Journal Homepage: - www.journalijar.com
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)
Article DOI: 10.21474/IJAR01/8129
DOI URL: http://dx.doi.org/10.21474/IJAR01/8129

RESEARCH ARTICLE

TOTAL PARATHROIDECTOMY WITH AUTOTRANSPLANTATION VERSUS SUBTOTAL PARATHYROIDECTOMY AS DIFFERENT MODALITIES IN MANAGEMENT OF SECONDARY HYPERPARATHYROIDISM.

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Manuscript Info

Manuscript History
Received: 01 October 2018
Final Accepted: 03 November 2018
Published: December 2018

Abstract

Background: secondary hyperparathyroidism is a common problem in patients with chronic renal failure. The optimal surgery in management of secondary hyperparathyroidism still controversial. Total parathyroidectomy with autotransplantation and subtotal parathyroidectomy may be employed.

Methods:This prospective study was conducted on 30 patients presented by manifestations of secondary hyperparathyroidism and admitted to Mansoura University Hospitals over three years (from May 2015 to May 2018).Our patients were divided to two groups:

Group (A) included 15 patients underwent total parathyriodectomy with cervical thymectomy and autotransplantation;(TPTX-AT)

Group (B) included 15 patients underwent subtotal parathyroidectomy with cervical thymectomy;(SPTX).

Results: TPTX-AT was associated with longer operative time than SPTX,(109.6 vs 94.9 $p<0.001$).the rate of complications was no significantly different between TPTX-AT and SPTX, recurrence of hyperparathyroidism,(SPTX: two patientsvsTPTX-AT: one patient P 1), hypoparathyroidism reported in three patients underwent TPTX-AT vsone patient underwent SPTX p 0.59.The two procedures markedly decreased serum PTH levels to normal ranges.

Conclusion: TPTX-AT and SPTX were effectively treating secondary hyperparathyroidism, nearly equal in safety, complications and in biochemical parameters improvement.

Introduction:-

Secondary hyperparathyroidism (sHPT) showing the adaptive and often the maladaptive response of the patients to control the disturbed homeostasis of serum calcium level, phosphorus and vitamin D metabolism caused by the affected renal functions. Dysregulation of calcium and phosphorus homeostasis causing elevated levels of the phosphatonin fibroblast growth factor 23 (FGF23), decreased renal phosphorus excretion, increased serum phosphorus, and diminished synthesis of calcitriol (1,25(OH)2D3), which is the active form of vitamin D. These changes cause increased synthesis and secretion of parathyroid hormone (PTH) and parathyroid cell hyperplasia (Cunningham et al., 2011). There is evidence that these disturbances in mineral metabolism lead to vascular (Goodman et al., 2000; Raggi et al., 2002) and valvular (Ribeiro et al., 1998) calcifications and are directly releated

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to an increased risk of cardiovascular morbidity and mortality (Covic et al., 2009). According to a recent systematic review, the risk of cardiovascular and all-cause mortality is high with elevated serum phosphorus followed by increased serum calcium level and PTH (Covic et al., 2009). Apart from extra-skeletal manifestations, sHPT also leads to marked alterations in bone metabolism which become obvious in the different types of renal osteo-dystrophy (Malluche&Faugere, 1990; Moe et al., 2006). This clinical syndrome including mineral, bone and cardiovascular changes has been termed CKD-related Mineral and Bone Disorder (CKD-MBD) (Moe et al., 2006). Furthermore, sHPT is thought to play a role in many other complications of end-stage renal disease as bone ache , bone fractures, sexual dysfunction, muscle dysfunction, disturbed hematopoiesis, immune disturbance, pruritus and calcific uremic arteriolopathy (calciphylaxis) (Rodriguez & Lorenzo, 2009).

Patients and methods:-

This prospective study was conducted on 30 patients presented by manifestations of secondary hyperparathyroidism and admitted to Mansoura University Hospitals over three years (from May 2015 to May 2018).
All patients were submitted to careful history taking, complete clinical examination, laboratory and radiological investigations.

