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Original Research Paper

Pharmacy

SCRUTINIZING CKD ASSOCIATED SECONDARY HYPERPARATHYROID DOSSIER

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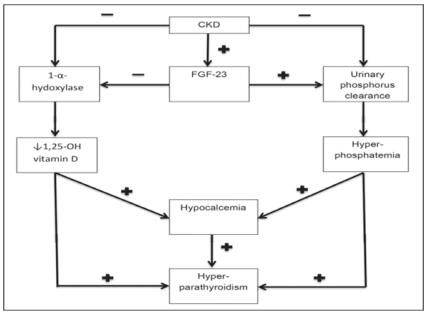
ABSTRACT

The kidney: improving global outcome guideline recommended that screening of renal hyperparathyroidism(rHPT) should be considered during CKD stage 3. Renal hyperparathyroidism (rHPT) or secondary hyperparathyroidism is a common complication of chronic kidney disease characterized by elevated parathyroid hormone levels secondary to derangements in the homeostasis of calcium, phosphate, and vitamin D.A 55 years old male patient presented with swelling in the neck associated with difficulty in speaking and sleeping, Reduced appetite(since 15days), Anasarca(since 15days), Shortness of breath(since 15days), Nausea, Vomiting(1 episode before hospitalization), Associated with 2 cm thyroid nodule and with comorbidities (Chronic Kidney Disease(CKD) , Hypertension(HTN) and Cardiovascular Disease(CVD).Patients with rHPT have high risk of developing cardiovascular and bone diseases, This case study shows that there is a need in improving therapeutic strategies and Patient's medical compliance, which makes a critical component in improving outcome and patients quality of life.

KEYWORDS :Renal hyperparathyroidism (rHPT), Anasarca, Chronic Kidney Disease(CKD) , Hypertension(HTN), Cardiovascular Disease(CVD).

INTRODUCTION:-

- Secondary hyperparathyroidism or renal hyperparathyroidism(rHPT) occurs when the parathyroid glands become enlarged and release too much PTH, causing a high blood level of PTH6. There are several reasons why this happens in patients with kidney disease:
- Higher blood phosphorus levels
- The kidneys cannot make active vitamin D (needed to absorb calcium)
- Lower blood calcium levels
- Secondary hyperparathyroidism can cause bone disease. It can also cause calcium to build up in tissues and organs such as the heart and blood vessels5.
- Chronic Kidney disease(CKD) is the progressive, irreversible deterioration of renal function usually resulting from long-standing kidney disease.
- CKD sometimes derives from ARF that does not respond to treatment
- Left ventricular dysfunction is a condition that often leads to heart failure. It may either be asymptomatic or also have symptoms of heart failure. It is characterized by dilation of the left ventricle and vasoconstriction.



- Figure 1: Schematic representation of the pathogenesis of renal hyperparathyroidism6

CLASSIFICATION:-

- CKD is defined as kidney damage or GFR 60ml/mint/1.73m2 for % 3months
- Kidney damage is defined as pathological abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies, CKD has been classified as stageI to V to denote the severity of renal impairment.
- Generally, CKD, if left untreated, progresses at a predictable, steady rate from steady rate from stage I through stage V
- Stage I is defined as kidney damage with a normal or increased GFR1. The corresponding GFR in stage I CKD is usually and 90Ml /Mint/1.73m2
- Stage II is defined as Kidney damage or a mildly decreased GFR(60 - 89ml /mint/1.73m2
- Stage III signifies moderate reductions in GFR (30-59mL / mint /1.73m2)
- Stage IV connates a GFR of 15-29mL /mint /1.73m2
- StageV is kidney failure3 or a GFR of 15mL / mint /1.73m2

CAUSES OF CKD IN ADULTS:-

- Diabetic Nephropathy
- Hypertension
- Glomerulonephritis
- Polycystic kidney disease
- Long standing vascular disease(eg-renal artery stenosis)
- Long standing obstructive uropathy(eg-renal calculi0\
- Exposure to Nephrotoxic agents2
- CLINICAL MANIFESTATIONS:-
- A. Metabolic Abnormalities:
- Hyponatremia or hypernatremia(based on relative sodium or water intake)
- Hyperkalemia

