Case report

MULTIPLE DISEASES REQUIRE VIGILANT MONITORING AND PROTOCOLS; A CASE REPORT

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ABSTRACT

High blood pressure is regarded as "the silent killer" because it often has no warning signs or symptoms. About 60% of people who have diabetes also have high blood pressure. Diabetes mellitus and metabolic syndrome are common in patients with chronic obstructive pulmonary disease (COPD) because COPD directly increases the insulin resistance. Insulin resistance commonly occurs with obesity, dyslipidaemia and hypertension. Together these make up the 'metabolic syndrome', which is a major determinant of cardiovascular morbidity and mortality. Thus; the purpose of this case study is to understand the complexity of diseases that can arise problems in treatment regimes to avoid clinical errors for optimizing the therapy plans. A 58 year old male was presented in the medical ward of semi-private hospital, Rawalpindi, Pakistan with chief complaints of acute exacerbation of COPD, uncontrolled hypertension, known carotid artery stenosis and left sided chest pain. On the basis of his medical investigation, the physician prescribed him tablet Theograde(theophylline) 350mg ½ BID(twice a day), tablet Rast (rosuvastatin) 10mg 1 × HS (at night), Tablet Lasix (furosemide) 40mg 1 × O.D (once a day), tablet Minipress (prazosin) , tablet Panadol (paracetamol) 2× TDS(three times a day), tablet Famot (famotidine) 40mg 1 × O.D, Atem (Ipratropium bromide) nebulization three times a day, Ventolin (salbuatamol) nebulization four times a day, Brufen (ibuprofen) cream, steam inhalation three times a day and Injection Leflox(levofloxacin) 500mg IV × O.D. vital signs showed temperature 99°F, respiratory rate 21 breaths/ minute, Blood pressure 150/105, pulse 86/minute and PEFR 250 L/minute. Cyanosis and edema were observed. CVS= S1+S2+ loud R2. There were certain clinical and pharmaceutical inaccuracies were noted during the treatment. Thus; a rational clinical practice needed to implement health care system. Specially; the avoidable clinical errors are required to be addressed to optimize the regimens. The need of hour is a qualified pharmacist side by side with an experienced prescriber which will help to avoid the undesired health related consequences.

Key Words; Blood pressure, diabetes, COPD, metabolic syndrome, pharmaceutical care

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INTRODUCTION

Blood pressure is the force of blood against the artery walls as it circulates through the body. High blood pressure or hypertension is the constant pumping of blood through blood vessels

with excessive force. It can harden the arteries, decreasing the flow of blood and oxygen to the heart. This reduced flow can cause angina, heart failure, heart attack. [1]

Although no direct cause has been identified, there are many factors such as sedentary lifestyle**,** [2] smoking, stress, potassium deficiency [3] (hypokalemia), obesity [4]**,** salt (sodium) sensitivity [5], alcohol intake [6], and vitamin D deficiency [7] that increase the risk of developing hypertension. Hypertension can be hereditary.

Hypertension is usually without any symptoms, but could give rise to early-morning headache, nosebleed, irregular heartbeats and buzzing in the ears. Other Symptoms of include tiredness, nausea, vomiting, confusion, anxiety, and chest pain and muscle tremors. [1]

Globally, nearly one billion people have high blood pressure (hypertension); of these, two-thirds are in developing countries.[1] High blood pressure is one of the common cardiovascular risk factors in Pakistan affecting one in three individuals over the age of 45 years.The National Health Survey of Pakistan (NHSP-1990-94) shows that 5.5 million men and 5.3 million women were hypertensives. [8] According to a cross-sectional survey of Gulshan-eSikanderabad, a squatter settlement situated near Ziauddin Medical University (ZMU), Karachi. Blood pressure was measured in 63 (38%) males and 135 (83%) females.Out of which, 11 (17.5%) males and 19 (14%) females were screened hypertensives. Hypertensives were older as compared to normotensives. Hypertensives were 9.7 times more likely to be diabetic as compared to normotensives in this study. [9]

