Parathyroidectomy is a reliable treatment option for chronic kidney disease patients with secondary hyperthyroidism (SHPT)

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Abstract

Background: Secondary hyperthyroidism (SHPT) is a common complication in chronic kidney disease patients undergoing peritoneal dialysis. It develops as a result of distortions in the regulation of calcium, phosphorus and parathyroid hormone (PTH). SHPT increases with decreasing kidney function. Factors that affect the levels of calcium, phosphorus, and PTH include diet, residual renal function, peritoneal transport properties, and dialysate calcium concentration. Treatment options for SHPT include pharmaceutical and surgical removal of parathyroid glands. Although there are treatment options for kidney disease patients with SHPT, little improvement has been made in the overall outcome of the patients. **Method:** Here, we present that parathyroidectomy is a treatment option for patients with SHPT. A test group (peritoneal dialysis patients with SHPT who had surgery plus forearm transplantation) were compared with control group (normal peritoneal dialysis patients without surgery). In both groups, clinical, biochemical and haematological profile assessments were done. **Results:** The test group after surgery show improved clinical, biochemical and haematological profile comparing with the control (non-surgery) group. **Conclusion:** parathyroidectomy (PTX) is a reliable treatment option for patients with SHPT, which brings about improvement in the biochemical, haematological, physiological and clinical parameters as compared with peritoneal dialysis patients with secondary hyperthyroidism without parathyroidectomy plus forearm transplantation.

Background

Secondary hyperparathyroidism (SHPT) is one of the commonest complications in chronic kidney patients undergoing dialysis. It is involved in skeletal metabolism, cardiovascular and soft-tissue calcification in patients with dialysis. It creates a compounded problem and greatly reduces the quality of life as well as increases the mortality rate of people with chronic kidney disease **(1)** There are many factors affecting calcium, phosphorus, and parathyroid hormone (PTH) metabolism in maintenance of peritoneal dialysis patients, including diet, residual renal function, peritoneal transport properties, calcium concentration in dialysate and application of phosphorus binders **(17)**. The role of parathyroid hormone involves absorption of calcium from the gut, demineralization of the bones and other connective tissues and absorption and reabsorption of minerals in the kidney during excretion. Secondary hyperparathyroidism develops from the distortions in the regulation of calcium, phosphorus, parathyroid hormone and vitamin D **(19)**.

Parathyroid dysfunction associated with biochemical and bone disorders continues to cause much morbidity including cardiovascular diseases, bone pain and fractures in chronic kidney disease (CKD) patients. **(8, 9, 10, 11, 12)**. Uncontrolled SHPT results in up to 20% of increased mortality **(10, 11)** and a four-fold increase in the incidence of bone fractures due to impaired bone quality in dialysis patients compared with non-dialysis patients **(13, 14, 15)**. Many studies support a global trend in SHPT: 29.48% among continuous ambulatory peritoneal dialysis (CAPD) patients in Thailand **(3)**, 60% in Argentina **(5)** and 47% in a review studies in Canada **(4)**. Early diagnosis and reasonable treatment (mainly drug therapy and parathyroidectomy plus forearm transplantation) are important methods to delay such

complications. Many therapeutic strategies in the management of mineral bone disease in chronic kidney disease (CKD-MBD) patients target the control of SHPT including the use of calcimimetics, vitamin D sterols **(18)**, phosphate binders and surgical procedures **(6, 7)**. Pharmacological treatment of SHPT presents with high cost **(16)**, many side effects, non-compliance and several reported cases of resistance to vitamin D analogs. Parathyroidectomy (PTX) is fast becoming the medical treatment of choice among chronic kidney disease patients with secondary hyperparathyroidism despite the contribution of pharmaceutical therapy. PTX brings relief and considerable improvement in the laboratory and clinical well-being of peritoneal dialysis (PD) patients. In a recent article by Eidman and Wetmore, even though parathyroidectomy may be beneficial as a remedy for secondary hyperparathyroidism, they cautioned that care must be taken to monitor clinical symptoms and laboratory values in these patients. Parathyroidectomy as a common method for the treatment of secondary hyperparathyroidism following chronic kidney diseases, lacks enough clinical and laboratory evidence. This study therefore seeks to bring to bear the clinical, biochemical, haematological and physiological support for parathyroidectomy in people living with chronic kidney disease undergoing peritoneal dialysis.

