF THE MALAYSIAN DIALYSIS AND TRANSPLANT REGISTRY 2013*, the number of new dialysis patients showed a linear increase over the last 10 years from 2901 patients in 2004 to 6541 patients in 2012 and at least 6222 patients in 2013. The number of prevalent dialysis patients showed a steeper linear almost 12 thousand in 2004 to about 32 thousand in 2013. (2)

Renal failure is associated with severe secondary hyperparathyroidism in majority of patient. Parathyroidectomy has an important role in the treatment of secondary hyperparathyroidism that is refractory to medical treatment. Post operative hypocalcemia is a well know and important complication after parathyroidectomy. (3, 4)

Despite the advent of new therapeutic agents, patient with secondary hyperparathyroidism often required parathyroidectomy. Rate of parathyroidectomy did not change significantly between 1991 and 2001 despite progression in medical therapy with phosphate binder and vitamin D analogue. Overall parathyroidectomy is required in about 20% of patient after 3 to 10 years of dialysis and up to 40 % after 20 years. (5-7)

Subtotal parathyroidectomy(SPTX) and total thyroidectomy with autotransplantation (TPTX +AT) was consider as standard surgical procedures for hyperparathyroidism before this . But due to it higher recurrence rate, some author recommend total parathyroidectomy without autoimplantation (TPXT) as the standard procedure nowadays. (7)

Recurrence rate of different parathyroidectomy approach:

- SPTX → 12%
- TPXT+ AT → 10%
- TPXT → 4%

Shih MI et al concluded that total parathyroidectomy without autoimplantation for secondary hyperparathyroidism is the option for treating patient with symptomatic secondary hyperparathyroidism who are not expected to receive kidney transplantation. In his study, 94 patients were assigned to 2 groups (44 patients in TPTX group, 50 patient in SPTX group) and recurrent rate was recorded. Recurrence rate over 60 months post op were significantly lower in TPTX group compare with SPTX group (4.5% Vs 18% respectively with p-value 0.028). There was no significant difference in term of post operative complication and symptom relief rate. (8)

Incidence of post-operative hypocalcaemia among patients with primary hyperparathyroidism underwent parathyroidectomy has been reported to be 10 to 46% and among patient with secondary hyperparathyroidism has been reported to be up to 95%. Patient with secondary hyperparathyroidism develop more profound post-operative hypocalcaemia so pre-operative predictor of hypocalcemia is particular important for postoperative management in patient with secondary hyperparathyroidism. (9)

Many previous studies evaluating the predictor of postoperative hypocalcemia in patient with primary hyperparathyroidism, but there are limited data regarding predictors for secondary hyperparathyroidism. A regional study conducted by Loke SC et al.(10) involved 2 tertiary institutions (Tan Tock Seng Hospital Singapore and Kuala Lumpur General Hospital) show strong relationship between ALP and post operative hypocalcaemia in patients with primary hyperparathyroidism. Loke SC at al also recommended that pre-operative ALP to be used to complement clinical protocol for post –operative hypocalcemia management in parathyroidectomy patient. (10)

A study by Hamouda et al.(11) which involved 76 patients in Arab Saudi try to identify the risk factors for developing early post-operative hypocalcemia after parathyroidectomy for secondary hyperparathyroidism. In that study, Hamouda concluded that age, level of pre-operative calcium, alkaline phosphatase and serum albumin correlated with early post-operative hypocalcaemia. (11)

Hypocalcaemia or even hungry bone syndrome are well known and serious complication in patient post-parathyroidectomy especially in patient with secondary hyperparathyroidism, so it is clinically useful if we can identify some mean that reliably predicting it occurrence so that necessary preventive protocol can be devised in the future.

