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BIOCHEMICAL CHANGES IN PATIENTS UNDERGOES THYROID SURGERY

Dr. Mohammed Meteab Mughir Al-karawi
M.B.CH.B,MS
JALAWLA GENERAL HOSPITAL
mohammedmetib0@gmail.com

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Abstract:

Once death from thyroid operation became an exception, specific pitfalls of the procedure, namely, injuries to the laryngeal nerves and damage to the parathyroid glands became obvious. Halsted is credited for his studies of surgical anatomy and blood supply of the parathyroid glands and the introduction of the technique of capsular dissection that implemented preservation of the vascular pedicle of a parathyroid gland and led to a safer approach to thyroid and parathyroid surgery. Today morbidity remains a subject of concern for surgeons performing thyroid and parathyroid procedures. Injury of the recurrent laryngeal nerve and hypoparathyroidism are the most frequent complications.

Patients and method This is a cross sectional study of 112 patients (98 females and 14 males) underwent different thyroid surgeries for different indication over a period of eight months (November 2014-july 2015) in baquba teaching hospital in Diyala governorate.

Results Regarding the changes that occurs in the serum level of calcium, phosphorous and parathyroid hormone following subtotal ,near total and total thyroidectomy .the results were significant to highly significant with a p-value < 0.05_ < 0.001 with respect to increase serum level of phosphorous and decrease in serum calcium and parathyroid hormone levels

Conclusions

- Nearly all patients did not prescribe neither oral calcium nor vitamin D as a routine in patients undergoes near total to total thyroidectomy.
- Significant number of patients develops subclinical hypocalcaemia and this can deceive the surgeon that there is no hypocalcaemia at all.

Recommendation We recommend routine supplementation of oral calcium and/or vitamin D in patients underwent extensive thyroid surgery to decrease the risk of postoperative hypocalcaemia.

Aim of the study The aim of this study is to evaluate and have an idea about the changes regarding calcium ,phosphorus and parathyroid hormone following different thyroid surgeries.

Keywords: Thyroid surgeries, parathyroid hormone, calcium ,phosphorus..

INTRODUCTION

Mortality from thyroid and parathyroid surgery is virtually disregarded nowadays. During the eighteenth century, however, the mortality rate of thyroid surgery was as high as 40% from bleeding and sepsis **[Becker WF 1977]**. As a consequence, in 1850 the French Academy of Medicine recommended its routine use be abandoned, and many leading surgeons would not perform it. The greatest advance in thyroid surgery is to be credited to **Theodor Kocher** who first recognized the importance of anti- and aseptic handling, hemostasis, and precise operative technique. Within a decade, his overall operative mortality decreased from 15% to 2.4%. With the exclusion of complicated cases, in 1898 he reported a mortality rate of only 0.18%. Following Kocher's principles, William Halsted, Charles Mayo, George Crile, and others contributed further to the development of thyroid surgery.

Once death from thyroid operation became an exception, specific pitfalls of the procedure, namely, injuries to the laryngeal nerves and damage to the

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parathyroid glands became obvious. Halsted is credited for his studies of surgical anatomy and blood supply of the parathyroid glands and the introduction of the technique of capsular dissection that implemented preservation of the vascular pedicle of a parathyroid gland and led to a safer approach to thyroid and parathyroid surgery. Today morbidity remains a subject of concern for surgeons performing thyroid and parathyroid procedures. Injury of the recurrent laryngeal nerve and hypoparathyroidism are the most frequent complications. The key issue of an effective and safe surgical approach is a profound knowledge of specific anatomy and pathophysiology in combination with meticulous handling and dissection of tissue.

The overall permanent complication rate should not exceed 1% in centers providing expertise **[Sosa JA, et al 1998, Rios-Zambudio A, et al 2004, Udelsman R, et al 2004].**

The relationship between volume of operations and outcome has been extensively examined by Sosa et al. in the State of Maryland **[Sosa JA, et al 1998].** They demonstrated a significant inverse relationship between the volume of thyroidectomies performed by individual surgeons and complication rates, postoperative length of stay, and hospital charges.

Also surgeons who performed more than 100 thyroidectomies over a 6-year period had the lowest hospital charges, compared with those performing 30–100 cases, 10–29 cases, and between one and nine cases.

1-1 HYPOPARATHYROIDISM

The reported rate of hypocalcemia after thyroid surgery varies from 1% to over 50% **[Reeve T, Thompson NW 2000, Harness JK, et al 2000, Ozbas S, et al 2005].** While the majority of instances of postoperative hypocalcemia are transient, permanent hypoparathyroidism is decidedly unusual and should amount to less than 1%.

