Spironolactone Induced Gynecomastia: A Case Report

S. Sahera¹, Dr. Y. Vijaya Bhaskar Reddy², D. Sathish Kumar³, Dr. V. Ramana⁴, Dr. S. Kusuma Kumari⁵

¹Pharma D, Department of Pharmacy Practice, Dr. K.V. Subba Reddy Institute of Pharmacy, Dupadu, Kurnool, AP.
²Professor and HOD, Department of Pharmacology, Kurnool Medical College, Kurnool, AP.
³Patient Safety Pharmacovigilance Associate, Kurnool Medical College, Kurnool, AP.
⁴Professor, Department of Pharmaceutics, Dr. K.V. Subbareddy Institute of Pharmacy, Kurnool, AP.
⁵Assistant Professor, Department of Pharmacy Practice, Dr. K.V. Subbareddy Institute of Pharmacy, Kurnool, AP.

Corresponding Author: Dr. S. Kusuma Kumari
Assistant Professor, Department of Pharmacy Practice,
Dr. K.V. Subbareddy Institute of Pharmacy, Kurnool, AP.

Abstract: Gynaecomastia is generally caused by increased ratio of free circulating oestrogens/androgens or altered effects of these hormones on their correspondent intracellular receptors in the mammary tissue. The pathologies influencing the levels of circulating sexual hormones (i.e. testicular or adrenal neoplasias, hepatic cirrhosis, hyperthyroidism hypogonadism obesity, refeeding syndrome. The active principles known for most frequently causing gynaecomastia are exogenous oestrogens, antiandrogens, 5 alpha reductase inhibitors, spironolactone and cimetidine. Medical history plays a fundamental role in the diagnosis of drug induced gynaecomastia. A large variety of drugs have been implicated in its pathogenesis and they may induce gynaecomastia by decreasing testosterone production, increasing peripheral conversion of testosterone to estradiol and displacing estradiol from sex hormone binding globulin. We present a case report of 41 old male patient affected by spironolactone induced gynaecomastia and discuss its pathogenetic mechanism.

Key Words: Gynaecomastia, Spironolactone, Decreased Testosterone Production, Conversion of Testosterone to estradiol, Spironolactone induced Gynaecomastia, Drug induced Gynaecomastia

Date of Submission: 19-10-2019
Date of Acceptance: 05-11-2019

I. Introduction

Gynaecomastia is clinically defined as benign enlargement of male breast due to proliferation of glandular component with deposition of fat. Gynaecomastia is a well described adverse effect of spironolactone and is related to dose and duration of treatment.

Spironolactone induces gynaecomastia by decreasing testosterone production, increasing peripheral conversion of testosterone to estradiol and displacing estradiol from sex hormone binding globulin.

A Large variety of drugs are known to cause gynaecomastia among them spironolactone are rarely reported. Here in we report a case of 41 years old male patient with spironolactone induced gynaecomastia.

II. Case Report

A 41 Year old male patient was referred to General Medicine Department Government General Hospital Kurnool with the chief complaints of fever, fatigue, black colored stools, swelling around umbilicus. He has similar complaints in the past since 1 yr known case of HBV related Decompensated cirrhosis of liver disease with portal hypertension with esophageal varices grade 3-2 column, Acute kidney injury shortness of breath recovered, known case of pulmonary TB one yr back. On physical examination He showed enlargement of male breast was present GYNECOMASTIA Medical History revealed that the patient had received Spironolactone 50mg/ day from 30 may 2018 for Decompensated cirrhosis of liver with portal hypertension and from 6 months there was slowly enlargement of breast was observed but no pain was appeared.

The patient had been taking spironolactone 50mg/day for 2yrs as a part of his medication regimen for Decompensated Cirrhosis of Liver Disease with Portal Hypertension.

The patient reported the chief complaints of fever, fatigue, black colored stools, swelling around umbilicus from 1 yr.

There was enlargement of male breast was also reported.

DOI: 10.9790/0853-1811015659
Based on the physical examination and on the relationship between the drug and onset of gynecomastia a diagnosis of drug induced Gynaecomastia was made. Withdrawal of the culprit drug and short term tablet Inderol 40 mg/ day was given led to complete and permanent remission of the disease. Rechallenge was done to avoid unnecessary risk to the patient.