Methods

Study subjects

65 peritoneal dialysis patients from November 2013 to June 2016 in Jiangsu Province Hospital were enrolled. Peripheral plasma was obtained from all enrolled patient. 25 patients eventually get parathyroidectomy plus forearm transplantation surgery due to secondary hyperparathyroidism (surgery group), while another 40 without secondary hyperparathyroidism did not get this surgery (non-surgery group). Moreover, the 25 patients were followed up to 72h after surgery. The writing consents were obtained from each patient, and this study was approved by the Ethics Committee of Jiangsu Province Hospital.

Observed parameters

Age, height, gender, liver function parameters (ALT, AST and ALP), hematological profiles (Hb, RBC, WBC, PLT, HCT and blood iron), total protein, albumin, globulin, triglycerides, cholesterol, HDL and LDL, phosphate calcium, kidney function parameters (urea creatinine and uric acid) are compared between surgery and non-surgery group.

Statistical analysis

SPSS 19.0 software package was used to analyze the data from this study. T test was used to compare the quantitative data between two groups. To examine the qualitative data between surgery and non-surgery group, the Chi-square test was used. A two-tailed probability less than 0.05 was inferred as statistically significant.

Results

Comparison on clinical parameters between surgery and without surgery groups. We analyzed if the groups will have a significant impact on the clinical parameters of the patients. The mean age for the surgery group was 44.80 years as compared to the non-surgery group which was 46.45 years ($P=0.67$) (**Sup. Table 1**). There was no significant height difference between the surgery group (162.60 cm) and non-surgery group (164.17 cm) ($p=0.58$) (**Sup. Table 1**). The mean difference between the two groups with respect to weight ($p=0.72$) and gender ($p=0.47$) was not significant (**Sup. Table 1**). The liver function parameters (ALT, AST and ALP) between the surgery and non-surgery groups were highly significant ($p=0.001$) with levels lower in surgery groups compared to non-surgery groups with the exception of ALP (557.72 vs 130.79) (**Table 1**). There was also no significant difference between the groups with regards to hematological profiles (Hb, RBC, WBC, PLT, HCT and blood iron) (**Table 1**). Significant difference was observed in the mean values for total protein ($p=0.001$), albumin ($p=0.001$) and globulin ($p=0.03$) between the surgery and non-surgery groups (**Table 1**). The mean values of triglycerides ($p=0.91$), cholesterol ($p=0.34$), HDL ($p=0.10$) and LDL ($p=0.73$) were not significantly differently between both groups (**Table 1**). Patients in the surgery group had a lower mean phosphate (2.23 mmol/L) compared to the non-surgery group (1.68 mmol/L) ($p=0.001$) (**Table 1**). The mean levels of calcium between the groups were not different. Kidney function parameters were not different between both groups as demonstrated by the mean values of urea ($p=0.17$), creatinine ($p=0.56$) and uric acid ($p=0.48$) (**Table 1**).

Dialysis method and composition affects the overall performance of SHPT patients after surgery. The method of dialysis plays a key role in the SHPT patients' responses. In **Table 2**, there is a significant correlation between continuous ambulatory peritoneal dialysis (CAPD) and daytime ambulatory peritoneal dialysis (DAPD) ($p=0.01$) in both pre-surgery and surgery groups. The volume of dialysis had no significant correlation between patients in both groups ($p=0.47$) irrespective of the amount, 6L, 8L, 10L or 12L (**Table 3**). The glucose composition (1.5%, 1.5% + 2.5% mix or 2.5%) of the dialysis fluid however, showed a significant correlation between the patients in the surgery and pre-surgery groups ($p=0.01$) (**Table 3**).