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood sugar. It is classified into Type 1 diabetes (insulin dependent) whose symptoms include: excessive excretion of urine (polyuria), thirst, constant hunger, weight loss, and fatigue and type 2 diabetes (non-insulin-dependent) and is largely the result of excess body weight and physical inactivity. Symptoms may be similar to those of Type 1 diabetes, but are often less marked. [10]

Currently DM affects 240 million people worldwide and this number is projected to increase substantially to 380 million by 2025, with 80% of burden in low and middle income countries [11]. Pakistan currently ranks at 7th position in the list of countries with major burden of DM. Pakistan belongs to high prevalence area, currently having 6.9 million affected people, with projected estimates expected to double by 2025 and affect 11.5 million people[12].

Chronic obstructive pulmonary disease (COPD) is a lung ailment that is characterized by a persistent blockage of airflow from the lungs- it is more than a “smoker’s cough”. It is not one single disease but an umbrella term used to describe chronic lung diseases that cause limitations in lung airflow. [13]The primary cause of chronic obstructive pulmonary disease (COPD) is tobacco smoke (80-90%) [14][15].Other factors include Occupational dusts and chemicals, [16] [17] [18] air pollution, [19] [20], and frequent lower respiratory infections. The most common symptoms of COPD are breathlessness, abnormal sputum, wheezing, chest tightness, tiredness and a chronic cough. [13]

Diabetes mellitus and metabolic syndrome are common in patients with chronic obstructive pulmonary disease (COPD). COPD may directly increase insulin resistance through effects of chronic inflammation on insulin receptor signalling and through chronic hypoxia and systemic corticosteroid treatment. COPD patients with diabetes have increased risk of pulmonary infection, structural lung damage, hospitalisation and death. Insulin resistance

commonly occurs with obesity, dyslipidaemia and hypertension. (Makarevich AE, et al.,2007).An estimated 64 million people have COPD worldwide in 2004.More than 3 million people died of COPD in 2005.Almost 90% of COPD deaths occur in low- and middle-income countries. According to new estimates for 2030, COPD is predicted to become the third leading cause of death. [13]

CASE REPORT

A 58 year old male was presented in the medical ward of semi-private hospital, Rawalpindi, Pakistan with chief complaints of acute exacerbation of COPD, uncontrolled hypertension, known carotid artery stenosis and left sided chest pain. His physical examination showed temperature 99°F, respiratory rate 21 breaths/ minute, Blood pressure 150/105, pulse 86/minute and PEFR 250 L/minute. Cyanosis and edema were observed. CVS= S1+S2+ loud R2. Abdomen= soft, tendor left hypochondrium (LHC). Chest bilateral crackles and bronchi observed. Sputum was decreased in quantity and whitish in color. He was belonging to a middle class family. His diagnosis showed that he was a patient of diabetes mellitus, hypertension, COPD and IHD.

Patient history showed that he was an Ex-smoker and quit smoking 1 year back (smoking period=30-45 years). His history of present illness (HOPI) showed that the patient was alright 1 year back when he starts developing shortness of breath. It was moderate in intensity and was mildly relieved on taking inhaler. There was also associated productive cough. No history of fever. No history of TB. No orthopenia. Patient also complained of left sided chest pain, raditory to left arm. Pain was aggravated in exertion and relieved on rest. He was taking sublingual Angisid. He was also taking medicines for COPD, hypertension and IHD for one year. Patient was adviced Thallium seen for IHD.