Although the pathogenesis of post- thyroidectomy hypocalcemia is multifactorial:

- Damage to the parathyroid glands in the form of direct injury or inadvertent removal, or;
- Indirectly by devascularization of the gland is the most common cause followed by the first one.
- Other causative factors are **(1)** negative calcium balance due to calcium absorption by bones in repair of osteodystrophy in hyperthyroid patients, **(2)** decreased serum albumin levels caused by hemodilution, **(3)** increased secretion of calcitonin during thyroid mobilization, or **(4)** conditions associated with increased renal excretion of calcium **[McHenry CR, et al 1994].**

A mild case of postoperative hypocalcaemia is self-limiting and may not be recognized unless routine calcium determination is carried out. Nevertheless we would recommend measurement of serum calcium levels routinely in every patient prior to and after bilateral thyroid surgery.

After an uncomplicated unilateral thyroid resection, hypocalcemia will virtually never be observed. Recently it was shown that intraoperative parathyroid hormone (PTH) determination allows prediction of postoperative hypocalcemia (PTH <10 pg/ml) and the necessity of early vitamin D supplementation in order to reduce the risk of postoperative symptomatic hypocalcaemia **[Quiros RM, et al 2005].**

Intraoperative PTH monitoring facilitates early discharge and reduces the costs of following up postoperative serum calcium levels. Patients exhibiting clinical signs of hypocalcemia, such as circumoral or acral paresthesia, muscle cramps, or numbness of the hands and feet, may be orally treated with calcium carbonate or calcium lactate in divided doses to a total of 2–8 g per day. Additionally, calciferol or dihydrotachysterol may be required in order to enhance calcium absorption.

After normalization of serum calcium levels, oral calcium therapy is continued until stabilization of calcium homeostasis is achieved. Severe symptoms require immediate intravenous therapy with 10 ml 10% calcium gluconate over 3–5 minutes and subsequent continuous infusion of 0.9% saline containing 30–40 ml 10% calcium gluconate per 24 hours. Permanent hypocalcemia (more than 6 months postoperatively) is a major concern since it may be associated with significant impairment of life quality, chronic gastrointestinal discomfort, changes in bone metabolism, and development of cataracts. Single reports on heterologous transplantation of parathyroid tissue after microencapsulation with amitogenic alginate exist; however, reliable clinical systems are not yet widely available **[Hasse C, et al 2000].**

1-2 Indications of thyroid surgery

Various indications for thyroidectomy exist.

- One of the major indications is a diagnosis of thyroid cancer, usually biopsy-proven by fine-needle aspiration of a nodule.
- In patients with all but the most minimal (low-risk) biopsy-proven papillary thyroid cancer, and all medullary thyroid cancer, a total thyroidectomy is indicated.

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- Patients with a fine-needle aspiration showing either Hürthle cells or follicular neoplasm require at least a thyroid lobectomy of the side ipsilateral to the nodule and possibly a total thyroidectomy if the permanent operative specimen shows signs of malignancy.
- In addition to these malignancies, anaplastic thyroid cancer can occasionally be an indication for thyroidectomy, if no significant extension and infiltration into the surrounding structures is found. **[Lai SY, et al 2010]**
- Beyond malignancies, thyroidectomy is also a viable option for patients with symptomatic thyroid masses or goiters. Patients who have compressive symptoms including dysphagia, dyspnea, shortness of breath, and/or hoarseness due to a large goiter should undergo a thyroidectomy
- Aesthetic concerns due to a goiter may be an indication for thyroidectomy.
- Another indication includes patients with medically refractory Graves' disease ,toxic multinodular goiter or hyperthyroidism. **[Myers, Eugene.2010]**

1-3 Contraindications

There is no absolute contraindication for thyroidectomy; it is only a matter of timing **as** uncontrolled severe hyperthyroidism (i.e. Graves' disease) due to concerns for intraoperative or postoperative thyroid storm.

Another example is that although thyroidectomy can be performed during pregnancy for malignancy, many authors cite post ponding surgery until after delivery if possible, secondary to risks to the fetus from the anesthesia (congenital anomalies or abortion or premature labor). Indications for surgery during pregnancy include aggressive cancers or airway compromise. If elective thyroid surgery is undertaken during pregnancy, it should be performed during the second trimester if possible. **[Owen RP,et al 2010, Kuy S,et al 2009]**

Another contraindication for thyroidectomy is when it is not possible as in anaplastic carcinoma which invades the adjacent muscles and the trachea or even the esophagus (patient beyond thyroidectomy).

