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Telmisartan Induced Myotoxicity: A Case-Report

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

The precise incidence of drug-induced myopathy is still not known, only few reports with the use of Telmisartan. There are likely around 150 agents that are associated to cause myotoxicity like statins, corticosteroids, anti-retroviral, and immunosuppressants. Therefore, as recommended by the guidelines, therapeutic drug monitoring of Telmisartan is required after the initiation of the therapy. However, the rise in serum creatinine up to 20-30% is accepted. But if serum creatinine level increases >30% then withdrawal of the therapy is recommended.

Suspicious with the previous therapy of Tab. Telmisartan as no other pathology could be detected. A causality analysis was done using the Naranjo's algorithm and WHO-UMC Scale and the present ADR was found to be 'Probable' with Telmisartan. Tab. Telmisartan was withdrawn completely and was switched by another Antihypertensive -Tab. Enalapril (5mg). Gradually, the condition of the patient showed improvement in terms of both- the clinical symptoms and laboratory abnormalities. However, re-challenge of the drug was not performed in order to avoid further toxicity. After 15 days, the patient had visited Medicine Outpatient Department (OPD) again the creatinine and uric acid levels where checked which were normal and further advised to follow up every month. To be conclude, adverse drug reaction of myotoxicity associated with telmisartan is rare but quite significant. So, close monitoring is necessary to ensure safety of drug therapy especially in long term use.

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Keywords: Drug therapy; telmisartan; myotoxicity.

1. INTRODUCTION

The precise incidence of drug-induced myopathy is still not known but it ranges from mild myalgia with or without mild weakness to chronic myopathy with severe weakness and to massive rhabdomyolysis with acute renal failure [1,2]. There are likely around 150 agents that are associated to cause myotoxicity like statins, corticosteroids, anti-retroviral, and immunosuppressants [3]. Angiotensin Receptor Blockers (ARBs) are the class of drugs known to cause myotoxicity. The rise in CPK (Creatine phosphokinase) with Telmisartan has been reported as common adverse event (≥ 1/100, < 1/10) while it is uncommon with other ARBs like Losartan, Olmesartan, Candesartan, Valsartan [4,5]. However, BP-lowering treatment is also associated with decrease in renal function and rise in the serum creatinine and uric acid in a long term. It is supported by the evidence that after starting with an angiotensin receptor blocker (ARB) or angiotensin-converting enzyme (ACE) inhibitor is associated with an increased incidence of adverse cardio renal outcomes during 10-year follow-up in one of the recent cohort studies conducted in primary care population [6]. Therefore as recommended by the guidelines, therapeutic drug monitoring of Telmisartan is required after the initiation of the therapy. However, the rise in serum creatinine up to 20-30% is accepted. But if serum creatinine level increases >30% then withdrawal of the therapy is recommended [7,8,9]. Previous studies have shown Losartan as the safer alternative among the class of ARBs for the patients at high risks of myotoxicity but it would be naïve to consider and for that requires the further research [10,11].

2. CASE DESCRIPTION

A 50-year-old female came to the hospital with complaints of myalgia, muscle weakness, vomiting and loss of appetite from last 2 months. Her medical history revealed that she had hypertension from last 12 years and diabetes for last 3 years and is on regular medication of the fixed dose of Tab.Telmisartan 40mg and Tab. Metformin 500 mg BID. Her lab report revealed abnormalities like hyperuricemia (uric acid - 11.4 mg/dl) and hypercreatinemia (creatinine- 6.7 mg/dl). Blood pressure was found to be 150/80 mmhg on examination. The clinical parameters like his complete blood count, serum electrocytes, erythrocyte sedimentation rate, peripheral smear, urine test, chikungunya antigen test was found to be within clinically acceptable limits but serum CPK and potassium levels were found to be slightly elevated, 262 U/L and 5.8mmol/L respectively. Hence, hospitalised with the provisional diagnosis of the nephrotic syndrome. As the treatment for the nephrotic syndrome consists of Diuretics, Antihypertensive medication, Statin and Immunosuppressive drugs; the patient was started with Tab. Furosemide 40mg, Tab. Ranitidine, Tab. Folic acid and Tab. Rosuvastatin and continued with the Tab. Telmisartan. Further, there was no improvement observed in the symptoms along with the same abnormalities in laboratory parameters. The patient never had the similar complain in the past with no history of statin or any other medical therapy, alcohol intake, smoking or vigorous exercise. Further other diagnostic tests were even performed like TSH, T3, and T4 to rule out the possibility of any other diseases which again were found to be normal. Even RBS, FBS, and HbA1c was also measured which were found within reference range, hence proving Metformin being actively working. Hence, proving something suspicious with the previous therapy of Tab. Telmisartan as no other pathology could be detected. Tab. Telmisartan was withdrawn completely and was switched by another Antihypertensive -Tab. Enalapril (5mg). Gradually, the condition of the patient showed improvement in terms of both- the clinical symptoms and laboratory abnormalities. However, re-challenge of the drug was not performed in order to avoid further toxicity. After 15 days, the patient had visited Medicine Outpatient Department (OPD) again the creatinine and uric acid levels where checked which showed the gradual declination in the levels and further advised to follow up every month.

3. DISCUSSION

There are only few reports of myotoxicity with the use of Telmisartan. In our case the myotoxicity occurred after continuously taking the medication Tab. Telmisartan for 12 years, thus the prolong exposure with the agent was responsible for the toxicity. This is supported by the evidence in which ARBs is responsible for cardiorenal outcomes in 10 years of study and suggested the withdrawal of offending drug [6].