On the basis of his medical investigation (primary diagnosis), the physician prescribed him tablet Theograde(theophylline) 350mg ½ BID(twice a day), tablet Rast (rosuvastatin) 10mg 1 × HS (at night), Tablet Lasix (furosemide) 40mg 1 × O.D (once a day), tablet Minipress (prazosin) , tablet Panadol (paracetamol) 2× TDS(three times a day), tablet Famot (famotidine) 40mg 1 × O.D, Atem (Ipratropium bromide) nebulization three times a day, Ventolin (salbuatamol) nebulization four times a day, Brufen (ibuprfen) cream, steam inhalation three times a day and Injection Leflox(levofloxacin) 500mg IV × O.D. on 2nd day of therapy , patient was complaint of left sided chest pain.his vital signs showed temperature 99°F, blood pressure 160/100, pulse 85/min and shortness of breath.the physician continued the treatment. On 3rd day, patient complained of body aches and shortness of breath.the Blood pressure was 140/100 with left sided chest pain, pulse 82/min, temperature 98°F and respiratory rate 20breath/min with persistant bronchi bilateral. On 5th day of therapy, shortness of breath was improved and one chest physiotherapy session was done. Vital signs showed temperature 98°F, blood pressure 150/100, pulse 86/min and respiratory rate 22 breath/min with Persistant bronchi bilateral.thus; the treatment continued.

DISCUSSION

The BNF (British National Formulary) is one the standard books used to design the treatment plans. The dose regimen of Tablet Rast, Tablet Famot, tablet Lasix and tablet Panadol prescribed according to the specifications but; the dose of tablet Theograde was

noticed lower than the recommended dose. The doses of Ventolin nebulization, Atem nebulization and tablet Minipress were not mentioned in the treatment regimen.

Cui H et al, (2011) reported the highest prevalence of hypertension (40.3%) among 4960 COPD patients, followed by diabetes/impaired glucose tolerance (18.8%) [21]

The concomitant administration of theophylline, levofloxacin and salbutamol causes hypokalemia that may prone to cause myalgias (body aches) and ventricular fibrillation and thus requires intensive electrolytes monitoring but; he was also prescribed furosemide that also causes hypokalemia and also no potassium supplements were prescribed. Along with hypokalemia, furosemide also causes hypocalcaemia, hypomagnesaemia, hyponatraemia, and hyperglycemia. [22]

Besides this, concomitant administration of levofloxacin and theophylline increases the risk of convulsions because levofloxacin inhibits the metabolism of theophylline by inhibiting CYP2D6 enzyme thus increases concentration of theophylline**.** Also levofloxacin injection must be given over atleast 60minutes for 500mg to avoid transient hypotension and counsel the patient to avoid a dairy product which was not followed. [22]

The patient history showed that he is also diabetic but no anti-diabetic drug was prescribed. Moreover; salbutamol increases blood glucose level and should be used with caution in diabetes and hypertension and requires regular monitoring of blood glucose level but; the frequency of nebulization was QID. [22]

Also furosemide and prazosin are prone to cause increase hypotensive effect especially 1st dose hypotension so there concomitant use should be avoided. In addition, drugs like theophylline, salbutamol, furosemide and levofloxacin also cause hypotension and should be monitored (blood pressure) time to time.

This study is substantiated by Kushner, Peckman and Snyder (2001) who reported two cases of seizures following administration of levofloxacin. They reported that after five doses, patient experienced seizures. [23] While Moorthy, Raghavendra and Venkatarathnamma (2008) reported

Levofloxacin-induced acute psychosis in 50-year-old man, with uncontrolled diabetes mellitus and hypertension on 3rd day of therapy following administration of oral levofloxacin (500 mg/day) [24].

This study is further substantiated by Whyte, Reid, Addis, Whitesmith, Reid (1988) who reported salbutamol induced hypokalemia due to stimulation of the beta-2 adrenergic receptor linked to a membrane bound Na^+/K^+ ATPase pump which transfers potassium into cell(Struthers & Reid, 1984) in combination with theophylline in a single-blind, randomized and placebo controlled clinical trials. They reported that theophylline significantly increases salbutamol induced hypokalemia and tachycardia while in some individuals profound hypokalemia (< 2.5 mmol 1-1) was observed with relatively low doses of salbutamol and theophylline. [25] While Lai, Legge, Friend (1991) reported hypokalemia and tachycardia in 9 patients with severe COPD due to air-driven nebulised high-dose salbutamol combined with oral theophylline.[26] In addition, Zuccalà, G (2000) reported that loop diuretics are one of the factors that cause hypokalemia in patients along with age and diabetes in a multicentre survey. [27]