1-4 Extent of thyroid surgery:

Thyroid surgery could involve:

- Lumpectomy
- Lobectomy
- Lobectomy plus isthmusectomy
- Subtotal thyroidectomy(Removal of both lobes leaving 4gm. on each side plus isthmusectomy)
- Near total thyroidectomy (total lobectomy on one side plus isthmusectomy plus subtotal lobectomy on the contralateral side)
- Total thyroidectomy (Removal of the whole thyroid tissue on both sides).

PATIENTS AND METHOD

This is a cross sectional study of 112 patients (98 females and 14 males) underwent different thyroid surgeries for different indication over a period of eight months (November 2014-july 2015) in baquba teaching hospital in Diyala governorate. **Table 1,2 The extent of surgery depend upon the indication of the surgery**

3-1 The indications for thyroid surgery were:

- Pressure symptoms over the trachea as feeling of dyspnea (even if the pressure is caused by unilateral large lump)
- Thyrotoxicosis (Graves or multinodular)
- Large diffuse euthyroid goitre
- Proved malignancy on (Fine Needle Aspiration Cytology)FNAC
- FNAC shows Hurthle cell tumor
- FNAC smear shows abundant follicular cells
- FNAC suspect malignancy as the result was atypia
- The patient wish the goitre to be removed (For aesthetic purposes)

Table 1 Distribution of the patients according to the extent of thyroid surgery

Type of surgery (Extent of thyroid surgery)	Number
Lupectomy	8
Lobectomy	24

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Subtotal thyroidectomy	46
Near total thyroidectomy	14
Total thyroidectomy	20

Note: The extent of thyroid surgery is surgeon's policy

The age group 23-74 years

- All the patients included in this study had a formal surgical indication for thyroidectomy, independently of the extent of the surgery.
- Patients who were excluded in this study involve:
  - Those with an incomplete preoperative assessment;
  - Those who presented with preoperative abnormalities (hypo, or hyper.) in the serum calcium, phosphate, parathyroid hormone or total serum protein.
  - Patients who already are known cases of renal failure as renal failure lead to secondary hyperparathyroidism secondary to decrease serum calcium level.
  - Patients who are known cases of vitamin D deficiency. This information is obtained from the patient by asking her/him a direct question or by asking whether she/he is receiving supplements for calcium or vitamin D as a medication prescribed by her/his doctor.

So that, in addition to the routine examinations that are performed prior to any thyroidectomy, the preoperative assessment for these patients included measurement of serum calcium, serum phosphorus, serum parathyroid hormone and total serum protein. The postoperative assessment included measurement of total serum calcium and phosphorus ion levels, 24 hours and 48 hours after the operation.

The normal reference range of serum calcium ,phosphorus, parathyroid hormone and total serum protein depended in the study and also in baquba teaching hospital main lab and with which our results are compared are as follow:

- Calcium – reference value: 2.1 mmol/L to 2.6 mmol/L.
  8.5 - 10.5mg/dL
- Phosphorus – reference value: 0.81 - 1.45 mmol/L
  2.5 mg/dl to 4.5 mg/dl.
- Total protein: 36-52 grams/L
- Albumin: 35–50 g/L
- Serum parathyroid hormone 11 - 54 pg/ml

The decision whether there is any difference in the serum level of both calcium and phosphorus depends upon blood investigations (serum level). It doesn't depend upon development of symptoms related to the changes in those two ions.

STATISTICAL ANALYSIS

The data collected in tables then computed applying the t-Test to extract the calculated t value, and then tabulated t value which the last used to extract the p-value.

A p-value <0.05 is considered significant, while p-value >0.05 is considered non-significant.

RESULTS

112 patients (98 females and 14 males) underwent different thyroid surgeries for different indication over a period of eight months (November 2014-july 2015) in baquba teaching hospital. **Table 1,2**

The extent of thyroid surgery is surgeon's policy

Table 1 Distribution of 112 patients according to the type (extent) of thyroid surgery

Type of surgery (Extent of thyroid surgery)	Number

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Lumpectomy	8
Lobectomy	24
Subtotal thyroidectomy	46
Near total thyroidectomy	14
Total thyroidectomy	20
Total number	112

Table 2 Detailed distribution of 112 patients underwent thyroid surgery according to the extent of surgery depending on the indication (The extent of thyroid surgery is surgeon's policy)