Various drugs are responsible for causing myotoxicity including other Anti-hypertensives

like ACE inhibitors (Captopril, Ramipril, Enalapril) and also ARBs. However, fewer studies have shown beneficial effects of prescribing Losartan and Olmesartan over Telmisartan or any other ARBs [10,11]. However, we avoided using same class of drug (ARBs) in replacement of Telmisartan thinking about their similar effects on renin-angiotensin system.

But the drug induced myotoxicity can be due to both on-target and off-target mechanisms of drugs. For example, few subsets of ARBs show off-target action by potentiating peroxisome proliferator-activated receptor- gamma (PPAR-γ). Now this activation of PPAR-γ demonstrates the novel actions of certain ARBs, providing a potential mechanism for their insulin-sensitizing/antidiabetic effects. Increased activation of PPAR-γ is responsible for causing myalgia and rhabdomyolysis whose similar effects have been observed in drugs like pioglitazone and rosiglitazone based on previous studies [12,13]. Activation of PPAR-γ occurs at the normal therapeutic levels of telmisartan and irbesartan which high drug concentration of losartan is required for the same purpose. Whereas, Eprosartan, Olmesartan, valsartan shows no activity on PPAR-γ receptors [14,15]. Also, lipophilic drugs have more affinity towards PPAR-γ receptors and all the ARBs shows lipophilicity at some extent. Telmisartan is highly lipophilic in nature and thus might be the reason for myotoxicity that occurred in our case.

A causality analysis was done using the Naranjo's algorithm and WHO-UMC Scale and the present ADR was found to be 'Probable' with Telmisartan.

4. CONCLUSION

Adverse drug reaction of myotoxicity associated with telmisartan is rare but quite significant. So, close monitoring is necessary to ensure safety of drug therapy especially in long term use. And the withdrawal of the drug is recommended in case of toxicity is observed and to prevent further complications. The drug regime can be switched to other safer options like Olmesartan or Losartan. However, further research should be done for the valid supportive evidence proving the significant association of the ADR.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

ETHICAL APPROVAL AND CONSENT

As per international standard or university standard guideline patients consent and ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Zuckner J. Drug-related myopathies. Rheumatic Diseases Clinics of North America. 1994;20(4):1017-32.
2. Prendergast BD, George CF. Drug-induced rhabdomyolysis-mechanisms and management. Postgraduate Medical Journal. 1993;69(811):333
3. Curry SC, Chang D, Connor D. Drug-and toxin-induced rhabdomyolysis. Annals of Emergency Medicine. 1989;18(10): 1068-84.
4. Telmisartan. In: Boehringer-Ingelheim. [Online]. [Burlington, Ontario]: Available:http://www.boehringeringelheim.ca/content/dam/internet/opu/ca_EN/documents/humanhealth/product_monograph/MicardisPlusPMEN.pdf. [amended 2013 Apr 29; cited 2014 Oct 31].
5. Olmesartan. In: Merck. [Online]. [Kirkland, Québec]: Available from: Available:http://www.merck.ca/assets/en/pdf/products/olmetec-pm_e.pdf. [prepared 2013 Nov 5; cited 2014 Oct 31].
6. Schmidt M, Mansfield KE, Bhaskaran K, Nitsch D, Sørensen HT, Smeeth L, Tomlinson LA. Serum creatinine elevation after renin-angiotensin system blockade and long term cardiorenal risks: Cohort Study. Bmj. 2017;356.
7. Kidney Disease: Improving global outcomes (KDIGO) blood pressure work group. KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease. Kidney Int Suppl. 2012; 2:337– 414.

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8. ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/ PCNA Guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: A report of the american college of cardiology/american heart association task force on clinical practice guidelines. Hypertension. 2018;71:e13–e115. DOI: 10.1161/HYP.0000000000000065.
9. Bakris GL, Weir MR. Angiotensin-converting enzyme inhibitor-associated elevations in serum creatinine: is this a cause for concern? Arch Intern Med. 2000;160:685–693. DOI: 10.1001/archinte.160.5.685
10. Barvaliya MJ, Naik VN, Shah AC, Tripathi CR. Safety of olmesartan in a patient with telmisartan-induced myotoxicity: A case report. British journal of clinical pharmacology. 2015;79(6):1034
11. Nishida Y, Takahashi Y, Susa N, Kanou N, Nakayama T, Asai S. Comparative effect of angiotensin II type I receptor blockers on serum uric acid in hypertensive patients with type 2 diabetes mellitus: a retrospective observational study. Cardiovascular Diabetology. 2013;12(1): 159.
12. Slim R, Salem CB, Zamy M, Biour M. Pioglitazone-induced acute rhabdomyolysis. Diabetes Care. 2009; 32(7):e84.
13. Kennie N, Antoniou T, Berger P. Elevated creatine kinase and myalgia in a patient taking rosiglitazone. Annals of Pharmacotherapy. 2007;41(3):521-5.
14. Schupp M, Janke J, Clasen R, Unger T, Kintscher U. Angiotensin type 1 receptor blockers induce peroxisome proliferator-activated receptor-gamma activity. Circulation. 2004;109:2054-7.
15. Erbe DV, Gartrell K, Zhang YL, Suri V, Kirincich SJ, Will S, Perreault M, Wang S, Tobin JF. Molecular activation of PPARγ by angiotensin II type 1-receptor antagonists. Vascular Pharmacology. 2006;45(3):154-62.

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