CONCLUSION

The rational therapy of multiple diseases is a serious issue and need unusual intention of health professionals. Specially; the avoidable clinical errors are needed to be addressed for optimizing the therapy plans. There is also a need of degree holder competent pharmacists in hospitals in Pakistan who can help physician in selecting the rational therapy. The need of hour is a qualified pharmacist side by side with an experienced prescriber. Therefore; the comprehensive clinical examination and pharmaceutical care will help to avoid the undesired health related consequences.

REFERENCES

1. Hypertension Fact Sheet, WHO, September 2011. WHO Head quarters Geneva, Switzerland: *http://www.searo.who.int/linkfiles/non_communicable_diseases_hypertension-fs.pdf*
2. Kyrou I, Chrousos GP, Tsigos C (November 2006). "Stress, visceral obesity, and metabolic complications". *Annals of the New York Academy of Sciences* 1083: 77–110.doi:10.1196/annals.1367.008.pmid 17148735.
3. Wu G, Tian H, Han K, Xi Y, Yao Y, Ma A. Potassium magnesium supplementation for four weeks improves small distal artery compliance and reduces blood pressure in patients with essential hypertension. *Clin Exp Hypertens*. 2006 Jul; 28(5):489-97.
4. Wofford MR, Hall JE (2004)."Pathophysiology and treatment of obesity hypertension".*CurrentPharmaceuticalDesign* 10 (29):362137.doi:10.2174/13816120 43382855. pmid 15579059.
5. Lackland DT, Egan BM (August 2007). "Dietary salt restriction and blood pressure in clinical trials". *Curr. Hypertens. Rep.* 9 (4): 314–9.doi:10.1007/s11906-007-0057-8.pmid 17686383.
6. Djoussé L, Mukamal KJ (June 2009)."Alcohol consumption and risk of hypertension: does the type of beverage or drinking pattern matter?" *Revista Española De Cardiología* 62 (6): 603–5.doi:10.1016/S1885-5857(09)72223-6.pmid 19480755.
7. Lee JH, O'Keefe JH, Bell D, Hensrud DD, Holick MF (2008). "Vitamin D deficiency an important, common, and easily treatable cardiovascular risk factor?" *J. Am. Coll. Cardiol.* 52 (24): 1949–56.doi:10.1016/j.jacc.2008.08.050.pmid 19055985.
8. Pakistan Medical Research Council. National Health Survey of Pakistan (NHSP 1990-94): Health profile of the people of Pakistan. Islamabad, Pakistan 1998
9. Hemna Siddiqui, Qudsia Anjum, Amir Omair, Jawed Usman, Raza Rizvi, Tabinda Ashfaq, Risk factors assessment for hypertension in a squatter settlement of Karachi. Vol. 55, No. 9, September 2005
10. Diabetes Fact Sheet, WHO, November 2008. WHO Head quarters Geneva, Switzerland: *http://www.who.int/mediacentre/factsheets/fs312/en/*

11. International Diabetes Federation. Prevalence estimates of diabetes mellitus (DM), 2010 - MENA. IDF Diabetes Atlas, 2010. International Diabetes Federation. 3-9-2010. Brussels, Belgium: *http://www.idf.org/diabetesatlas/5e/the-global-burden*

12. Khuwaja AK, Fatmi Z, Soomro WB, Khuwaja NK. Risk factors for cardiovascular disease in school children: a pilot study. J Pak Med Assoc 2003 53; 396 ± 400

13. Chronic obstructive pulmonary disease (COPD) Fact Sheet, WHO, November 2011. WHO Head quarters Geneva, Switzerland: *http://www.who.int/mediacentre/factsheets/fs315/en/index.html*

14. Young RP, Hopkins RJ, Christmas T, Black PN, Metcalf P, Gamble GD (August 2009). "COPD prevalence is increased in lung cancer, independent of age, sex and smokinghistory". *Eur.Respir.J.* 34 (2):3806. doi:10.1183/09031936.00144208.pmid 19196816.