- Fluid overload
- Edema
- Metabolic acidosis
- Calcium and phosphate metabolism is altered due to hyperparathyroidism3
- Neurological Manifestations:
- Short attention span
- Loss of memory
- Listlessness
- Confusion
- Stupor2
- Seizures
- Coma
- Peripheral neuropathy and pain
- Itching and a burning sensation(particularly in the feet and legs)3
- C.Cardiovascular Problems:
- Arterial hypertension
- Peripheral edema
- CHF and pulmonary edema2
- D. GI Manifestations:
- Hiccups
- Anorexia
- Constipation
- Stomatitis2
- E.Respiratory Problems:
- Dyspnoea
- Pulmonary edema
- Pleuritic pain1
- Uremic pleuritis2
- F.Integumentary Findings:
- Pale yellowish,dry, scaly skin
- Ecchymoses,
- Purpura
- Brittle nails and hair3
- G.Musculoskeletal Changes:
- Muscle and bone pain
- Calcifications in the brain, heart, eyes , joints and vessels
- Soft tissue calcifications and renal
- Osteodystrophy1
- H. Haematological Disturbances:
- Anaemia
- Pallor of the skin, nail beds,Palms conjunctivae and mucosa1
- Abnormal bruising or ecchymoses
- Uremic bleeding due to the platelet inactivation2

- **Case study**:
- PATIENT DEMOGRAPHIC PROFILE:
- AGE:55YEARS
- GENDER: MALE
- UNIT: NEPHROLOGY
- DATE OF ADMISSION: 12-2-2017
- DATE OF DISCHARGE: 19-02-2017
- CHIEF COMPLAINTS;
- Asymptomatic 2months back and noticed swelling in the neck associated with difficulty in speaking and sleeping
- Reduced appetite(since 15days)
- Anasarca(since 15days)
- Shortness of breath(since 15days)
- Nausea
- Vomiting(1 episode before hospitalization)

PMHX:

- Hypertension(since 2 years, patient on Lasix-Furosemide 40mg OD)
- Swelling in the neck

FMHX:

- No known family history of CAD, Diabetes mellitus

PHX:

- Reduced appetite
- PROVISIONAL DIAGNOSIS::HASHIMOTOS THYROIDITIS with CHRONIC KIDNEY DISEASE 3A(GFR:30-59ml/Min/1.73m2)& **HYPERTENSION**
- DAY WISE TREATMENT

- **DAY 1:**
- C/O: Shortness of breath, reduced appetite, Anasarca, Nausea, Vomiting
- O/E: Patient conscious, coherent ,oriented
- Temp: 98.6F
- PR: 86b/mint
- BP:160/90mmHg
- RR:22/mint
- Adv: Sr.creatinine, Sr.electrolytes, CBP, USG Abdomen, HIV I &II antibodies,Thyroid Profile, HBsAg test, USG Abdomen and pelvis, 2D Echo. LFT, CUE.

- **DAY 2:**
- C/O: One episode of Generalized Tonic Clonic Seizures(GTCS). Hypoglycemia
- MANAGEMENT: Patient was shifted to CCU and loading dose of Epitril 0.5mg(Clonazepam) and Inj. Midazolam bolus 2cc was given; 2 pint 25% dextrose was given (stat) followed by 1pint 5%dextrose @20ml/hr
- O/E: GRBS 39mg/Dl,
- Thyroid Profile
- T3:1.0nmol/L(0.92-2.33)
- T4:99nmol/L(60-120)
- TSH: 2.1 mU/L(0.4-5.2)
- MEDICATIONS: CST.
- Surgery has it's place and efficacy in the treatment of selected patients with Hashimoto's thyroiditis and compression symptoms or nodular forms with dominant nodules over 2 cm

- **DAY 3:**
- C/O: No fresh complaints, no episode of seizure, general condition better
- O/E: Patient conscious & Coherent
- MEDICATIONS: CST

- **DAY 4 AND DAY 5:**
- C/O: No fresh complaints
- O/E: Patient underlying Hemodialysis
- BP:150/90mmHg
- RR:21/mint
- PR:82b/mint

- **DAY 6:**
- C/O:No fresh complaints
- Adv: Add Inj.MVI in 100ml NS/OD(Multivitamin and Cap.Raricap forte(Iron +Folic acid50mg /0.3mg), Tab.Arkamin 0.1mg/BD(Clonidine)

- **DAY 7:**
- C/O: No fresh complaints
- O/E:Patient conscious, coherent
- MEDICATIONS:CST