History taking included;

1. Age
2. Sex
3. Occupation
4. Marital status
5. Menstrual history in females
6. Special habits
7. Medical and surgical history
8. History of previous neck irradiation or surgery
9. History of pathological fractures, bone aches or recurrent muscle cramps.
10. History of consanguinity, heridofamilial diseases or similar condition in the family.
11. Careful history taking about renal disease, duration of dialysis, place of dialysis, medications taken with dialysis.

Clinical examination;

All patients were submitted to thorough and complete preoperative general and local examinations to the neck.

Investigations;

All patients were submitted to the following preoperative investigations;

1. Laboratory investigations which included
2. Serum PTH
3. Serum Calcium
4. Serum phosphorus
5. Thyroid function tests (S. T3, T4 and TSH).
6. Complete blood count, Liver function tests.
7. E.C.G.
8. Neck U/S.
9. Tc-99m Sestamibi scan.

Inclusion criteria for our patients:

1. Age; no age selection
2. Sex; male or female
3. Patients with chronic renal failure
4. Patients on long term dialysis
5. Patients with high PTH more than 1000pg/ml level with low serum calcium

Our patients were divided to two groups:

Group (A) included 15 patients underwent total parathyriodectomy with cervical thymectomy and autotransplantation in the sternomastiod muscle or in the forearm ;(TPTX-AT)

Group(B) included 15 patients underwent subtotal parathyroidectomy by removing three and half of the parathyroid glands and leave half of one glandwith cervical thymectomy;(SPTX)

Follow up of all patients was done by measuring serum PTH, serum calcium and serum phosphorus in second postoperative day, two weeks postoperative, after one month, three months, six months and after one year.

Statistical analysis:-

1. Data were analyzed with SPSS version 21. The normality of data was first tested with Shapiro test.
2. Qualitative data were described using number and percent. Association between categorical variables was tested using Fischer exact test when expected cell count less than 5.
3. Continuous variables were presented as mean ± SD(standard deviation) for parametric data and median for non-parametric data. The two groups were compared with Student *t* test for parametric data and Mann Whitney test for non parametric.

Level of significance:

For all above mentioned statistical tests done, the threshold of significance is fixed at 5% level (p-value).
The results was considered:

1. Non-significant when the probability of error is more than 5% ($p > 0.05$).
2. Significant when the probability of error is less than 5% ($p \leq 0.05$).
3. The smaller the p-value obtained, the more significant are the results

Results:-

This study was done on 30 patients with secondary hyperparathyroidism and divided to two groups group A and group B each group had 15 patients. Group A underwent total parathyroidectomywith autotransplantation, (TPTX-AT), while Group B underwent subtotal parathyroidectomy (SPTX), bilateral cervical thymectomy was done routinely to all patients in the two groups.

As regard demographic and clinical data of the two groups we found that group A (TPX-AT) included 13 males (86.7%) and 2 females (13.3%) while group B (SPX) included 8 males (53.3%) and 7 females (46.7%).the mean age in group A was 44.7+/-7.8 and in group B the mean age was 43.2+/- 15.5 with significant difference between the two groups as regard age and sex of the patients. All patients in the two groups presented by either bone aches or pathological fractures (80% and 20% respectively), the pathology of parathyroid gland in all patients in both groups was hyperplasia.

The difference in the operative time between the two groups was slightly significant with slight increase in time in TPTX-AT than SPTX and p value was <0.001.there was no significant difference betweenthe two groups in hospital stay as all patients discharged from the hospital nearly at the fourth postoperative.

The two techniques were nearly equal in the complications after surgery as there were two patients showed temporary vocal cord affection in the form of hoarseness of voice, one patient after TPTX and another one after SPTX. Recurrence of manifestations of hyperparathyroidism with elevation in serum PTH level again occurred in one patient after TPTX-AT within the first year postoperative due to hyperplasia in the transplanted graft and occurred also in two patients after SPTX, while hypoparathyroidism reported in three patients after TPTX-AT may be due to failure of the transplanted graft and reported in one patient only after SPTX, also there was no significant difference between the two groups as regard other postoperative complications as wound infection and bleeding.

