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Original Research Article

VANCOMYCIN ASSOCIATED EOSINOPHILIA & RED MAN SYNDROME IN A TERTIARY CARE HOSPITAL

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Abstract

Vancomycin associated Red Man Syndrome (RMS) is a common infusion related adverse effect. A correlation has been proposed between vancomycin induced eosinophilia and occurrence of RMS. In such cases, it is identified that activated T-cells release cytokines, which tends to contribute to hypersensitivity reaction. A cross-sectional, retrospective study was conducted to evaluate the possible association of vancomycin induced eosinophilia with the occurrence of RMS at a local tertiary care cancer hospital. In this study the role of eosinophilia before the occurrence of RMS was focused. A twenty one month data was extracted from Jan, 2014 to Sep, 2015 and 8 patients were found to be reported for vancomycin induced RMS. Only one patient (12.5%) fulfilled the criteria for the drug rash eosinophilia and systemic symptoms (DRESS) among the 8 patients. This particular patient had eosinophilia preceding RMS. In the study sample, 2(25%) patients showed a rise in their eosinophil count but within the normal range. A correlation of eosinophilia and RMS could not be established in our study.

Keywords: red man syndrome, vancomycin, drug rash eosinophilia and systemic symptoms, eosinophilia.

Introduction

Vancomycin is a significant treatment option for Methicillin-resistant *Staphylococcus aureus* (MRSA) infection, and a first line therapy for Methicillin Resistant *Streptococcus pneumoniae* and *Corynebacterium jeikeium* infection [1-3]. For the treatment of methicillin-susceptible (MSSA) infections it is less preferred relative to beta-lactams [1-2].

In spite of an effective Antimicrobial Stewardship Program (ASP) carried out in different hospitals, the use of Vancomycin was increasing due to increased prevalence of MRSA cases. This may have happened due to irrational prescribing of antibiotics in third world countries leading to multi-drug resistance [4]. Thus, in patient receiving vancomycin it's important to establish the complications in antibiotic therapy from occurrence of DRESS.

Use of Vancomycin has led to two types of hypersensitivity reaction, one is the anaphylaxis and other is RMS. The latter is associated with face, neck and abdomen involvement, with prevalence of pruritus and rash. Patients tend to experience a feeling of burning, leading to discomfort. Symptoms also include headache, hyperthermia, itching and paresthesia, due to which patient becomes agitated [5].

Incidence of allergic reaction may also serve for clinical diagnosis of DRESS following drug use. The criteria for DRESS include hyperthermia, rash, eosinophilia, and existence of multi-organ association

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[6]. Other hematological changes may include leukocytosis or atypical lymphocytes. The usual organ involvement tends to appear within 2 weeks of skin erythema [7-8]. In RMS eosinophilia generally occurs, however, in case of vancomycin induced RMS it is important to distinguish the route cause. Generally, RMS is correlated to the higher infusion rates. Thus, the claim that eosinophilia is the cause for RMS may be questionable.

A study was conducted at Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore (SKMCH&RC), Pakistan, a local tertiary care hospital, with the aim to assess the significance of eosinophilia in patients experiencing RMS with vancomycin use.

MATERIALS AND METHODS

A retrospective cross-sectional study was conducted to evaluate the adverse drug reactions in terms of Vancomycin induced RMS, reported from Jan, 2014 to Sep, 2015. A total of 2,666 patient data gathered, who received vancomycin during the sample period.

Results

In the study sample (n= 2666) 8 patients were reported to suffer from vancomycin induced RMS. Among these patients, 2(25%) patients had their eosinophil count slightly deviated but it was within normal range and showed rise in eosinophil count. Only 1(12.5%) patient had prevalence of eosinophilia along with RMS, fulfilling the criteria of DRESS. The data collected of patients who had RMS post-vancomycin, is depicted in Figure 1.