- **DAY 8:-**
- C/O:No fresh complaints
- Adv: Discharge the patient
- MEDICATIONS: CST

S.NO	TESTS	LAB VALUE(1st day)	LAB VALUE (5th day)	NORMAL VALUE	
1.	Serum calcium	6.5mg/dL	7.6mg/dl	8.5-10.2mg/dL	
2.	PTH	77pg/ml	68pg/ml	10-65pg/ml	

3.	Hb%	5.3g/dl	7.8g/dl	11.5-17g/dl	
4.	RBC count	1.72lakhs/mm3	2.8lakhs/mm3	3.8-6.5lakhs/mm3	
5.	Sr.Creatinine	5.8mg/dl	3.5mg/dl	0.6-1.2 mg/dl	
6.	Sr.Phosphous	9mg/dl	4mg/dl	2.1-5.6mg/dl	
7.	Sodium	136mmol/L	138mmol/L	135-145mmol/L	
8.	Potassium	4.1mmol/L	4.2mmol/L	3.5-5.0mmol/l	
9.	Chloride	97mmol/L	101mmol/L	96-106mmol/L	
10.	Alkaline phosphate	109 I/U	82I/U	38-94I/U	
11.	Blood Urea	87U/L	72U/L	10-45U/L	
12.	Urine pus cells	1-2/HPF	0-2/HPF	0-4/HPF	
13.	Urine Epithelial cells	1-2/HPF	0-1/HPF	0-4/HPF	
14.	Urine albumin	++++	+++	0	
15.	RBS	57mg/dl	72mg/dl	80-150mg/dl	

OTHER INVESTIGATIONS:-

- ULTRASOUND: Abdomen and Pelvis
- MICROBIOLOGY: HIV I & II Antibodies, HBsAg
- 2D Echo:

Mildly dilated cardiac chambers
Mild apical septal hypokinesia
LV systolic and Diastolic dysfunction
Sclerotic aortic valves with no significant stenosis(Age related)
FINAL INVESTIGATION:-
Secondary Hyperparathyroidism , Chronic Kidney Disease with Hypertension & Left Ventricular Dysfunction

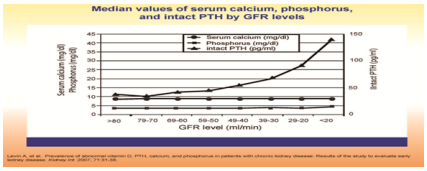
CASE STUDY: SOAP FORMAT:

SUBJECTIVE:-

- A 55years old male was admitted in Nephrology department with chief complaints of shortness of breath(since 15 days),decreased appetite , anasarca, nausea and vomiting(1 episode).
- There was a known history of Hypertension(since 2 years)
- No known history of Coronary artery disease , diabetes and epilepsy
- The patient was non-smoker and a non-alcoholic

OBJECTIVE:-

- Abdomen and Pelvis ultrasound revealed bilateral grade II- III renal parenchymal changes
- 2D Echo showed dilated left ventricle, concentric left ventricular hypertrophy, global hypokinesia , moderate LV dysfunction and Ejection fraction 40%
- Haemoglobin levels and RBC count were decreased indicating anaemia(5.3gm/dl , 1.72lakhs/mm3)
- Elevated Serum phosphorus and Alkaline Phosphatase indicated secondary hyperparathyroidism
- Increased blood urea(120mg/dl) and Serum Creatinine (5.8, 7.3mg/dl) indicates chronic renal failure.
- Presence of pus cells, epithelial cells and albumin in urine indicates underlying kidney disease.



ASSESSMENT:-

- **PROBLEM 1: ANASARCA:**
- Patient showed signs of anasarca on admission
- **MEDICATION :**Tab. Lasix(Furosemide) 40mg/OD

- **PROBLEM 2:NAUSEA AND VOMITING:**
- Patient had 1 episode of vomiting in day 1
- MEDICATION: No medication were given

- **PROBLEM 3:-HYPERTENSION:**
- Hypertension, or high blood pressure, is present in 80-85% of people with CKD
- Patient had a known history of hypertension since 2 years and was taking Furosemide 40mg OD
- **MEDICATION:** Tab. Arkamin (Clonidine) 0.1mg