Table (1): Demographic and clinical data of the studied group

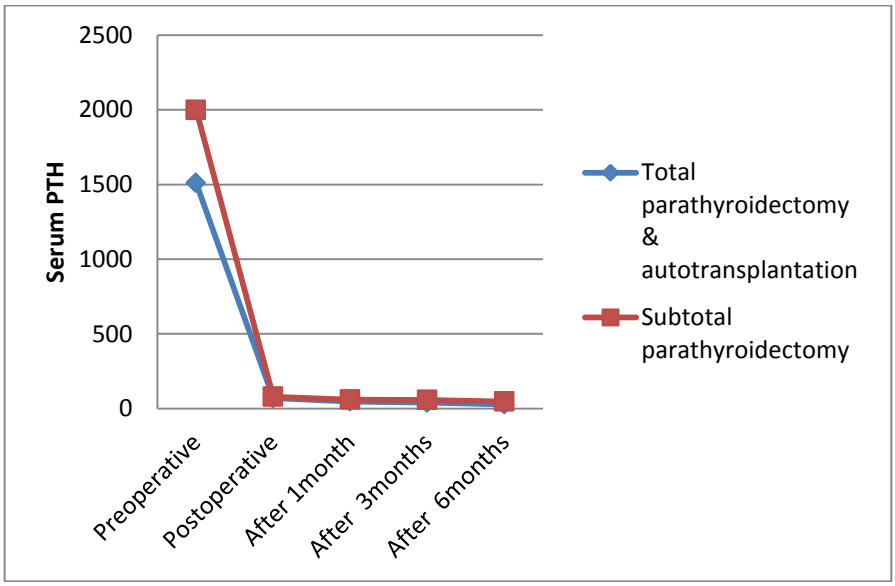
Demographic and clinical data	Total parathyroidectomy & autotransplantation (n=15)	Subtotal parathyroidectomy (n=15)	p-value
Age/ years Mean ± SD Min-Max	44.73±7.85 28-56	43.27±15.57 20-65	0.747
Sex Male Female	13 (86.7%) 2 (13.3%)	8 (53.3%) 7 (46.7%)	0.109
Complaint Bone aches Pathological fractures	12 (80.0%) 3 (20.0%)	11 (73.3%) 4 (26.7%)	1 1
Chronic kidney disease	15 (100%)	15 (100%)	1
Site Upper Lower All	- - 15 (100%)	- - 15 (100%)	1
Radiological findings Adenoma Hyperplesia	- 15 (100%)	- 15 (100%)	1
Operative time Mean ± SD	109.67±9.53	94.93±6.23	<0.001*
Hospital stay Mean ± SD	3.0±0.0	3.13±0.51	0.326
Failure or recurrence	1 (6.7%)	2 (13.4%)	1
Hypoparathyroidism	3 (20%)	1 (6.7%)	0.598
Associated thyroid disease	1 (6.7%)	1 (6.7%)	1
vocal cord affection	2 (13.4%)	1 (6.7%)	1

Effect on serum PTH levels:
Serum PTH showed marked decrease and became within the normal values after both surgical procedure without significant difference between in lowering of serum PTH between TPTX-AT and SPTX and during follow up period serum PTH level showed more decrease in patients underwent TPTX than in patients underwent SPTX.

Table 2:-PTH level among Total parathyroidectomy & autotransplantation and Subtotal parathyroidectomy groups

PTH Median (Min-Max)	**Total parathyroidectomy & autotransplantation (n=15)**	**Subtotal parathyroidectomy (n=15)**	**p- value**
Preoperative	1510 (1272-1917)	2000 (1019-2000)	0.126
Postoperative	70 (33-90)	80 (55-130)	0.008*
After 1month	48 (4-60)	60 (5-70)	0.005*
After 3months	40 (28-70)	58 (15-70)	0.032*
After 6months-1 year	28 (18-500)	48 (18-400)	0.003*

