ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 03 | March - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

LEVETIRACETAM INDUCED CUTANEOUS RED RASHES: AN EXTREMELY RARE ADVERSE DRUG REACTION

Neurosurgery

Dr R. K. Barooah Associate professor, Department of Neurosurgery, GMCH Guwahati.

Dr Ankur Anand* Senior Resident, Department of Neurosurgery, GMCH Guwahati. *Corresponding Author

ABSTRACT

The goal of anti epileptics is to achieve sustained seizure freedom with well tolerated doses. All kind of adverse drug reactions should be fully defined and established[1]. Levetiracetam is one of the newer second-generation antiepileptic drugs with multiple mechanisms of action. Levetiracetam is generally considered safe and became one of the most commonly prescribed medications for the treatment of partial and generalized epilepsy. We report a rare undesirable cutaneous adverse reaction secondary to levetiracetam. Our Patient, 23 year male developed drug resistant focal seizures with secondary generalisation, Post traumatic was started on Levetiracetam developed Skin Hyperpigmentation and rashes. To date there are very few cases reported involving Skin reactions from Levetiracetam. The prescribing physicians should inform the patients regarding all potential adverse effects of levetiracetam including skin hyperpigmentation. Further studies have to be conducted to explore the pathophysiology of this rare cutaneous adverse effect.

KEYWORDS

Levetiracetam, Cutaneous adverse drug reactions, red rash, anti epileptics reactions.

INTRODUCTION

Epilepsy is the second most common and frequently encountered neurological condition that imposes heavy burden on individuals, families, and also on healthcare systems. As per a recent study, 70 million people have epilepsy worldwide and nearly 90% of them are found in developing regions. With a conservative estimate of 1% as prevalence of epilepsy, there are more than 12 million persons with epilepsy (PWE) in India, which contributes to nearly one-sixth of the global burden. [1]

The goal of epilepsy treatment is to achieve sustained seizure freedom and to achieve this using tolerated antiepileptic drug (AED) schedules.[1]

It is, therefore, very important to fully define and establish the adverse effects profile of drugs using, where possible, best evidence such as level I (randomized controlled trial) evidence and systematic review with meta-analysis.

Levetiracetam is one of the newer second-generation antiepileptic drugs with multiple mechanisms of action. It is a broad-spectrum antiepileptic drug that was approved by the United States Food and Drug Administration in 1999 and became one of the most commonly prescribed medications for the treatment of partial and generalized epilepsy (first choice and add-on) [2].

Levetiracetam has a favorable adverse effects profile with the 5 most common adverse effects being nasopharyngitis, somnolence, asthenia/fatigue, dizziness, and nervousness/irritability. Its minimal drug interactions, few side effects, and broad-spectrum efficacy contributed to its wide use for the treatment of seizures.[3]

Cutaneous adverse drug reactions (cADRs) are commonly associated with antiepileptic drugs (AEDs) particularly the aromatic Carbamazepine (CBZ), Phenytoin (PHT), Phenobarbitone (PB), and Lamotrigine (LTG). They range from minor maculopapular exanthem (MPE) to severe life-threatening reactions like Drug reaction eosinophilia and systemic symptoms (DRESS), Stevens Johnson Syndrome (SJS) and Toxic epidermal Necrolysis (TEN), and manifest within a few hours to weeks of the AED being initiated.[9]

As was mentioned then, the adverse effects profile of any new drug will change as more experience is gained and as more time has passed [4]. This report adds to that literature by updating the numbers through adding trials published since those older reviews.

CASE REPORT: -

A 23 year male, presented to the hospital following Road Traffic Accident. On Presentation patient was having moderate Traumatic head injury. Non Contrast Computed Tomography Scan of Head was done according to trauma Protocol of our institution. He had hemorrhagic contusions for which he was managed conservatively with Oral antiepileptics tablet Levetiracetam 500mg twice daily, Patient had an episode of focal Seizure having impaired consciousness with secondary generalizations on the day of injury.

He was prescribed Levetiracetam 500mg tablets twice daily following discharge approximately 2 months ago. Patient was followed monthly in our Neurosurgery OPD at GMCH, Guwahati, all other drugs were discontinued after 1 month of 1st follow -up. Patient was on Levetiracetam only after 1 month of discharge with the same doses. After approx. 7 weeks of daily medications with decrease in intensity and frequency of Seizure episodes, Patient Came to OPD having maculopapular red rash with pruritic lesions. These Skin Lesions were sudden in onset Started in distal Part of all 4 extremities and within the Span of 1-2 day, it involved approx. 70% of the whole body Sparing face, mucous membranes, nails, and retina. This complaint interfered to some degree with her social and marital relationships. His past medical, family, and medication history were unremarkable.

