ejpmr, 2019,6(12), 449-450

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Case Study

ISSN 2394-3211

EJPMR

PIOGLITAZONE-INDUCED PULMONARY OEDEMA IN POST MASTECTOMY PATIENT

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Article Received on 25/09/2019 **Article Revised on 15/10/2019** **Article Accepted on 05/11/2019**

ABSTRACT

Pioglitazone is a commonly used anti diabetic drug. It is a proven insulin sensitizer which lowers the glucose level in the blood. Here we report a case of patient who suffered pulmonary oedema with normal cardiac functioning due to the use of pioglitazone. A 87 year old, female, who had a history of breast cancer (stage 1), and underwent mastectomy (right breast) along with several cycles of chemotherapy one year back. She was diabetic for the past 24 years and is on oral hypoglycaemic agents (OHA). The patient also had a history of Hypertension since 12 years; she was on antihypertensive. The patient got admitted in the emergency department with breathlessness and pedal oedema. All blood parameters except potassium levels were normal. Cardiac markers (d-dimer and troponins) were on the normal range, ECG leads was also normal. Chest X-ray revealed pulmonary oedema with effusion in both lungs. Computed tomography of chest showed dilated pulmonary arteries along with glassy round patches as a classical symptom of pulmonary oedema. Although the patient was treated with intravenous antibiotics and other supportive care, repeated chest X ray didn't showed any improvement. Hence pioglitazone was suspected as a potential cause and was discontinued in the same day. The patient's conditions improved in the following days. Chest X-ray repeated on the sixth day showed clinical improvement. Hence we conclude that all patients in the aged population and with or without a compromised cardiac function have to be monitored closely to prevent such adverse events due to pioglitazone.

INTRODUCTION

Pioglitazone is a commonly used antidiabetic drug. It is a proven insulin sensitizer which lowers the glucose level in the blood. The glycation inhibiting property of pioglitazone gives the drug an additional anti ageing property.[1] it also act as a ligand for the PPAR-gamma receptor, which aids in the uptake of lipid components into adipocytes, and can be beneficial in dyslipedemic and arthrosclerosis patients.[2]

Thus pioglitazone is having many more clinical utility other than its antidiabetic property. These properties make it a preferential agent in patients who are suffering with other life style diseases along with diabetics. In spite of all these benefits, physicians hesitate to prescribe this drug because of its increased reports of adverse drug events like the incidence of urinary bladder cancer. The postulated mechanism of carcinogenic property of pioglitazone is the ability to provide a tumour promoting environment by its PPAR -gamma receptor activity which boost the denovo synthesis of nutrients in the urinary bladder.[3] Because of the higher incidence of urinary bladder risk, the pioglitazone is marketed with boxed warning in India. But clinical use of pioglitazone is further reduced due to other reported side effects related to fluid retention, heart failure, weight gain etc.[4] Here we report a case of patient who suffered pulmonary oedema with normal cardiac functioning due to the use of pioglitazone.

CASE REPORT

A 87 year old, female, who had a history of breast cancer (stage 1), and underwent mastectomy (right breast) along with several cycles of chemotherapy one year back. She was diabetic for the past 24 years and is on oral hypoglycaemic agents (OHA). The patient also had a history of Hypertension since 12 years; she was on antihypertensive. The patient got admitted in the emergency department with breathlessness and pedal oedema. Bystanders reported that the patient had these symptoms for past 3 days and breathlessness was found to be progressive. Patient did not report any chest pain or any fever episodes.

From the medication history, she was on valsartan 20mg, BD, carvidelol 3.125mg OD, metformin 500 mg + teneligliptin 20 mg OD, pioglitizone 15 mg OD for last one year. At the time of hospitalization pulse was 92

beats / minute, blood pressure was 130/90 mm/hg. But his SpO_2 was reported to be 81%. Patient was afebrile. On physical examination, he didnot show any tenderness in the abdominal areas. Blood reports showed that total counts 10,600/L, GRBS 159mg/ml, Sodium 135meq/L, potassium 2.9meq/L, serum creatinine 1.1 mg%, Blood urea nitrogen 43%. This reports showed the patient had hypokalemia and all other blood parameters were normal. Cardiac markers (d-dimer and troponins) were on the normal range, ECG leads was also normal. Chest X-ray revealed pulmonary oedema with effusion in both lungs. Computed tomography of chest showed dilated pulmonary arteries along with glassy round patches as a classical symptom of pulmonary oedema.

