International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 9; Issue 06(A); June 2020; Page No.22404-22406
DOI: http://dx.doi.org/10.24327/ijcar.2020.22106.4416

Research Article

PATIENT SPECIFIC DOSING: A FITTER MODEL IN DIALYSIS PATIENT WITH TUBERCULOSIS

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A R T I C L E I N F O

Article History:
Received 4th Mrach, 2020
Received in revised form 25th April, 2020
Accepted 18th May, 2020
Published online 28th June, 2020

Key words:
Tuberculosis (TB) haemodialysis, clinical pharmacist, pharmaceutical care

A B S T R A C T

Tuberculosis (TB) is an airborne infectious disease caused by Mycobacterium tuberculosis and is a major cause of morbidity and mortality in developing countries. There are no randomized controlled trials that provide evidence to guide TB treatment in renal failure.
Case report: A 69 year old male patient was admitted in a secondary care hospital on 6th October and discharged on 21st October having 52.2kg body weight. He presented with hiccups and unresponsiveness. He had a past medical history of Diabetes mellitus (25 years), Hypertension (23 years) and Pulmonary Tuberculosis (2013). At present he also presented with complaints of End stage renal disease and pleural effusion tuberculosis (4 months) and was on medicines such as Tab. AKT4 (Isoniazid, Rifampin, Pyrazinamide and Ethambutol), Tab. Arkamin (clonidine), Tab. GTN (Nitroglycerin), Tab. Shelcal (Calcium carbonate and vitamin D3), Tab. Pyridexin (vitamin B6), Tab. Nicardia (Nifedipine). The tuberculosis medicines were discontinued without informing the doctor few weeks ago and restarted prior to this admission. The patient was on haemodialysis twice weekly due to End- Stage Renal Disease (ESRD). The critical evaluation of patient by clinical pharmacist the patient recovered and the therapy was modified according to patient condition and the errors were rectified. **Conclusion**: This case report illustrates the need of thorough monitoring by Clinical Pharmacist in the patient oriented management and pharmaceutical care that should be provided for vulnerable population

INTRODUCTION

Tuberculosis (TB) is an airborne infectious disease caused by *Mycobacterium tuberculosis* and is a major cause of morbidity and mortality in developing countries. It commonly affects the lungs, but can also cause damage to other parts of the body. Patients with active pulmonary TB may be asymptomatic, some have mild or progressive dry cough, or present with multiple symptoms, such as fever, fatigue, weight loss, night sweats, and a cough which produces bloody sputum[1]. In India the prevalence of pulmonary tuberculosis among men aged 15 years and over is 2 to 4 times higher than in women of the same age[2]. In 2001, about 60 % of the new TB cases worldwide were in Asia[3]. Based on the pathogenesis Tuberculosis infection may be of two types latent and active. In latent phase TB germs are dormant in the body and this phase can last for long time even decades. The patients usually experience no signs and symptoms and are unable to spread the disease. In active phase TB germs rapidly reproduce and multiply in the body, leading to a variety of symptoms. TB can be spread to other parts of the body such as gastrointestinal tract, liver, bones and brain, however pulmonary TB is more common[3].

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The risk of acquiring tuberculosis is increased in immunocompromised patients including patients on dialysis and those who have undergone kidney transplantation[4].

Tuberculosis, although an uncommon cause of progressive renal failure, is an important one because, unlike many renal conditions, it is potentially preventable and easily treatable. Evidence as to the extent to which tuberculosis is a cause of end stage renal failure worldwide is scanty. The incidence of tuberculosis in haemodialysis was found to be 105.9 per 1000 patient years. The other significant risk-factors on univariate analysis were observed to be Male gender, diabetes mellitus, past history of tuberculosis, mining as an occupation, low serum albumin and duration of haemodialysis more than 24 months[5].

There are no randomized controlled trials that provide evidence to guide TB treatment in renal failure. Current treatment guidelines are based on reports from case series, the known pharmacological characteristics of the drug used and recommendations of experts in the area, including international agencies involved in TB control[6]. There are some factors that affect the therapy of renal failure tuberculosis patient. Drug pharmacokinetics, especially the proportion of drug excreted by kidneys and its clearance by dialysis (both haemodialysis and peritoneal dialysis), which affects the serum levels of drugs and consequently the toxicity[7]. Co-morbid illness and

possible drug interaction which may affect the drug therapy. There are number of reports about tuberculosis developing in patients on regular haemodialysis. Commonly the patient present with fever, anorexia and weight loss and usually either is known to have had pulmonary or other forms of tuberculosis or is a member of a high-risk ethnic or social group. Often the recrudescence is extra pulmonary, so it is likely that, in most cases, the disease is due to reactivation of past disease rather than a primaryinfection[8].