Work up for systemic disorders causing hyperpigmentation including thyroid function tests, electrolytes, serum cortisol, and renal function tests were unremarkable. Changes in treatment were done and he was Started with a mild dose of Steroid along with antihistaminic and lacto-calamine lotion for local applications and Patient was followed on OPD Basis. Another anti-epileptic valproic acid 500mg was started, Patient responded quite well and skin maculopapular rash subsided in 3-4 days of initiating the treatment along with decrease in intensity and frequency of Seizure were noted.

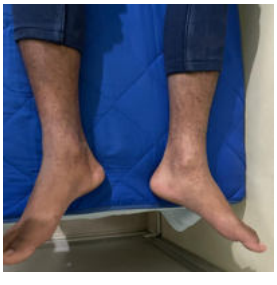

Figure 1: Demonstration of Maculopapular rashes seen on both lower limb.

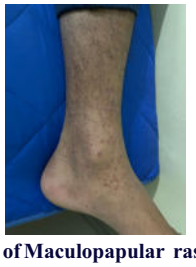

Figure 2 : Distribution of Maculopapular rashes in left lower limb.

DISCUSSION:-

The pathogenesis of drug-induced hyperpigmentation is unknown in some cases. However, the accumulation of melanin in the dermis instead of the basal layer of the epidermis is considered the end result in most of the cases [4]. The accumulation of melanin may result from overproduction by epidermal melanocytes that are stimulated by the drug (melanocytic hypermelanosis). It may also represent a nonspecific cutaneous inflammatory reaction to the medication. Another possibility is the formation of a stable drug-melanin complex which prevents melanin clearance in the dermal macrophages. Another mechanism may be the accumulation of the triggering medication without melanin. Synthesis of other pigments such as lipofuscin under the direct influence of the drug with subsequent deposition may cause hyperpigmentation. Additionally, the deposition of iron as a result of drug-induced damage to dermal vessels may lead to hyperpi gmentation. [3,7,8]

Cutaneous side effects are commonly associated with antiepileptic drugs such as carbamazepine, phenobarbitone, phenytoin, and lamotrigine. These side effects may be mild such as maculopapular rash or more severe and life-threatening such as drug reaction eosinophilia and systemic symptoms. These cutaneous manifestations may appear within a few hours to weeks of the initiation of the antiepileptic drug.[9]

Cutaneous drug reactions due to LEV are rare, and only case reports and small series are published [5,6]

In a systematic review of ten randomised controlled trials by Mbizvo et al, adverse effect profile of LEV in patients of drug-resistant epilepsy was studied, and rash due to LEV was reported in only two studies.[10] The prescribing physicians should inform the patients regarding all potential adverse effects of levetiracetam including skin hyperpig mentation. Further studies have to be conducted to explore the pathophysiology of this rare cutaneous adverse effect.

REFERENCES:

1. Ngugi AK, Bottomley C, Kleinschmidt I, Sander JW, Newton CR. Estimation of the burden of active and life-time epilepsy: A metaanalytic approach. Epilepsia 2010;51:883-90.
2. Crepeau AZ, Treiman DM. Levetiracetam: a comprehensive review. Expert Rev Neurotherapeutics 2010;10(2):159–71.
3. NICE. National Institute for Clinical Excellence. NICE Clinical Guideline 137. The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care, January 2012. www.guidance.nice.org.uk/CG137
4. Krause W. Drug-induced hyperpigmentation: a systematic review. J Dtsch Dermatol Ges 2013;11:644-51.
5. Briggs DE, French JA. Levetiracetam safety profiles and tolerability in epilepsy patients. Expert Opin Drug Saf 2004;3(5):415–24.
5. Duong TA, Haddad C, Valeyrie-Allanore L, Sbidian E, Chosidow O, Wolkenstein P. Levetiracetam: a possible new inducer of toxic epidermal necrolysis and Stevens-Johnson syndrome in 2 cases. JAMA Dermatol 2013;149:113-5.
6. FDA Approved Labeling text dated 16 Dec 2011. Reference ID: 3060029, www.fda.gov/downloads/Drugs/DrugSafety/UCM152832.pdf.
7. Dereure O. Drug-induced skin pigmentation. Epidemiology, diagnosis and treatment. Am J Clin Dermatol 2001;2:253-62.
8. Garin Shkolnik T, Feuerman H, Didkovsky E, et al. Blue-gray mucocutaneous discoloration: a new adverse effect of ezogabine. JAMA Dermatol 2014;150:984-9.
9. Ramanujam B, Ihtisham K, Kaur G, et al. Spectrum of cutaneous adverse reactions to levetiracetam and human leukocyte antigen typing in North-Indian patients. J Epilepsy Res 2016;6:87-92.
10. Mbizvo GK, Dixon P, Hutton JL, Marson AG. Levetiracetam add-on for drug-resistant focal epilepsy: an updated Cochrane Review. Cochrane Database Syst Rev 2012;9: CD001901