TABLE 1: DRUGS MOST FREQUENTLY INVOLVED IN DRUG INDUCED GYNECOMASTIA

1. POTASSIUM SPARING DIURETICS: Spironolactone
2. CALCIUM CHANNEL BLOCKERS: Nifedipine
   Amlodipine
   Diltiazem
   Verapamil
3. ANGIOTENSIN CONVERTING ENZYME INHIBITORS: Captopril
   Enalapril
4. ALPHA RECEPTOR BLOCKERS: Doxazosin
   Prazosin
5. CENTRALLY ACTING AGENTS: Clonidine
   Methyldopa
   Reserpine
6. ANTIANDROGENS: Bicalutamide
   Flutamide
7. 5 ALPHA REDUCTASE INHIBITORS: Finasteride
   Dutasteride
8. H2 HISTAMINE RECEPTOR BLOCKER: Cimetidine
9. PROTEASE INHIBITORS OF ANTIRETRO VIRAL THERAPY : Saquinavir
   Lopinavir
10. ANTIPSYCHOTIC DRUG : Haloperidol
11. SEVERAL CHEMOTHERAPY DRUGS: Methotrexate
    Carmustine
    Etoposide
    Cytarabine
12. ANTIRETRO VIRAL DRUGS REVERSE TRANSCRIPTAS INHIBITORS: Stavudine
    Zidovudine
    Lamivudine
13. ENVIRONMENTAL EXPOSURE : Phenothrin
    anti parasitical
14. EXOGENOUS HORMONES : Oestrogens
    Androgens
15. ANTIFUNGAL DRUG : Ketoconazole
16. PROTON PUMP INHIBITORS : Omeprazole
17. CARDIOVASCULAR DRUGS: Phytoestrogens
18. DRUGS RARELY CAUSING GYNECOMASTIA :

III. Discussion

Gynecomastia is clinically defined as benign enlargement of male breast due to proliferation of glandular component with deposition of fat. Normally estrogen stimulates the proliferation of breast epithelial cells and androgens have an inhibitory. Gynecomastia usually results due to imbalance between actions of estrogens and androgen on the breast tissue. The causes for gynecomastia can be either physiological (neonatal , pubertal or involutinal ) or pathological conditions ( drug induced endocrine disorders such as testicular , adrenocortical or pituitary tumors , hyperthyroidism , and non-endocrine causes such as cirrhosis ,starvation , stress and renal failure .

Drugs associated with gynecomastia are bicalutamide , flutamide , nilutamide , leuprolide ,metronidazole ,ketoconazole ,isoniazide, minocycline, digoxin , spironolactone, amlodipine ,nifedipine , verapamil , captopril , enalapril , amiodarone, methyldopa, minoxidil, methotrexate , vincristine, diazepam,
phenytoin, androgens, anabolic steroids, estrogen, theophylline, d-penicillamine, cimetidine, and metoclopramide.

Spironolactone does alter the peripheral metabolism of testosterone resulting in changes in the ratio of testosterone to estradiol which could contribute to the production of gynecomastia.

Spironolactone is a well known cause of gynecomastia and may act by displacing androgen from the androgen receptor and sexual hormone binding globulin and by causing increased metabolic clearance of testosterone and higher estradiol production.

The patients spironolactone was replaced with indelol that lowers the incidence of gynecomastia.

Spironolactone induces gynecomastia by blocking androgen production, by blocking androgens from binding to their receptors and by increasing both total and free estrogen levels.

Production of testosterone is decreased by inhibiting 17 alpha hydroxylase and 17, 20 – desmolase, which are enzymes in the testosterone synthesis pathway.

Oestrogens levels are increased by enhancing the peripheral conversion of testosterone to estradiol and by displacing estradiol from sex hormone binding globulin.

IV. Conclusion

Spironolactone causing bilateral gynecomastia is well established. Eliciting proper history and performing examination can result in correct diagnosis. Stopping the offending drug resolves the problem and thereby can save the patient from embarrassment, anxiety, physical discomfort of investigations. Patients should be informed about this side effect while prescribing this drug, and alternatively indelol can be used.

Physician should discuss about serious adverse drug reactions while prescribing a medication, if he get any adverse drug reaction he will discontinue the drug and consult the physician.

References