1.3 - RATIONALE FOR THE STUDY

Prevalence for Secondary hyperparathyroidism is increasing nowadays because number of patient with renal failure increased over the year in Malaysia.(12) To the best of our knowledge, there is no local study was done to identify risk factors for developing post operative hypocalcemia in patients with secondary hyperparathyroidism. As the consequences of post operative hypocalcemia are potentially serious, it is clinically useful if we can identify some mean that reliably predicting it occurrence so that necessary preventive protocol can be devised and reduced the incidence of post-operative hypocalcaemia.

2-STUDY PROTOCOL

2.1- DOCUMENT SUBMITTED FOR ETHICAL APPROVAL

Predictors of early post –operative hypocalcemia after total parathyroidectomy in renal failure patient with secondary hyperparathyroidism

NMRR-16-250-29616(IIR)

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Introduction

Hyperparathyroidism is a disease characterized by elevated serum calcium and inappropriate elevated parathyroid hormone (PTH) level. Prevalence for hyperparathyroidism is around 0.3% in general population.(1)

There are 3 type of hyperparathyroidism -Primary, Secondary and Tertiary. Secondary hyperparathyroidism (SHPT) refers to excessive secretion of parathyroid hormone in response to hypocalcaemia and associated hyperplasia of the parathyroid glands. SHPT will enhance vascular calcification with increased cardiovascular mortality.

Chronic renal failure, hypermagnesiumia, osteoporosis and osteomalacia/ ricket can cause SHPT. By far the most common cause of SHPT is chronic renal failure but its clinical effects were not well elucidated until recently. Chronic renal failure or stage 5 chronic kidney disease is defined as glomerular filtration rate (GFR) less then 15ml/min/1.73m² or required dialysis. Chronic renal failure patient with SPTH have variant presentation, range from completely asymptomatic to severe bone pain and pruritus. Patient also may present with osseous lesion such as fracture, growth retardation and osteitis cystica.

Pathogenesis of secondary hyperparathyroidism is complex, every aspect of renal failure from the decreased synthesis function to metabolic abnormalities to even treatment of renal failure contribute to it. Factors that lead to hypertrophy and hyperplasia transformation of the parathyroid gland with subsequent elevation of PTH in an attempt to normalized serum calcium level such as:

- Hyperphosphatamia and hypocalcemia
- Reduce renal 1-alpha hydroxylase and calcitriol

- Bony resistance to PTH (if excessive PTH)
- Change in PTH set point (rise in set point)
- Aluminium intoxication

Initial treatment for SHPT is medical treatment with the aim to bringing the serum calcium and phosphate to a physiological level to prevent overstimulation of parathyroid glands and hence over production of parathyroid hormone. Medical therapy includes calcium supplement, vitamin D supplement, phosphate-poor diets, aluminium-binding agents, haemodialysis with calcium enriched dialysate and calcimimetic agent eg, Cinacalcet. Surgical therapy for secondary hyperparathyroidism includes renal transplant (definite therapy) and operative Parathyroidectomy.

Despite the advent of the new therapeutic agents, patient with long term SHPT secondary to renal failure often require parathyroidectomy. Rate of parathyroidectomy did not change significantly for the past 20 years despite the introduction of new medical therapy agents. Parathyroidectomy is indicated in patient who failed medical treatment, patient with intractable bone pain/pruritus, fracture and patient with symptomatic ectopic calcification.

Hypocalcaemia or even hungry bone syndrome are well known and serious complication post-parathyroidectomy, but not all patient will develop this complication. So it will be very helpful and clinically significant if we can identify which patient is more prone to develop post operative hypocalcaemia/hungry bone syndrome.

Rationale of this study

- Prevalence for secondary hyperparathyroidism is increasing nowadays because patient with Renal failure patient increased over the year.(12)
- No local study was done regarding risk factors for developing post operative hypocalcemia in secondary hyperparathyroidism.
- As the consequences of post operative hypocalcemia are potentially serious, it is clinically useful if we can identify some mean that reliably predicting it occurrence so that necessary preventive protocol can be devised.

Objective of study

- To study the possible predictors of early post-operative hypocalcemia after parathyroidectomy and the clinical presentation of secondary hyperparathyroidism in renal failure patient.