Parathyroidectomy reduces PTH levels in a time-dependent manner whereas calcium levels improve with time. SHPT patients report with increased levels of PTH and hypocalcaemia. Improving these clinical parameters is crucial to the survival of the patients. Parathyroidectomy reduced blood PTH levels from a mean value of 1,591.86 pg/ml to 63.45 pg/ml within 24 hours. PTH levels were further reduced on day 3 (72 hours) post-surgery to 39.44 pg/ml ($p=0.0001$) (**Table 4**). Mean calcium level in the pre-operative group was 2.39 mmol/L; however, 24 h post-surgery, mean calcium level further reduced to 1.94 mmol/L. The level started rising after day 3 post-surgery to 2.15 mmol/L ($p=0.0001$) (**Table 5**). Moreover, we did the comparison on mean calcium and PTH levels (pre-surgery and post-surgery) among different groups of patients receiving parathyroidectomy. We firm confirm that parathyroidectomy reduces PTH levels after 24h ($p<0.05$) and 72h ($p<0.05$). Whereas calcium levels reduce to 1.94 mmol/L at 24h after parathyroidectomy but increase to 2.15mmol/L at 72h after surgery and the difference is significant (**Table 6**).

Discussion

SHPT is a common complication among people with chronic kidney disease undergoing some form of maintenance dialysis (including peritoneal dialysis). SHPT heightens as kidney function declines. Secondary hyperparathyroidism presents with laboratory and clinical modifications in the physiological parameters of the body. The treatment of SHPT involves both pharmaceutical and surgical methods. Some studies show that high cost of drugs, side effects, resistance to some drugs is increasing the choice of surgical treatment for SHPT. This study sought to establish the impact of parathyroidectomy with or without forearm transplantation on clinical, physiologic and laboratory parameters.

The study is a comparative study that compares test group (peritoneal dialysis patients with SHPT who had surgery done as a treatment method) with a control group (normal peritoneal dialysis patients with no secondary hyperthyroidism and for that matter had no surgery). Data was collected at two levels of the study (the preoperative and postoperative data). At the preoperative level, basic information was collected on both participants in the surgery and non-surgery groups. At the postoperative level, data was collected on only surgery group participants. After parathyroidectomy, chronic kidney disease patients with SHPT experience a decrease in the levels of PTH after 24 hours. The levels of PTH even decreased further to 39.44 pg/mL after 72 hours. This suggests those peritoneal dialysis patients with SHPT who undergo surgery see PTH improvement in a time-dependent manner. Although PTH levels decrease after 24 hours, calcium levels which are expected to rise in a time dependent manner doesn't. It decreases at 24 hours post-surgery but gradually increases after 72 hours post-surgery. The glucose composition of the dialysis fluid also plays a key role in the overall outcome of SHPT patients. There was a significant difference between the glucose composition used in the dialysis process ($p=0.01$) but not the volume of dialysis fluid ($p=0.47$). This information will provide clinicians the better option when considering the optimal dialysis method to improve patient care while reducing PTH levels and improving calcium levels.

From the results gathered during the study, we have demonstrated that parathyroidectomy is a treatment alternative for the management of secondary hyperthyroidism among peritoneal dialysis patients. It brings about improvement in the biochemical, haematological, physiological and clinical parameters as compared with peritoneal dialysis patients with secondary hyperthyroidism without parathyroidectomy plus forearm transplantation. The study however is limited by the small sample size and one dialysis centre bias. We suggest therefore similar study be repeated in a large sample size cross sectional multi-centre dialysis points to eliminate biases.