- **PROBLEM 4: LV DYSFUNCTION**
- **MEDICATION:** Tab. Nicardia (Nifedipine) 10mg BD
- Tab. Cardivas (Carvedilol) 3.125mg OD
- Tab.Lanoxin (Digitoxin) 0.25mg alternate day

- **PROBLEM 5: SECONDARY PARATHYROIDISM IN KIDNEY DISEASE:**
- In the course of CKD, the body begins to retain phosphate . As the disease progresses, high blood phosphate levels can develop.
- **MEDICATION:**-Cap. Bio D3 plus(Calcitriol + calcium)

- **PROBLEM 6: ANAEMIA:-**
- People with CKD are at risk for anaemia. This occurs because improperly functioning kidneys produce reduced amounts of a substance called Erythropoietin. Anaemia can lead to fatigue and other complications.
- Complete Blood picture: Hb% was 5.3gm/dl
- **MEDICATION:** Tab. Livogen-XT(Ferrous fumarate +folic acid)
- Cap. Raciper forte(Iron +Folic acid)

- **PROBLEM 7: DECREASED APPETITE**
- **MEDICATION:** Inj.MVI(Multivitamin)10ml OD

- **PROBLEM 8: PEPTIC ULCER PROPHYLAXIS:**
- **MEDICATION:** Tab. Pan(Pantoprazole)

- **PROBLEM 9: CARDIOVASCULAR DISEASE PREVENTION**
- **MEDICATION:** Tan. Aztor(Atorvastatin)10mg OD HS

PLAN:-

S.NO	FORM	DRUG	DOSE	FREQUENCY	GENERIC NAME	INDICATION
1.	Capsule	Bio D3 Plus	250mg+0.25mg	OD	Calcitriol+Calcium	Hyperparathyroidism
2.	Tablet	Lasix	40mg	OD	Furosemide	Anasarca,Hypertension
3.	Tablet	Pan	40mg	OD	Pantoprazole	Peptic Ulcer Prophylaxis
4.	Tablet	Cardivas	3.125mg	OD	Carvedilol	Hypertension
5.	Tablet	Livogen	100mg+1.5mg+61.8mg	BD	Iron+Folicacid+Zinc Sulphate	Anaemia
6.	Tablet	Nicardia	10mg	BD	Nifedipine	LVD,Hypertension
7.	Tablet	Lanoxin	0.25mg	OD	Digoxin	LVDysfunction
8.	Tablet	Revlamer	800mg	OD	Sevelamer Hydrochloride	Hyperphosphatemia

DISCUSSION:

A 55 years old male patient was admitted to a tertiary care hospital with the chief complaints of swollen neck, difficulty in sleeping and eating (since 15days), Anasarca(since 15days), Nausea and vomiting. Patient's physical examination initially indicated that he might be suffering from **Hashimotos Thyroiditis** but these symptoms started appearing two months back.

Patients thyroid profile showed normal TSH, T3 and T4 but elevated PTH and phosphorus and decreased Haemoglobin levels, serum calcium and Random Blood Sugar(RBS) due to which patient suffered from hypoglycemia during second day of his visit and also an episode of Tonic **Clonic Seizure** for which 2 pint 25% Dextrose was given (stat) followed by 1pint 5%dextrose at 20ml/hr and Clonazepam 0.25mg. The thyroid gland is enlarged (with 2cm large follicle) with normal TSH which shows that it is Nontoxic nodular goiter and the associated lab values of Elevated Phosphorus, PTH with Low calcium levels which is an indicator of Secondary

Hyperparathyroidism

As the patient was suffering from CKD since two years as this condition disturbances the Homeostasis of phosphorus and calcium which leads to increase in PTH and is referred to as renal hyperparathyroidism rPTH). Patient was not suggested to diagnose for renal Osteodystrophy this condition has been mostly seen in CKD stage. As serum creatinine was also elevated causing Nausea and Vomitings.

Patient's Hypertension was not under control even though Antihypertensive drugs were given, this was due to Patients compliance, Patient was also reluctant to take any medication and fluid buildup due to which the body was exacerbated by the underlying CKD causing pressure and volume overload to the heart leading to Cardiovascular complications. 2D echo showed mildly dilated cardiac chamber due to fluid overload .