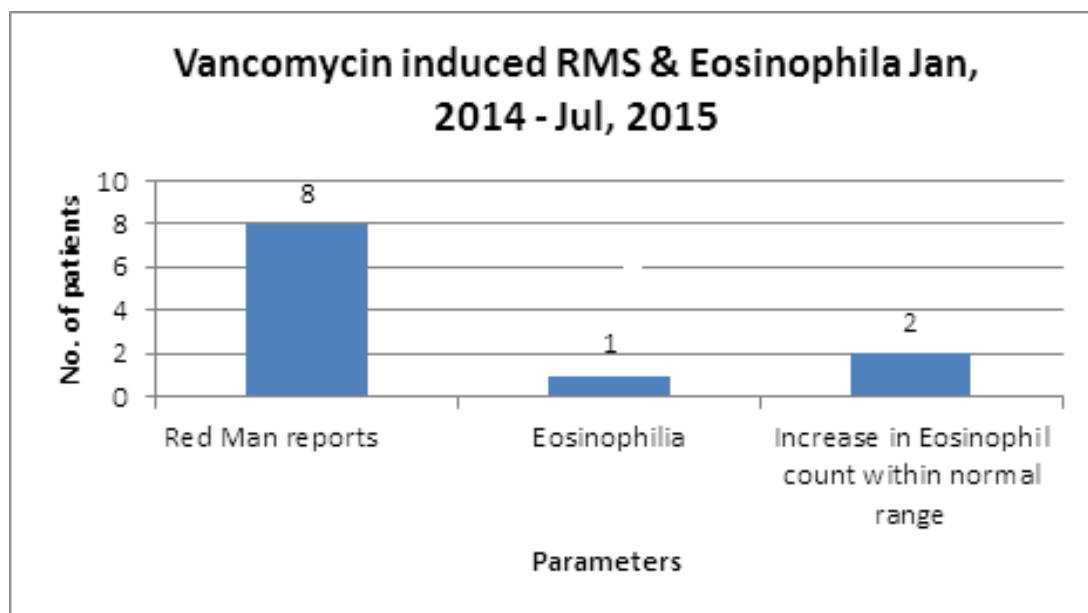


Figure 1: Data for RMS from Jan, 2014 to Sep, 2015

Discussion

In this study correlation of eosinophilia with occurrence of RMS in patients receiving vancomycin was evaluated. Eosinophilia may serve as a marker to the definitive occurrence of RMS and may facilitate the physician as evidence to discontinue the specific drug. In terms of the mechanism, RMS is a result of type IV hypersensitivity reaction due to cytokines released for the activated T-cells [9].

DRESS was earlier connected with the use of anticonvulsants [10-11], but now an increasing trend has been noticed for it in patients receiving antibiotics such as, β -lactams, vancomycin, sulfa-drugs, tetracycline and fluoroquinolone. In our study the focus was on vancomycin.

Vancomycin use is now increasing in hospitals as a result of growing number of multidrug resistant bacteria. In case of incidence of RMS, linezolid substitution is considered as one of the options. If the incidence is independent of eosinophilia then the most probable cause can be high rate of infusion, in which case the drug may be continued at a slower rate. The usual treatment for RMS is antihistamines and intravenous or topical corticosteroids.

A similar research conducted by KG Blumenthal et al showed a 4 years data collection for vancomycin induced DRESS, where 5 patients fulfilled the criteria. Comparative to this, our study had 1 patient, who had eosinophilia and fulfilled the criteria for DRESS [12].

neutropenia started with Piperacillin/Tazobactam 1900mg q6h as an empiric therapy. Later the patient developed fever and blood culture exhibited gram-positive *Micrococcus species* against which vancomycin was started. The patient's hematological test showed raised eosinophil count which consistently escalated as the therapy proceeded. On day 8 of vancomycin, he started to develop rashes with typical signs and symptoms of RMS, therefore, Vancomycin was stopped at once. Hydrocortisone and Pheniramine were administered for symptomatic management. Condition settled soon after vancomycin was discontinued and it was replaced with teicoplanin.

Two pediatric cases were discussed by Bauters T, et al [13] with cancer malignancy, receiving vancomycin. Both patients were infused drug over 60 minutes. Interestingly, none were on opioids, but they discussed the role of concomitant use of opioids in the occurrence of RMS [14]. In our case, Patient was receiving tramadol for pain management.

Conclusion

It was concluded that vancomycin may not influence eosinophil count. Also, raised eosinophil count is unlikely to contribute to RMS in patients treated with vancomycin. Further studies are recommended to establish the incidence of RMS secondary to eosinophilia in vancomycin treated patients.

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The single reported patient diagnosed T-cell Non-Hodgkin lymphoma, admitted with febrile



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