Indication of surgery	Extent of surgery	No.	No.
Pressure symptoms by unilateral large lump	Lumpectomy	7	26
	Lobectomy	19	
Thyrotoxicosis (Graves or multinodular)	Subtotal	32	52
	Near total	9	
	Total	11	
Large diffuse euthyroid goitre causing pressure symptoms	Subtotal	13	17
	Near total	3	
	Total	1	
Proved malignancy on FNAC	Total	3	3
FNAC shows Hurthle cell tumor	Total	1	1
FNAC smear shows abundant follicular cells	Lobectomy	3	6
	Total	3	
FNAC suspect malignancy as the result was atypia	Near total	2	3
	Total	1	
The patient wish the goitre to be removed	Lumpectomy	1	4
	Lobectomy	2	
	Subtotal	1	
Total number		112	112

Table 3 Total serum calcium for patients who underwent lumpectomy in mmol/l before surgery and 24 hours after surgery (number of patients was 8)

	Before surgery	**24 hrs after surgery**
1	2.2	2.3
2	2.1	2.1
3	2.3	2.2
4	2.2	2.1
5	2.2	2.3
6	2.1	2.2

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7	2.1	2.1
8	2.3	2.1
Number of patients who developed hypocalcaemia		**0 (out of 8)**

Table 4 Total serum calcium for patients who underwent lobectomy in mmol/l before surgery and 24 hours after surgery (number of patients was 24)

	Before surgery	**24 hrs after surgery**
1	2.2	2.3
2	2.1	2.1
3	2.3	2.2
4	2.2	2.1
5	2.2	2.3
6	2.1	2.2
7	2.1	2.1
8	2.3	2.1
9	2.2	2.1
10	2.3	2.2
11	2.1	2.1
12	2.2	2.2
13	2.2	2.2
14	2.2	2.2
15	2.3	2.2
16	2.3	2.2
17	2.2	2.3
18	2.1	2.1
19	2.3	2.2
20	2.2	2.2
21	2.1	2.1
22	2.2	2.1
23	2.3	2.2
24	2.3	2.2
Number of patients who developed hypocalcaemia		**0 (out of 24)**

Table 5 Total serum calcium for patients who underwent subtotal thyroidectomy in mmol/l before surgery and 24 hours after surgery (number of patients was 46)

	Before surgery	**24 hrs after surgery**
1	2.1	2.1
2	2.1	2.2
3	2.1	1.8
4	2.4	2.1
5	2.3	2.1
6	2.1	2.1
7	2.4	2.3
8	2.3	2.4
9	2.2	1.5
10	2.3	2.3
11	2.4	1.8

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12	2.1	2.2
13	2.3	1.9
14	2.2	2.1
15	2.2	2.4
16	2.3	1.9
17	2.2	2.3
18	2.2	1.9
19	2.4	2.1
20	2.2	2.2
21	2.2	1.8
22	2.4	1.9
23	2.3	2.2
24	2.1	1.9
25	2.2	2.2
26	2.2	2.4
27	2.4	2.4
28	2.3	2.2
29	2.3	2.3
30	2.1	2.2
31	2.3	2.1
32	2.3	2.1
33	2.3	1.5
34	2.3	2.0
35	2.2	1.5
36	2.4	1.5
37	2.3	2.3
38	2.1	2.2
39	2.4	2.1
40	2.2	2.1
41	2.3	2.3
42	2.2	2.3
43	2.4	2.4
44	2.3	2.2
45	2.2	2.1
46	2.4	1.8
Number of patients who developed hypocalcaemia		**Clinically clear (4)**
		Subclinical (8)
		(Total 12 out of 46)

Table 6 Total serum calcium for patients who underwent near total thyroidectomy in mmol/l before surgery and 24 hours after surgery (number of patients was 14)

	Before surgery	**24 hrs after surgery**
1	2.2	**2.2**
2	2.2	**2.1**
3	2.3	**1.5**
4	2.4	**1.9**
5	2.2	2.3
6	2.4	**2.2**
7	2.2	**1.8**

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8	2.1	**1.4**
9	2.2	**1.9**
10	2.1	2.2
11	2.4	2.1
12	2.3	**1.6**
13	2.3	2.1
14	2.3	**1.5**
Number of patients who developed hypocalcaemia		**Clinically clear (4)**
		Subclinical (3)
		(Total 7 out of 14)

Table 7 Total serum calcium for patients who underwent total thyroidectomy in mmol/l before surgery and 24 hours after surgery (number of patients was 20)