Specific objective

- To identify the predictors for developing early post-operative hypocalcemia after parathyroidectomy for secondary hyperparathyroidism in renal failure patients.
- To determine the common clinical presentation of secondary hyperparathyroidism.

Research questions

- Is there any factors (demographic or clinical) that can be use as predictors of early post-operative hypocalcemia after parathyroidectomy.
- What is the common clinical presentation in patients with secondary hyperparathyroidism.

Research hypothesis

- Ho- Age, gender, clinical symptoms, length of dialysis, pre-operative blood investigation and are not associated with post-operative hypocalcemia after parathyroidectomy for secondary hyperparathyroidism.
- HA- Age, gender , clinical symptom, length of dialysis, pre-operative blood investigation are associated with post-operative hypocalcemia after parathyroidectomy for secondary hyperparathyroidism.

Literatures Review

There is a linear increase of new dialysis patients over the last 10 years from 2901 patients in year 2004 to 6541 patients in year 2012. The number of prevalent dialysis patients showed a steeper linear increment at almost 12 thousand patients in 2004 to 32 thousand patients in 2013. (2)

Renal failure is associated with severe secondary hyperparathyroidism in majority of patient. Parathyroidectomy has an important role in the treatment of secondary hyperparathyroidism that is refractory to medical treatment. Post operative hypocalcemia is a well know and important complication after parathyroidectomy. (3, 4)

Despite the advent of new therapeutic agents, patient with secondary hyperparathyroidism often required parathyroidectomy. Rate of parathyroidectomy did not change significantly between 1991 and 2001 despite progression in medical therapy with phosphate binder and vitamin D analogue. Overall parathyroidectomy is required in about 20% of patient after 3 to 10 years of dialysis and up to 40 % after 20 years. (5-7)

Subtotal parathyroidectomy(SPTX) and total thyroidectomy with autotransplantation (TPTX +AT) was consider as standard surgical procedures for hyperparathyroidism before this . But due to it higher recurrence rate, some author recommend total parathyroidectomy without autoimplantation (TPXT) as the standard procedure nowadays. (7)

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Incidence of post-operative hypocalcaemia among patients with primary hyperparathyroidism underwent parathyroidectomy has been reported to be 10 to 46% and among patient with secondary hyperparathyroidism has been reported to be up to 95%. Patient with secondary hyperparathyroidism develop more profound post-operative hypocalcaemia so pre-operative predictor of hypocalcemia is particular important for postoperative management in patient with secondary hyperparathyroidism. (9)

Many previous studies evaluating the predictor of postoperative hypocalcemia in patient with primary hyperparathyroidism, but there are limited data regarding predictors for secondary hyperparathyroidism. A regional study conducted by Loke SC et al.(10) involved 2 tertiary institutions (Tan Tock Seng Hospital Singapore and Kuala Lumpur General Hospital) show strong relationship between ALP and post operative hypocalcaemia in patients with primary hyperparathyroidism. Loke SC at al also recommended that pre-operative ALP to be used to complement clinical protocol for post –operative hypocalcemia management in parathyroidectomy patient. (10)

A study by Hamouda et al which involved 76 patients in Arab Saudi try to identify the risk factors for developing early post-operative hypocalcemia after parathyroidectomy for secondary hyperparathyroidism. In that study, Hamouda concluded that age, level of pre-operative calcium, alkaline phosphatase and serum albumin correlated with early post-operative hypocalcaemia. (11)

Hypocalcemia or even hungry bone syndrome are well known and serious complication in patient post-parathyroidectomy especially in patient with secondary hyperparathyroidism, so it is clinically useful if we can identify some mean that reliably predicting it occurrence so that necessary preventive protocol can be devised in the future.

Methodology

Research design

This is a retrospective study involving patients with secondary hyperparathyroidism that underwent parathyroidectomy in Hospital Raja Perempuan Zainab II from 1st January 2007 to 31st December 2014.