As an initial symptomatic management patient was treated with intravenous furosemide 40 mg Q8hr along with oral spironalactone 25mg OD. Intravenous potassium supplementation was given to correct the hypokalemia. Patient was treated with intravenous antibiotics (ceftriaxone 1 gm + sulbactam 125mg BD. Oxygen support was also given to maintain the SpO_2 level in the range of 90%. On the first day. Patient was asked to continue with all own medications. On the third day patient showed breathlessness and SpO_2 was recorded to be 78% without oxygen. Repeated chest X-ray didn't show any improvement from initial condition. The C-reactive protein test and the total blood counts were in the normal range to suspect any infections. Pioglitazone was stopped on the same day in accordance with the reports regarding the induction of pulmonary oedema. Patients RBS and GRBS were maintained in the normal range after the discontinuation of the pioglitazone. The patient's conditions improved in the following days. Chest X-ray repeated on the sixth day showed clinical improvement.

As there were no other reasons for the pulmonary oedema, the possibility of pioglitazone to induce the pulmonary oedema was suspected. The clinical improvement the patient had after discontinuation of the same drug was also a key finding to suspect the drug as a causative agent for the pulmonary oedema. Pioglitazone was not rechallenged to this patient.

DISCUSSION

In India diabetics is a highly prevalent endocrine disorder. The treatment using classical OHA s still remain as the first line option for type two diabetics' mellitus. The high cost of new OHA s forces the patients to continue on these classical OHAs. Pioglitazone is one among the classical OHAs that are used widely among these populations. The trial reports of the PROactive (prospective pioglitazone clinical trial in macro vascular events) proved the beneficial properties of pioglitazone to prevent the complication of type two diabetes mellitus.[5]

The latest evidences regarding the adverse drug events with pioglitazone are alarming. Other than the risk of developing urinary bladder carcinoma, pulmonary oedema caused by the pioglitazone should be considered and dealt with caution. Studies and researches that focus on the adverse events of pioglitazone had to be performed to generate a strong signal.

The proposed pathogenesis of fluid retention induced by the pioglitazone is of multifactorial origin. These factors include vasodilatory effect of the drug that would increase the vascular permeability that could lead to the pioglitazone induced oedema. The physiological properties of the thiazolidinedions are mainly because of the PPAR gamma agonist property in the proximal tubules. This pharmacological action causes decreased sodium excretion which simultaneously increases the sodium reabsorbtion in the body.[5] These actions change the osmotic level physiology of the body and thus induce fluid retention in the body. But the mechanism of inducing pulmonary oedema in a patient without cardiac dysfunction is still unknown.

But from the similar case reports.[4] Use of pioglitazone for a period of more than 1 year are at risk of developing pulmonary oedema.

Hence we conclude that all patients in the aged population and with or without a compromised cardiac function have to be monitored closely to prevent such adverse events due to pioglitazone.

ACKNOWLEDGEMENTS

The author would like to thank the staff and the post graduate students of department of pharmacy practise, Nirmala college of pharmacy, muvattupuzha and Mrs Andrea Annie Tom for her support and encouragement.

CONFLICT OF INTREST: Nil.

REFERENCES

1. Jafari M, Khadoyari B, Felgner J, Bussel I, Rose M, Mueller L.Pioglitazone:an antidiabetic compound with anti aging properties. Biogerontology, 2007; 8: 639-651.
2. Guarente L, Picard F. Calorie restriction. Cell, 2005; 120: 473-482.
3. Chiu M, McBeth L, Sindwani P, Hinds T. Deciphering the roles of thiazolidinediones and PPAR gamma in bladder cancer. Hindawi, 2017; 4810672.
4. Jearath V, Vashisht R, Rustagi V, Raina S, Sharma R. Pioglitazone-induced congestive heart failure and pulmonary edema in a patient with preserved ejection fraction. Journal of pharmacology and pharmacotherapeutics, 2016; 7: 411-3.
5. Beltwski J, Rachanczyk J, Wlodarczyk M. Thiazolidinedione-induced fluid retention: recent insights into the molecular mechanisms. Hindawi, 2013; 628628.