	Before surgery	**24 hrs after surgery**
1	2.2	1.8
2	2.2	2.1
3	2.1	1.9
4	2.3	1.5
5	2.4	1.5
6	2.4	2.2
7	2.4	1.4
8	2.2	2.2
9	2.1	2.1
10	2.1	1.9
11	2.1	1.9
12	2.2	1.8
13	2.2	1.4
14	2.2	1.6
15	2.3	1.9
16	2.2	1.9
17	2.2	1.8
18	2.1	2.1
19	2.2	2.1
20	2.2	1.4
Number of patients who developed hypocalcaemia		**Clinically clear (6)**
		Subclinical (8)
		(Total14 out of 20)

Table 8 Values of calculated t, tabulated t and p-value for calcium changes after surgery according to the type of surgery (extent of thyroidectomy)

Type of surgery	Calculated t value	Tabulated t value	p-value
Lumpectomy	0.25	2.265	> 0.05
Lobectomy	1.8	2.056	> 0.05
Subtotal	4.6	3.5202	< 0.001
Near total	4.3	2.131	< 0.001
Total	5.65	2.030	< 0.02

P- Value > 0.05 is considered non-significant
P- Value < 0.05 is considered significant
P- Value < 0.001 is considered highly significant

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Table 9 Total serum phosphorus for patients who underwent lumpectomy in mmol/l before surgery and 24 hours after surgery (number of patients was 8)

	Before surgery	**24 hrs after surgery**
1	0.92	1.11
2	1.13	1.14
3	1.31	1.17
4	1.12	1.31
5	1.01	1.02
6	1.23	1.19
7	1.15	1.21
8	1.22	1.32
Number of patients with hyperphosphataemia		**0 (out of 8)**

Table 10 Total serum phosphorus for patients who underwent lobectomy in mmol/l before surgery and 24 hours after surgery (number of patients was 24)

	Before surgery	**24 hrs after surgery**
1	1.32	1.06
2	1.12	1.30
3	1.24	1.15
4	0.98	0.97
5	1.24	1.32
6	1.31	1.11
7	1.09	1.12
8	1.27	1.35
9	1.14	1.17
10	1.32	1.24
11	1.24	0.98
12	1.41	1.23
13	1.23	1.33
14	1.23	1.17
15	1.07	1.19
16	0.99	1.11
17	1.28	0.94
18	1.22	1.13
19	1.11	1.13
20	1.24	1.22
21	0.98	1.21
22	1.15	1.19
23	1.17	1.34
24		
Number of patients with hyperphosphataemia		**0(out of 24)**

Table 11 Total serum phosphorus for patients who underwent subtotal thyroidectomy in mmol/l before surgery and 24 hours after surgery (number of patients was 46)

	Before surgery	**24 hrs after surgery**
1	0.99	1.29

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2	1.32	1.38
3	1.26	1.24
4	0.98	1.34
5	1.31	1.23
6	1.26	1.26
7	1.16	1.31
8	1.31	1.39
9	1.19	**1.49**
10	1.33	1.29
11	1.19	1.21
12	1.25	1.37
13	1.18	1.33
14	1.28	1.17
15	1.09	1.21
16	0.94	1.11
17	1.28	0.94
18	0.94	1.13
19	1.18	1.21
20	1.34	1.22
21	1.44	1.21
22	1.39	**1.54**
23	1.31	1.37
24	1.25	1.31
25	1.24	1.35
26	1.21	**1.50**
27	1.31	1.19
28	1.21	1.11
29	1.22	0.94
30	0.98	1.43
31	1.15	1.21
32	1.37	**1.53**
33	1.40	1.21
34	1.29	1.19
35	1.29	1.34
36	1.25	1.23
37	1.24	0.97
38	1.31	**1.49**
39	0.97	1.43
40	1.16	1.24
41	1.29	1.33
42	1.29	1.22
43	1.31	1.17
44	1.21	1.39
45	1.21	1.32
46	1.12	0.94
Number of patients with hyperphosphataemia		**5(out of 46) All are asymptomatic**

Table 12 Total serum phosphorus for patients who underwent near total thyroidectomy in mmol/l before surgery and 24 hours after surgery (number of patients was 14)

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	Before surgery	**24 hrs after surgery**
1	0.99	1.31
2	1.32	**1.52**
3	1.31	**1.54**
4	0.98	1.19
5	1.24	1.42
6	1.28	**1.55**
7	1.14	1.39
8	1.37	1.39
9	1.21	1.38
10	1.25	1.43
11	1.17	**1.49**
12	1.29	1.39
13	1.24	**1.53**
14	1.23	**1.47**
Number of patients with hyperphosphataemia		**6(out of 14) All are asymptomatic**