In conclusion, our study indicates that PTX is a reliable treatment option for patients with SHPT, which brings about improvement in the biochemical, haematological, physiological and clinical parameters as compared with peritoneal dialysis patients with secondary hyperthyroidism without parathyroidectomy plus forearm transplantation.

Declarations

Ethics approval and consent to participate

The writing consents were obtained from each patient, and this study was approved by the Ethics Committee of Jiangsu Province Hospital.

Consent for publication

Written consent was provide by patients involving in this study and a copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and material

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Competing interests

All the authors declare there is no conflict of interest.

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Authors' contributions

Research design: Hongqing Cui, Jingjing Wu ; Conducted experiments: Hongqing Cui,Li Zhang, Chunxia Mao. Contributed analytic tools: Baodi Huang. Data analysis: Huijuan Mao, Ningning Wang. Manuscript writing: Haibin Ren, Changying Xing. All authors read and approved the final manuscript.

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Tables

Table 1: Partial comparison of quantitative data from surgical and nonsurgical groups with (paired *T* test)

Objects	1= surgical group 2=nonsurgical group	Number	average	Standard error	T value	df	Sig.(Bilateral)
Albumin	1	25	31.70	3.14			
g/L	2	40	36.11	5.26	-4.24	62.91	0.00
cholesterol	1	25	4.41	1.18			
mmol/L	2	40	4.71	1.23	-0.95	52.61	0.34
Triglyceride	1	25	1.64	0.78			
mmol/L	2	40	1.61	0.86	0.11	55.13	0.91
Urea	1	25	21.46	5.38			
(mmol/l)	2	40	19.52	5.75	1.38	53.68	0.17
Creatinine	1	25	1025.45	235.65			
(μmol/L)	2	40	1065.34	307.06	-0.59	60.23	0.56
Uric acid	1	25	427.00	74.21			
(μmol/L)	2	40	411.51	101.44	0.71	61.32	0.48
	1	13	10.42	4.60			
ALT(U/L)	2	38	16.09	7.06	-3.31	32.30	0.00
AST(U/L)	1	12	12.51	4.11			
	2	38	20.96	7.42	-5.00	34.49	0.00
High-density lipoprotein mg/L	1	25	1.01	0.26			
	2	34	1.13	0.29	-1.70	54.71	0.10
Low-density lipoprotein mg/L	1	25	2.99	0.79			
	2	34	3.08	1.06	-0.35	56.98	0.73
Ca(mmol/L)	1	25	2.39	0.24			
	2	40	2.39	0.32	-0.06	60.64	0.96
P(mmol/L)	1	25	2.23	0.53			
	2	40	1.68	0.50	4.09	48.78	0.00
K(mmol/L)	1	25	3.73	0.64			
	2	40	4.10	0.77	-2.13	57.96	0.04
Na(mmol/L)	1	12	140.29	3.43			
	2	40	139.28	3.09	0.92	16.74	0.37
Cl(mmol/L)	1	12	97.68	3.19			
	2	40	97.28	3.11	0.38	17.75	0.71
Mg(mmol/L)	1	11	0.98	0.16			
	2	39	0.98	0.19	0.02	18.12	0.99
CRP (mg/L)	1	20	9.77	17.59			
	2	32	14.80	26.55	-0.82	49.78	0.42
LDH	1	12	218.25	54.79			
	2	34	236.71	77.17	-0.89	27.33	0.38
Ferritin	1	22	403.63	477.83			
g/L	2	32	314.97	286.77	0.78	31.38	0.44
Transferrin saturation (%)	1	20	27.30	16.15			
	2	32	32.47	13.54	-1.19	35.18	0.24
Alkaline phosphatase	1	25	557.72	548.59			
	2	34	130.79	120.68	3.82	25.71	0.00
Hemoglobin	1	25	92.04	18.51			
G/L	2	40	97.31	20.80	-1.06	55.54	0.29