Source population

The study includes all renal failure patients with secondary hyperparathyroidism who underwent parathyroidectomy from 1st January 2007 to 31st December 2014 in Hospital Raja Perempuan Zainab II. The list of patients who underwent parathyroidectomies will be traced from the record in the operation theater. The data collection will be started after ethical approval.

Sampling frame

All patients that fulfilled the inclusion and exclusion criteria will be recruited

- Inclusion criteria:
 - All renal failure patients with secondary hyperparathyroidism who underwent total parathyroidectomy during the duration of study.
- Exclusion criteria:
 - Patients with renal hyperparathyroidism who underwent parathyroidectomy with incomplete data or missing data
 - Patient younger than 16 years old was excluded (have higher physiological alkaline phosphatase level)

Sampling methods

Convenient sampling

Sample size calculation

Sample size for research question

Sample size calculations were performed using PS software. “Studies that are analyzed by t-test with independent design” were chosen.

1. Associated factor : Age

δ = expected detectable difference between two groups

σ = standard deviation of either group

$\alpha = 0.05$ Power of study = 80% n = required sample size

m = ratio of patients of hypocalcaemia to normo-calcaemia(1 : 1)

Torer et.al¹ reported the mean age of patients in the hypocalcaemia group are

younger than those in the normo-calcaemia group (36.0 \pm 9.7 versus 49.2 \pm 13.2,p=0.006)

$\sigma = 9.7$ $\delta = 13$

Result of sample size calculation show that we will need 10 subjects for each group.

Utilizing 10% for drop out, the minimum sample size for each group is 11 subjects (which is equivalent with 22 subjects for the whole study).

2. Associated factor : pre operative Calcium level

δ = expected detectable difference between two groups

σ = standard deviation of either group

$\alpha = 0.05$ Power of study = 80% n = required sample size

m = ratio of patients of hypocalcaemia to Normo-calcaemia(1 : 1)

Torer et.al¹ reported the pre-operative Ca level (≤ 2.0 mmol) of patients in the

hypocalcaemia group developed hypocalcaemia compared to normo-calcaemia group

during post operative (9.6 ± 0.7 versus 10.4 ± 1.1 , $p=0.01$)

$\sigma = 0.7$ $\delta = 0.8$

Result of sample size calculation show that we will need 13 subjects for each group.

Utilizing 10% for drop out, the minimum sample size for each group is 15 subjects

(which is equivalent with 30 subjects for the whole study).

3. Associated factor : ALP

δ = expected detectable difference between two groups

σ = standard deviation of either group

$\alpha = 0.05$ Power of study = 80% n = required sample size

m = ratio of patients of hypocalcaemia to normo-calcaemia(1 : 1)

Hamouda et al reported the mean and SD pre-operative ALP level for

both group is 1100 ± 112 , $\sigma = 112$ $\delta = 100$

Result of sample size calculation show that we will need 21 subjects for each group.

Utilizing 10% for drop out, the minimum sample size for each group is 24 subjects (which is equivalent with 48 subjects for the whole study).

4. Associated factor : Albumin

δ = expected detectable difference between two groups

σ = standard deviation of either group

$\alpha = 0.05$ Power of study = 80% n = required sample size

m = ratio of patients of hypocalcaemia to normo-calcaemia(1 : 1)

Hamouda et.al² reported the mean and SD pre-operative Albumin level for

both groups is 37.2 ± 2.58

$\sigma = 2.58$ $\delta = 2.1$

Result of sample size calculation show that we will need 25 subjects for each group.

Utilizing 10% for drop out, the minimum sample size for each group is 28 subjects

(which is equivalent with 56 subjects for the whole study).

The highest sample size calculation will be chosen for the study. In this case, the total sample size required for both groups will be 56 subjects (28 subjects for each arm).