Table 13 Total serum phosphorus for patients who underwent total thyroidectomy in mmol/l before surgery and 24 hours after surgery (number of patients was 20)

	Before surgery	**24 hrs after surgery**
1	0.99	1.39
2	1.32	**1.48**
3	1.31	1.31
4	0.98	**1.45**
5	1.24	**1.49**
6	1.28	**1.51**
7	1.14	**1.53**
8	1.37	**1.49**
9	1.21	**1.58**
10	1.25	**1.54**
11	1.17	1.43
12	1.29	1.39
13	1.24	1.43
14	1.23	1.39
15	0.99	1.39
16	1.32	**1.51**
17	1.31	1.36
18	0.98	1.39
19	1.24	1.39
20	1.28	**1.45**
Number of patients with hyperphosphataemia		**10(out of 20) All are asymptomatic**

Table 14 Values of calculated t, tabulated t and p-value for phosphorous changes after surgery according to the type of surgery (extent of thyroidectomy)

Type of surgery	Calculated t value	Tabulated t value	p-value
Lumpectomy	1.45	2.262	> 0.05

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Lobectomy	0.71	2.056	> 0.05
Subtotal	1.923	3.2815	< 0.002
Near total	10.5	2.131	< 0.001
Total	8.27	2.030	< 0.001

P- Value > 0.05 is considered non-significant
P- Value < 0.05 is considered significant
P- Value < 0.001 is considered highly significant

Table 15 Total serum parathyroid hormone for patients who underwent lumpectomy in pg/ml before surgery and 24 hours after surgery (number of patients was 8)

	Before surgery	**24 hrs after surgery**
1	23	22
2	34	32
3	21	30
4	41	39
5	33	35
6	42	40
7	19	20
8	32	35
Number of patients who developed hypoparathyroidism		**0 (out of 8)**

Table 16 Total serum parathyroid hormone for patients who underwent lobectomy in pg/ml before surgery and 24 hours after surgery (number of patients was 24)

	Before surgery	**24 hrs after surgery**
1	18	17
2	17	19
3	26	27
4	28	26
5	39	35
6	31	33
7	17	18
8	18	17
9	26	24
10	41	39
11	36	38
12	32	34
13	29	31
14	38	36
15	36	31
16	41	39
17	19	18
18	17	21
19	16	22
20	21	20
21	24	23

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22	26	27
23	29	30
24	37	36
Number of patients who developed hypoparathyroidism		**0 (out of 24)**

Table 17 Total serum parathyroid hormone for patients who underwent subtotal thyroidectomy in pg/ml before surgery and 24 hours after surgery (number of patients was 46)

	Before surgery	24 hrs after surgery
1	42	39
2	35	9
3	33	32
4	19	10
5	24	8
6	33	29
7	37	9
8	42	41
9	15	15
10	19	19
11	20	17
12	21	10
13	26	10
14	32	11
15	17	8
16	19	12
17	29	10
18	38	31
19	48	46
20	42	38
21	49	10
22	35	34
23	33	31
24	24	21
25	19	17
26	23	10
27	32	29
28	33	31
29	43	40
30	47	42
31	19	16
32	25	21
33	27	9
34	29	28
35	27	10
36	36	39
37	39	10
38	37	39
39	39	36
40	31	30

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41	41	39
42	19	17
43	44	41
44	41	39
45	17	13
46	23	18
Mean		
Number of patients who developed hypoparathyroidism		12 (out of 46)

Table 18 Total serum parathyroid hormone for patients who underwent near total thyroidectomy in pg/ml before surgery and 24 hours after surgery (number of patients was 14)

	Before surgery	**24 hrs after surgery**
1	24	12
2	26	**10**
3	45	14
4	19	13
5	17	**8**
6	13	15
7	28	12
8	42	16
9	26	**10**
10	25	**9**
11	29	**8**
12	33	13
13	37	**10**
14	39	**10**
Number of patients who developed hypo-parathyroidism		**7 (out 0f 14)**

Table 19 Total serum parathyroid hormone for patients who underwent total thyroidectomy in pg/ml before surgery and 24 hours after surgery (number of patients was 20)