Hct	1	12	0.29	0.05			
%	2	40	0.30	0.06	-0.15	21.60	0.89
Plt	1	12	205.25	75.53			
10 ⁹ /L	2	40	200.83	79.27	0.18	18.89	0.86
PTH pg/ml	1	25	289.35	217.36			
	2	40	1609.80	508.71	12.30	29.55	0.00
25-hydroxy-vitamin D (blood level) (nmol/L)	1	25	14.52	9.15			
	2	30	16.87	11.76	-0.83	52.78	0.41
RBC	1	12	3.54	1.31			
(10 ¹² /L)	2	38	3.23	0.69	0.79	13.00	0.45
WBC	1	12	5.76	2.18			
(10 ⁹ /L)	2	38	6.80	1.92	-1.48	16.75	0.16
β-2microglobulin	1	9	38.42	9.38			
%	2	13	45.80	11.71	-1.64	19.47	0.12
Folic acid	1	4	33.39	25.37			
nmol/L	2	26	30.45	18.32	0.22	3.50	0.84

Table 2: Comparison among different dialysis method (CAPD and DAPD) (Chi-square test of counting data, Fisher's exact method).

Dialysis method			Chi-square value	Pvalue
	Surgical group(number)	Nonsurgical group(number)		
CAPD	13	26	13.63	0.001
DAPD	12	5		

Table 3: Comparison among different dialysis volume (6L, 8L, 10L, 12L) and glucose concentration of dialysis fluid (1.5%, 1.5% + 2.5% mix (2.5%)) (Chi-square test of counting data, Fisher's exact method)

Dialysisvolume	group		Chi-square value	Pvalue
	surgical group(number)	Nonsurgical group(number)		
6L	2	4	2.31	0.47
8L	20	22		
10L	2	5		
12L	1	0		
1.5%	4	11	10.20	0.01
1.5%+2.5% (mix)	15	16		
2.5%	6	4		

Table 4: Comparison between mean PTH levels amongst pre-surgery and post-surgery groups.

	Average	Standard error	number	Fisher's value	P value
PTH level(Pre-surgery)	1591.86	554.14	19	160.50	.000
PTH level of non-transplantation side(24h after surgery)	63.45	74.90	19		
PTH level of non-transplantation side (72h after surgery)	39.44	87.79	19		

Table 5: Comparison between mean calcium levels among pre-surgery and post-surgery groups

	Average value	Standard error	number	Fisher's value	P value
Ca ²⁺ level(Pre-surgery)	2.39	0.24	25	7329.62	.000
Ca ²⁺ level(24 h after surgery)	1.94	0.16	25		
Ca ²⁺ level (72h after surgery)	2.15	0.21	25		

Table 6: Comparison between mean calcium and PTH levels amongst pre-surgery and post-surgery groups: Analysis of variance of repeated measures of paired data.

Comparison between each other		Average value	Standard error	number	T value	P value
Pair 1	PTH level(Pre-surgery)	1602.49	518.31	24	14.57	0.00
	PTH level of non-transplantation side (24h after surgery)	74.34	120.72	24		
Pair 2	PTH level(Pre-surgery)	1591.86	554.14	19	12.47	0.00
	PTH level of non-transplantation side (72h after surgery)	39.44	87.79	19		
Pair 3	Ca ²⁺ level(Pre-surgery)	2.39	0.24	25	8.29	0.00
	Ca ²⁺ level(24 h after surgery)	1.94	0.16	25		
Pair 4	Ca ²⁺ level(Pre-surgery)	2.39	0.24	25	3.66	0.00
	Ca ²⁺ level(72 h after surgery)	2.15	0.21	25		
Pair 5	PTH level of non-transplantation (24h after surgery)	63.45	74.90	19	1.03	0.32
	PTH level of non-transplantation (72h after surgery)	39.44	87.79	19		
Pair 6	Ca ²⁺ level(24 h after surgery)	1.94	0.16	25	-4.08	0.00
	Ca ²⁺ level(72 h after surgery)	2.15	0.21	25		

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