15. Devereux, Graham (May 2006). "Definition, epidemiology, and risk factors". *BMJ* 332 (7550):11424.doi:10.1136/bmj.332.7550.1142. PMC 1459603.pmid 16690673.

16. Hnizdo E, Vallyathan V (April 2003). "Chronic obstructive pulmonary disease due to occupational exposure to silica dust: a review of epidemiological and pathological evidence". *OccupEnvironMed* 60 (4):23743. doi:10.1136/oem.60.4.237.PMC 1740506.pmid 12660371.

17. Loscalzo, Joseph; Fauci, Anthony S.; Braunwald, Eugene; Dennis L. Kasper; Hauser, Stephen L; Longo, Dan L. (2008).*Harrison's Principles of Internal Medicine* (17th ed.). McGraw-Hill Professional. ISBN 0-07-146633-9.

18. Halbert RJ, Natoli JL, Gano A, Badamgarav E, Buist AS, Mannino DM (September 2006). "Global burden of COPD: systematic review and meta-analysis". *Eur. Respir. J.* 28 (3): 523–32.doi:10.1183/09031936.06.00124605.pmid 16611654.

19. Kennedy SM, Chambers R, Du W, Dimich-Ward H (December 2007). "Environmental and occupational exposures: do they affect chronic obstructive pulmonary disease differently in women and men?" *Proceedings of the American Thoracic Society* 4 (8): 692–4. doi:10.1513/pats.200707-094SD.pmid 18073405

20. National Heart, Lung and Blood Institute, *COPD Learn More Breathe BetterÂ®*. National Heart, Lung, and Blood Institute , Health Information Center, Bethesda, MD 20892: http://www.nhlbi.nih.gov/health/public/lung/copd/what-is-copd/index.htm

21. Cui H, Wei ZM, Cai JF, Li Y, Fan L, Hu YX, Liu L, Zhang M, Liu AM. Prevalence of hypertension and glucose/lipid metabolism disorders in 4960 in patients with chronic obstructive pulmonary disease during 2000-2010. *Nan Fang Yi Ke Da Xue Xue Bao*. 2011 Sep; 31(9):1498-503. pmid:21945752

22. British National Formulary (BNF) 2007, BMJ publishing group Ltd and RPS publishing 2007. ed.54, p167. ISSN: 0260-535X

23. Kushner JM, Peckman HJ, Snyder CR. Seizures associated with fluoroquinolones, *The Annals of Pharmacotherapy* doi: 10.1345/aph.10359 Ann Pharmacother October 1, 2001 vol. 35 no.10 1194-1198.

24. Moorthy N, Raghavendra N, Venkatarathnamma PN. Levofloxacin-induced acute psychosis. *Indian J Psychiatry*. 2008 Jan; 50(1):57-8 pmid: 19771310.

25. Whyte KF, Reid C, Addis GJ, Whitesmith R, Reid JL. Salbutamol induced hypokalaemia: the effect of theophylline alone and in combination with adrenaline. Br J *Clin Pharmacol*. 1988 May; 25(5):571-8.pmid: 3408637.

26. Lai CK, Legge JS, Friend JA. Air-driven nebulised high-dose salbutamol in severe chronic obstructive airways disease: is it safe? *Respiration*. 1991; 58(5-6):249-54. pmid: 1792412

27. Zuccalà, G. Older Age and In-Hospital Development of Hypokalemia from Loop Diuretics Results from a Multicenter Survey. *J Gerontol A Biol Sci Med Sci (2000)* 55 (4): M232-M238.doi: 10.1093/gerona/55.4.M23