Patient developed Anemia for which iron supplement were given, and for Elevated Serum Phosphorus Sevelamer 800mg a phosphate binding agent was administered to the patient. Vitamin D supplement was also given for calcium depletion, An antioxidant N-acetyl cysteine would have been helpful in further reducing renal impairment, Probiotic has also been effective in reducing load on kidneys by clearing nitrogenous waste. Parathyroidectomy was performed to remove large follicle but there is also an option of radioactive iodine therapy instead of surgery for Nontoxic nodular goiter.

Patient's medical compliance and negligence of his attenders lead to this case of renal hyperparathyroidism if the patient would have taken medication then hypertension and CKD would have been under control and this Exacerbated constitutional symptoms lead to CVD. Better stratergies are needed to reduce patients compliance and in turn improve patients quality of life.

PHARMACISTS INTERVENTION:

1. **Carvedilol+ Furosemide:** Carvedilol increases and Furosemide decreases serum potassium. Potassium levels must be monitored carefully.
2. **Nifedipine +Atorvastatin:** Nifedipine will increase the level or effect of atorvastatin by affecting hepatic/ intestinal enzyme CYP3A4 metabolism. Significant interaction possible, monitor closely.
3. **Nifedipine+Carvedilol:** Carvedilol and Nifedipine both increase anti-hypertensive channel blocking. Potential for dangerous interaction. Use with caution and monitor closely.
4. **Furosemide+Folic acid:**Furosemide decreases levels of folic acid by increasing renal clearance.
5. **Pantoprazole+Digoxin:** Pantoprazole will increase the level or effect of digoxin by increasing gastric pH. Applies only to oral form of both the agents. Possible serious or life- threatening interaction. Monitor closely. Use alternatives if available.
6. **Atorvastatin+ Digoxin:** Atorvastatin will increase the level or effect of digoxin by P-Glycoprotein(MDRI) efflux transporter. Significant interaction possible,monitor closely.
7. **Nifedipine+ Digoxin:** Nifedipine will increase the level of the digoxin by P-Glycoprotein (MDRI) efflux transporter . Significant interaction possible, monitor closely. Significant interaction possible, monitor closely . Nifedipine will decrease digoxin clearance,increasing plasma concentration and the risk of toxicity. Adjust the digoxin dose as needed.
8. **Carvedilol+ Digoxin:** Carvedilol increases levels of digoxin by enhancing GI absorption. Applies only to oral form of both the agents. Significant interaction possible, monitor closely.
   Carvedilol increases levels of digoxin by decreasing renal clearance.
   Carvedilol increases effects of digoxin by pharmacodynamic synergism, Enhanced Bradycardia.
   Carvedilol and Digoxin both increase serum potassium.
9. **Furosemide+ Digoxin:** Furosemide increases effects of Digoxin by pharmacodymaic synergism.Significant interaction possible, monitor closely. Hypokalemia increases digoxin levels.
10. **Pantoprazole+ Digoxin:**Pantoprazole increases toxicity of digoxin by the other. Potential for interaction, monitor closely. Prolonged use of PPIs may cause hypomagnesemia and increased risk for digoxin toxicity.

PATIENT COUNSELLING:-

Regarding Disease: Chronic kidney disease(CKD), also called as Kidney failure is a condition in which the kidneys lose some of their ability to remove waste and excess water from the blood stream. As waste and fluids accumulate, other body systems are affected, potentially leading to complications.

The most common causes of CKD are diabetes and high blood pressure. In the early stages of CKD, there are no symptoms. The disease can progress to complete kidney failure, also called end-satge renal disease. This occurs when kidney function has worsened to the point that dialysis or kidney transplantation is required to maintain life.

LIFE STYLE MODIFICATIONS:

- Exercise for half an hour/day
- Reduce daily dietary sodium intake to less than or equal to 100mEq(not more than 3mg/day)
- Avoid green leafy vegetables,roots and tubers
- Avoid fruit juices, Squashes, Proprietary drinks like horlicks, Bournvita etc
- Avoid cocoa products like chocolate, coffee etc
- Avoid oil seeds like groundnut, Coconut, Sesame
- Avoid Coconut milk as it is rich in potassium
- Fruits like apple, Guava, Pine apple, Papaya and pears can be taken thrice a week
- Proteins in diet to be taken in moderate amounts such as dals and pulses(3 Serving/day)
- Avoid Pickles, Papads, Salted preserved foods, Soda and Dry fruits
- Water intake should be monitored accurately if urine output is less than intake
- Avoid red meat, Jams, Jellies, Jaggery.

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