Study Conduct

- After ethical approval, a list of patients who underwent parathyroidectomy in between January 2007 to December 2014 will be obtained from the record in the operation theater Hospital Raja Perempuan Zainab II.
- Patients who fulfill the inclusion and exclusion criteria will be recruited in the study.
- The data of patients will be obtained by retrospective study of patients' medical records. The data will be entered in a data collection form (Appendix 1)
- Clinical and biochemical parameters of eligible subjects will be recorded using a pre-tested data collection form. The variables of interest are age, gender, ethnicity, duration of dialysis, main complaint, occurrence of renal hyperparathyroidism, pre- and post-operative blood investigation, post-operative calcium level as well as operative information.
- Patients will be divided into two groups based on the post operative calcium level within 24 hour according to the definition proposed by Hamouda et al.
 - Normocalcemia (more than 2mmol/L) and
 - Hypocalcemia (2mmol/L or <2mmol/L) group.
- Data analysis using SPSS software. All results are expressed as mean value, standard deviation and percentage.
- P-value less than 5% were accepted to be significant
- Univariate statistical tests using simple logistic regression will be performed and P-value less then 5% will be accepted to be significant. Multivariate stepwise logistic regression will be use to identify predictive factors of early hypocalcemia

Privacy and confidentiality

Personal information and data will not be disclosed unless required by law. Subject's confidentiality will be protected, no name or identifiable information will be collected. The data collection form will have serial numbers instead of names of the subjects to prevent recognition.

Data will be protected through password setting to access the database and securely locked. The data is only accessible by researchers involve in this study. The data will be used and remain directly available up to completion of the study. Thereafter, the data will be compressed with encryption and archived in a flash drive after proper documentation. This is to destroyed by formatting the flash drive after a 3-years maintenance period determined by the date of its formal closure. We define the formal closure as the submission of a closure report to the National Medical Research Registry of Malaysia.

Subject's data and information will be kept confidential and will be known by research team only. Only aggregated (grouped) results will be presented and submitted to local or international peer-reviewed medical journals and relevant government ministries.

Flow chart

List of patients underwent parathyroidectomy between year 2007 to 2014 obtained from operation theater.



Recruitment of patients who fulfilling the inclusion and exclusion criteria



Review of medical records of patients that recruited in the study



Data from medical records entered in the data collection form



Data collection and statistical analysis



Report and manuscript write up

Gantt Chart of Research Activities

PROJECT ACTIVITIES	2015												2016											
	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D
Dissertation topic discussion at department and Ethic approval					→																			
Patient / Subjects Recruitment and Data Collection															→									
Data Analysis / Interpretation																→								
Presentation & Submission of Reports																	→							
Report Writing																	→	→						
Submission of dissertation Papers																		→	→					

Milestone of Research Activities:

- June 2015 : Proposal preparation and presentation
- March 2016 : Starting patient recruitment and Date collection
- April 2016 : Completion of data collection
- May 2016 : Completion of data analysis
- May 2016 : Preparation of dissertation write up
- July 2016 : Dissertation paper submission

Appendices

Appendix 1: Data Collection Form

Sample no : _____

Demographic:

Age: _____ Sex: M/ F Ethnic: _____

Pre-operative information:

1. Main complaint

- Renal stone
- Bone pain
- Polyuria/polydispsia
- Nausea/vomiting
- Constipation
- Pancreatitis
- Peptic ulcer
- Muscle weakness
- Psychosis

Duration of symptom: _____ months

2. Renal hyperparathyroidism

- Duration of renal failure: _____ years
- Duration of haemodialysis: _____ years
- Evidence of aluminium bone disease → Y/N

3. Pre-operative investigation

Serum calcium _____ mmol/L
Serum albumin _____ g/L
Serum phosphate _____ mmol/L
Serum ALP _____ IU/L
Serum iPTH _____ pg/ml
Serum creatinine _____ umol/L

Operative information:

Date of surgery: _____

Weight of resected specimen: _____ g HPE result : _____