	Before surgery	**24 hrs after surgery**
1	18	12
2	19	**10**
3	16	**8**
4	25	**8**
5	36	19
6	32	**7**
7	39	**10**
8	40	**9**
9	41	**8**
10	19	**10**
11	40	**10**
12	24	11
13	29	**9**
14	28	**10**

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15	18	**8**
16	39	17
17	44	**10**
18	18	**8**
19	19	17
20	41	15
Number of patients who developed hypoparathyroidism		**14 (out of 20)**

Table 20 Values of calculated t, tabulated t and p-value for parathormone changes after surgery according to the type of surgery (extent of thyroidectomy)

Type of surgery	Calculated t value	Tabulated t value	p-value
Lumpectomy	0.7	2.306	> 0.05
Lobectomy	0.2	2.056	> 0.05
Subtotal	5.87	3.5202	< 0.001
Near total	6.96	2.131	< 0.001
Total	8.5	2.075	< 0.001

P- Value > 0.05 is considered non-significant
P- Value < 0.05 is considered significant
P- Value < 0.001 is considered highly significant

Regarding the changes that occurs in the serum level of calcium, phosphorous and parathyroid hormone following subtotal ,near total and total thyroidectomy .the results were significant to highly significant with a p-value < 0.05_ < 0.001 with respect to increase serum level of phosphorous and decrease in serum calcium and parathyroid hormone levels.

While the results weren't significant in patients underwent lumpectomy or lobectomy with a p-value>0.05

DISCUSSION

Hypocalcemia after near total to total thyroidectomy is the most common transient complication among these related to thyroid surgery.[**Jacobs JK,et al 1983, Reeve T 2000]** Although being self-limiting in nature, it is of particular concern, due to its delayed manifestations of symptoms. As described in a study by (Grodski and Serpell, 2008) **[Grodski S, Serpell J. 2008]** incidence of hypocalcaemia is around 18-30%, and occurs after 24-48 hrs post-operatively. Normal serum calcium value ranges between 2.1 and 2.6 mmol/L. Symptoms of hypocalcaemia occur when serum calcium level lies below 2 mmol/L. Percentage of patients in whom hypocalcaemia occurs after near total to total thyroidectomy ranges between 10.2% and 80% approximately. [**Abboud B, 2002]** Thus, close monitoring of post-operative serum calcium concentration is usually recommended in high-risk patients. **[Kihara M, et al 2005]**
In most patients hypocalcaemia after thyroid surgery is self-limiting but in some it may be potentially dangerous. **[Mittendorf EA,et al 2004]** Parathyroid injury/ removal is the most common cause of hypocalcaemia. **[Lindblom P, et al 2002]**

Various strategies for diagnosing and managing post thyroidectomy hypocalcaemia have been used. More recently measurement of parathyroid hormone (PTH) after total thyroidectomy has been utilized to try to predict those patients at the risk of developing post thyroidectomy hypocalcaemia. **[Grodski S, Serpell J. 2008]**
Many studies support our study in which there is large percentage of patients who undergoes thyroid surgery extending from subtotal to total thyroidectomy shows up t0 45% decrease in serum calcium.[Reeve T,et al 2000]
Many studies based on the fact that large percentage of patients developed post thyroidectomy hypocalcaemia advocate routine prescription of vitamin D and calcium post thyroidectomy to avoid the adverse features of hypocalcaemia. Such studies

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include:

1- Study done by Bellantone R1, Lombardi CP, Raffaelli M, Boscherini M, Alesina PF, De Crea C, Traini E, Princi P. named Is routine supplementation therapy (calcium and vitamin D) useful after total thyroidectomy? [Bellantone R,et al 2002]
The study involve seventy-nine patients who underwent total thyroidectomy were randomly allotted to one of the following groups: (1) group A, no treatment; (2) group B, given oral calcium 3 g per day; (3) group C,given oral 3 g + Vitamin D 1 mg per day. Treatment was started on postoperative (PO) day 1 in groups B and C. The results was fewer patients in groups B and C experienced symptoms when compared with group A (P <05). Patients in groups B and C had only minor symptoms, whereas 2 patients in group A experienced major symptoms and 6 required intravenous calcium (P <.01).;
2- Another study done by Roh JL1, Park JY, Park CI. Prevention of postoperative hypocalcemia with routine oral calcium and vitamin D supplements in patients with differentiated papillary thyroid carcinoma undergoing total thyroidectomy plus central neck dissection. [Roh JL,et al, Park JY, Park CI. 2009]
The study involves 197 patients with differentiated papillary thyroid carcinoma, 49 underwent total thyroidectomy alone, and 148 underwent total thyroidectomy plus central neck dissection (CND). The latter were randomized to oral calcium 3 g/day plus vitamin D 1 mg/day (Group A, n=49); calcium alone (Group B, n=49); or no supplements (Group C, n=50). Hypocalcemic symptoms, serum calcium, and parathyroid hormone (PTH) levels were compared among the groups.
The results were: group C had significantly higher incidences of symptomatic (26.0% vs 6.1%; P<.015) and laboratory (44.0% vs 14.3%; P<.015) hypocalcemia than the group without CND. The incidences of symptomatic and laboratory hypocalcemia were significantly decreased in Groups A (2.0% vs 8.2%, respectively) and B (12.2% vs 24.5%, respectively) (P<.05) in comparison with group C. Serum calcium levels decreased in most patients after surgery, but recovered earliest in Group A.
3- Another study done by Roh JL1, Park CI. (Routine oral calcium and vitamin D supplements for prevention of hypocalcemia after total thyroidectomy). [Roh JL, , Park CI. 2006]
The study involve ninety patients who underwent total thyroidectomy were randomly assigned to routinely receive or not receive a supplement containing oral calcium (3 g/d) and vitamin D (1 g/d) for 2 weeks. Hypocalcemic signs and symptoms, serum calcium, and parathyroid hormone (PTH) levels were monitored and compared between the 2 groups.
The results were the incidences of symptomatic and laboratory hypocalcemia were significantly lower in the oral calcium/vitamin D group than in the group not receiving the supplement: 3 of 45 patients (7%) versus 11 of 45 (24%) and 6 of 45 (13%) versus 16 of 45 (36%), respectively (P < or < 0.02). The hypocalcemic symptoms were minimal in the supplement group but more severe in the group not receiving the supplement. Serum calcium levels decreased in both groups after surgery but recovered earlier in the supplement group.
4- Others who prove post-thyroidectomy hypocalcaemia and the need for routine postoperative supplementation of vitamin D and calcium are:
A. Tartaglia et al. demonstrated that oral administration of calcitriol and calcium salts after total thyroidectomy significantly decreases the risk of severe postoperative hypocalcemia,
[Tartaglia F ,et al 2005]
B. Pisaniello et al. concluded that early and combined oral administration of both calcium and vitamin D seemed to have major efficacy in preventing and treating postoperative hypocalcemia, demonstrating mean serum calcium levels higher than those of patients who received only oral calcium administration.[Pisaniello D ,et al 2005]
C. Uruno et al. mentioned that a prophylactic infusion of calcium solution after total thyroidectomy may be useful in reducing the development of symptomatic hypocalcemia and reducing a patient's risk of discomfort and anxiety due to hypocalcemia.
[Uruno T, et al 2006]

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D. Kurukahvecioglu et al. showed that routine postoperative calcium and vitamin D supplementation therapy may be useful for the prevention of symptomatic hypocalcemia after total thyroidectomy and may allow for a safe and early discharge from the hospital.[Kurukahvecioglu O,et al 2007]

All of the above studies proved post extensive thyroidectomy hypoparathyroidism and clinical and subclinical hypocalcaemia which mandate the need for routine supplementation of calcium with or without vitamin D Regarding hyperphosphataemia; as we read in the literature review, the most important regulator of phosphate homeostasis is Fibroblasts Growth Factor-23 (FGF-23) and it doesn't completely depend upon parathyroid hormone.

In the presence of normal renal function exra-phosphate in the blood will be excreted in the urine even in patients with hypoparathyroidism. This is why we seldomly face the problem of hyperphosphataemia in practice at the time there is severe hypoparathyroidism and symptomatic hypocalcaemia.

CONCLUSIONS

- A significant postoperative hypocalcaemia and hypoparathyroidism was identified in patients who undergoes subtotal, near total and total thyroidectomy.
- Nearly all patients did not prescribe neither oral calcium nor vitamin D as a routine in patients undergoes near total to total thyroidectomy.
- Significant number of patients develops subclinical hypocalcaemia and this can deceive the surgeon that there is no hypocalcaemia at all.
- No single patient developed symptomatic hyperphosphataemia. This is explained by being the homeostasis of phosphorus doesn't depend solely on parathyroid hormone but others plays major role as fibroblast growth factor 23.

RECOMMENDATION

We recommend routine supplementation of oral calcium and/or vitamin D for at least two weeks in patients underwent extensive thyroid surgery to decrease the risk of postoperative hypocalcaemia.

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