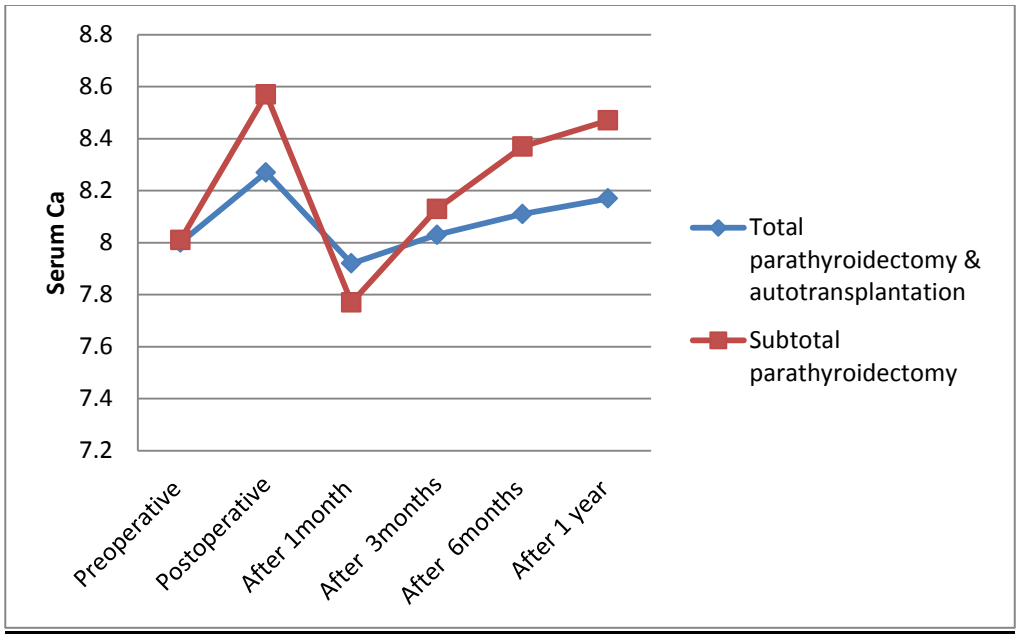
Significant p <0.05



Effect on serum calcium levels:
Serum calcium levels remain within normal range after both techniques and during the follow up period there was no marked hypocalcaemia even in patients had hypoparathyroidism after TPTX –AT and SPTX.

Table (3):-Serum Calcium among Total parathyroidectomy & autotransplantation and Subtotal parathyroidectomy groups

Serum Calcium	**Total parathyroidectomy & autotransplantation (n=15)**	**Subtotal parathyroidectomy (n=15)**	**p- value**
Preoperative	8.00±0.46	8.01±1.05	0.986
Postoperative	8.27±0.52	8.57±0.70	0.195
After 1month	7.92±0.63	7.77±0.90	0.610
After 3months	8.03±0.65	8.13±0.72	0.675
After 6months	8.11±0.78	8.37±0.82	0.371
After 1 year	8.17±0.28	8.47±0.75	0.161



Discussion:-

In our study there was no significant difference between patients underwent TPTX-AT and patients underwent SPTX in their demographic data which cope with the study done by Chen J, et al, in 2015.

We found that both surgical techniques had no significant difference as regard postoperative complications eg: vocal cord affection, bleeding and infectionwhich similar to the results reported by Meltzer C, et al, 2016.

Hypoparathyroidism was detected in TPTX-AT technique more than SPTX,while recurrence of hyperparathyroidism was reported in patients underwent SPTX more than TPTX-AT, but overall there was no significant difference in the rate of complications between the two techniques this results cope with results reported by, Meltzer C, et al, in 2016.

In our study we found that serum PTH markedly decreased postoperatively after both surgical techniques reaching normal values and during the follow up periodserum PTH levels after SPTX slightly higher than TPTX-AT, also serum calcium levels showed no significant difference between both techniques and still within normal ranges, this biochemical changes was similar to that reported by, Wetmore JB, et al, 2016 and the study done by Liang Y, et al, in 2015.

Conclusion:-

Both TPTX-AT and SPTX were effective in treating secondary hyperparathyroidism and preventing recurrence.

The difference between the two surgical procedures in recurrence, persistence of hyperparathyroidism or occurrence of hypoparathyroidism after surgery was insignificant.

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