Case Report

A 69 year old male patient was admitted in a secondary care hospital on 6th October and discharged on 21st October having 52.2kg body weight. He presented with hiccups and unresponsiveness. He had a past medical history of Diabetes mellitus (25 years), Hypertension (23 years) and Pulmonary Tuberculosis (2013). At present he also presented with complaints of End stage renal disease and pleural effusion tuberculosis (4 months) and was on medicines such as Tab. AKT4 (Isoniazid, Rifampin, Pyrazinamide and Ethambutol), Tab. Arkamin (clonidine), Tab. GTN (Nitroglycerin), Tab. Shelcal (Calcium carbonate and vitamin D3), Tab. Pyridexin (vitamin B6), Tab. Nicardia (Nifedipine). The tuberculosis medicines were discontinued without informing the doctor few weeks ago and restarted prior to this admission. The patient was on haemodialysis twice weekly due to End- Stage Renal Disease(ESRD). The significant laboratory reports are in table no.1. There were elevated level of urea, creatinine and electrolytes and the Doctor advised for haemodialysis and prescribed medications for the presented complaints. Inj. Perinorm 5mg/ml stat, Inj. Pantop 40mg stat were administeredat the time of admission and the treatment plan was:Tab. Nicardia 10 mg 1-0-1 –(6-20), Tab. Arkamin 100 mg 1-0-1-(6-20), Tab. GTN CR 2.6 mg 1-0-1 -(7-20), Tab. Shelcal 500 mg 1-1-1 -(7-20), Tab. Pyridexin 20 mg 1-0-0 -(7-20), Tab. Liofen 5 mg 1-0-1 -(6-7), Inj. Zolheal 20 mg 1-0-1 -(7-20), Tab. AKT4 1-0-0-(6-10).

Tableno 1 Significant Laboratory test values on hospital admission time to discharge

Date	6/10	7/10	8/10	10/10	12/10	13/10	16/10	19/10	20/10
Hemoglobin (gms/dl)	8.9	8.8	8.8	8.9					
Potassium (mEq/L)	5.9	4.6	4.5	4.6	4.8	4.7	4.8	4.5	4.3
Sodium (mEq/L)	134	132	130	133	134	130	134	133	134
Creatinine (mg/dl)	45.5	4.7	4.5		4.3				4.1
Urea(mg/dl)	120	110	108		80				75

The haemodialysis was done on the date of 7th, 10th, 13th, 16thand 19th.On 14th -16th the temperature of patient elevated in the range of 99-101F and no treatment were given. The patient was unresponsive till 10/10 and the vital signs were normal on other dates except7th, 10th, 13th, 16th and 19thdue to increased pressure by haemodialysis. The FBS was normal throughout the hospital admission. The OHA or insulin was not taken by patient for a while by the order of doctor. By the critical evaluation of patient by clinical pharmacist the patient recovered and the therapy was modified according to patient condition and the errors were rectified in between the therapy Tab. Pantoprazole were changed to Rabeprazole during the course of stay at hospital.

DISCUSSION

The clinical pharmacist operates with a patient centered medication therapy management model to provide care for patients with chronic kidney disease and patients undergoing dialysis. Even before analyzing the case chart, the clinical pharmacist took all previous history of medical conditions and medications of the patient and interviewed the bystander for further details like social habits, family history, etc. As we know the patient is at ESRD, the creatinine clearance should be monitored to assess the functioning of kidneys. Using Cockcroft-Gault formula the creatinine clearance was assessed to be9 ml/hr.

The patient was at unresponsive state, and it was suspected that this may due to excessive elimination of hormone cortisol from the body but on checking, cortisol level was found to be normal.Ifincreasedamountofcortisoleliminatedfrombodyitwilll eadtohypotension, hyponatremia and other severe complications [9]. As the serum electrolytes levels were elevated due to ESRD, the doctor suddenly suggested Dialysis to reduce the amount of waste products. But even after dialysis the urea level wasn't reduced which led to the suspicion that high urea levels may be the reason for unresponsiveness and it was identified as an ADR of anti-tubercular drugs. The patient was taking combination of TB medication which was stopped in between the therapy and restarted prior to this incident. Combined effect of suddenly provoked TB medication along with ESRD may have led to the increase in urea to a higher level which caused unresponsiveness. By using Naranjo scale it was interpreted and the doctor was advised to discontinue the Anti-tubercular drugs for a time. On holding medication the patient recovered from unresponsive state and after a week the same drug reintroduced to patient without re-challenging as the patient was at high risk. The dose was adjusted for the combination as the developed ADR is dose dependent and there was chances for reoccurring. As the particular combination of drug were not available at everywhere and the prescription was directed to Ernakulum district hospital.

The drug which was administered on admission time for hiccups (metoclopramide) requiredonlya dose of 3.75mgbutwas administered5mg/10mldose.This was reportedto the doctor by the Pharmacist and the dose was reduced for further administration. The other observations which was found were that, for the prescribed medicine for hypertension GTN CR, the dosing is only required in q72-96hrs because there is highly protein binding. Also the dosing of vitamin B12 was adjusted after dialysis. In between the therapy the pantoprazole was changed to rabeprazole which was unwanted, as both have same mechanism of action and effects and the both drugs were administered at the same time as the stop order for Pantoprazole was not noticed by the Nursing Staff until intervention was done by the Pharmacist.

All the oral medications were crushed and administered to the patient because of non- adherence as he was unabletotakeit. The drug GTNCR is an on-crushable drug which too was crushed and given. The pharmacist advised to doctor to convert oral form to transdermal patch of 10mg/24hr rate of drug release. As the patient was having ESKD, the level of hemoglobin was low due to the decreased production of erythropoietin. Erythropoietin supplement was suggested but due to patient's financial status, it was not followed. The pharmacist powdered all the drugs and packed them in to

different packets and labelled appropriately as per time and day. The bystander was counseled about the administration of drug and other precautions that should be followed. To increase the adherence and correct administration of medications, alarms were set by pharmacist on the bystander phone. On discharge the patient was normal except from the complaints of ESKD and tuberculosis.

Table 2 Dose modification for AKT4

Drug	Normal dose/day	Dose/Kg for patient	Total best	Frequency
Isoniazid	300mg	5mg/kg	300mg	Daily
Rifampicin	450mg	10mg/kg	1500mg	Daily
Pyrazinamide	1500mg	30mg/kg	1500mg	Three times weekly q7hr
Ethambutol	800mg	15mg/kg	800mg	Three times weekly q7hr

Naranjo Adverse Drug Reaction Probability Scale

Sl. No	Questions	Yes	No	Don't Know	Score
1	Are there previous conclusive reports of this reaction?	+1	0	0	0
2	Did the adverse event appear after the drug was given?	+2	-1	0	+2
3	Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?	+1	0	0	+1
4	Did the adverse reaction reappear upon re-administering the drug?	+2	-1	0	0
5	Were there other possible causes for the reaction?	-1	+2	0	-1
6	Did the adverse reaction reappear upon administration of placebo?	-1	+1	0	1
7	Was the drug detected in the blood or other fluids in toxic concentrations?	+1	0	0	0
8	Was the reaction worsened upon increasing the dose? Or, was the reaction lessened upon decreasing the dose?	+1	0	0	+1
9	NO	+1	0	0	0
10	Was the adverse event confirmed by any other objective evidence?	+1	0	0	+1
TOTAL SCORE					**5**

CONCLUSION

This case report illustrates the need of thorough monitoring by Clinical Pharmacist in the patient oriented management and pharmaceutical care that should be provided for vulnerable population. The ESRD population has many unique issues, which puts them at special risk for drug- related problems and associated increase in morbidity and mortality. Simple activities such as medication profile reviews have been shown to be successful in streamlining drug therapy. By suitably involving in the therapy, the Pharmacist was able to avoid serious life threatening complications and helped the doctor to modify the therapy. Collaboration between physicians and pharmacists has been advocated to improve health care and it has contributed to better patient outcomes. The expertise of clinical pharmacists in pharmacotherapy may help to improve treatment responses and reduce adverse events in patients with reduced kidney function[10].

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