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CASE REPORT OF VANCOMYCIN INDUCED FLUSHING SYNDROME

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ABSTRACT

Red man syndrome (RMS) also known as vancomycin flushing syndrome(VFS) is a type of physiological disorder which can be mostly seen in patients with rapid IV(intravenous) infusion of first dose of the antibiotic drug vancomycin which may lead to certain physiological complications due to allergic reactions and histamine release.at first it was initially attributed to the impurities present in the vancomycin but after enhancing the purity of the drug the symptoms of red man syndrome still persists in 3%-47% of patients who receive the treatment. Other drugs like amphotercinB, rifampicin,ciprofloxacin etc or other drugs that stimulate histamine when combined with vancomycin show the very same reaction in the patients. Discontinuation of vancomycin and administration of diphenyhydramine can counter most of the reactions induced by vancomycin. Thus slow infusion of vancomycin can minimize the risks of any sort of allergic or hypersensitivity reactions. A 9-month old patient came to the hospital with chief complaint of trauma to the head after experiencing a fall from a car and had four episodes of vomiting before visitng the hospital.After a thorough examination of brain was done using MDCT scan acute sub-dural hematoma was seen and the patient was subjected to a conservative treatment When the clinical pharmacist learned about the case, they compared the symptoms at that time to a review of previous cases in the literature and made the tentative assumption that the patient was suffering from red man syndrome due to vancomycin infusion. Then it was brought to the notice of medical team where it was discussed in detail & finally diagnosed with red man syndrome and thus the syndrome was treated with appropriate measures.

INTRODUCTION:-

Health professionals often utilize the intravenous infusion of drugs since that enables them to give drugs at a much better rate and subsequently improving the effectiveness of the drug as well as its bioavailability. With the IV infusion, the treatment of the disease is quick to act.Well, aside from the obvious psychological complication of Edemas, the majority of complications of IV infusion are limited to pain upon injection, erythema, and rarely infection at the site of iv infusion. Vancomycin can cause two types of hypersensitivity reactions, anaphylaxis and red man's syndrome. In most cases, red man's syndrome has been noted in association with the fast intravenous infusion of the first dose of the medication, and its causes were thought to be due to contaminants present in vancomycin preparations. Vancomycin is associated with a particular infusion reaction termed red man syndrome. It typically consists of pruritus, an erythematous rash that involves the face, neck, and upper torso. Less frequently, hypotension and angioedema can occur[1]. Practitioners using vancomycin should be aware of this drug reaction, its prevention, and treatment.

This activity describes the evaluation, diagnosis, and management of vancomycin flushing syndrome and stresses the role of team-based interprofessional care for affected patients[2].vancomycin hypersensitivity is an anaphylactic reaction. Anaphylaxis is an immunologically mediated reaction involving drug-specific immunoglobulin E (IgE) antibodies and is independent of the infusion rate[3].Rarely, VIR has been caused by topical administration of vancomycin powder[4]. RMS includes a different array of signs and symptoms. These may include milder reactions involving flushing, urticaria and pruritus, or more severe ones comprising, for example, total body redness, severe itching, and sometimes, low blood pressure. Although there is general consensus on clinical features included in the symptom complex of RMS, there is no standard definition based on a required constellation of features that constitutes this ADR. The lack of a precise phenotype may account for widely reported estimates of incidence in the literature[5].

Case Presentation:-

A 9-month old patient was admitted to pediatric ward of the hospital with C/O of trauma to the head due to an automobile accident and reportedly had four episodes of vomiting before visiting to the hospital.The patient was subjected to MDCT scan of the brain such that acute sub-dural hemorrhage measuring 4mm in maximum thickness was noted along the left parieto-occipetal convexity.There was also presence of mild extension of hematoma along the intra-hemispheric fissure along with communited undisplaced fracture of the right occipital bone . Complete blood count,coagulation profile, urine examination, renal and liver function tests were also in normal limits. A conservative approach was made to treat the patient whereby the treatment consisted of IV infusion of mannitol(100 ml),meropenem(600 mg) and vancomycin(500 mg).The patient's vitals where all in the normal limits. After the first dose of vancomycin the physical examination revealed rash on the face, neck and upper torso which was diagnosed as the red man syndrome (RMS).There was also presence of fever, chills, weakness, dizziness, nausea, vomiting and a rapid heart rate. Clinically, the syndrome developed at the end of the infusion in the patient, but appeared as early as 15 minutes after initiation of the infusion. By observing the adverse drug reaction of the patient the total regimen was changed and the vancomycin was totally aborted and IV infusion of diphenyhydramine was made in order to correct the complications. With the change in regimen. The situation of RMS was reversed within a few hours of administration of diphenyhydramine. Further care and periodic assessment of vitals was undertaken in order to prevent any sort of allergic reactions to the body. the case of RMS is best described in the following images.

DISCUSSION:-

Hypersensitivity reactions due to vancomycin are of many variations including localized skin reactions and generalized cardiovascular collapse. The most frequently encountered side effect is the reaction of infusing vancomycin (VIR). It is caused by infusion of the drug at a fast rate and is not an actual hypersensitivity reaction as such. Administration route -

Principal if not exclusive cause of VIR is the parenteral or intravenous administration of vancomycin. Very rarely, topical application of vancomycin powder has been reported to cause VIR.In contrast, oral administration of vancomycin in subjects with *Clostridioides difficile* infections does not usually result in systemic absorption. However, for some patients, especially those with impaired kidney function or other abnormalities, oral administration can lead to detectable serum levels of the medication, and VIR to oral vancomycin may be possible[4]. The predominant side effect of Vancomycin use is red man syndrome(RMS) and there have been a number of studies carried out to explore this overbearing toxicity. A prospective study was done to evaluate the incidence, aetiology, and possible prevention of this phenomenon. Thirty-three patients were followed for their first two doses (1 g over 60 min) of vancomycin. Prior to the first infusion, the patients were randomized to receive double-blind pretreatment with either diphenhydramine (50 mg) or a placebo. Patients were re-evaluated in a short time span, and blood was collected to monitor histamine levels at 0, 30 and 60 minutes during infusion of the first dose. Patients experiencing first dose reactions were cross-randomised for additional prophylaxis and histamine levels were assessed during a second infusion. Of 17 received placebo before infusion, 8 (47%) had RMS. None of the 16 received diphenhydramine prophylaxis had any first-dose reaction (P = .003). Three out of the eight patients who experienced first dose reactions evidenced an RMS reaction after the second dose; in one such case, the second dose was minimal compared to the first RMS despite diphenhydramine prophylaxis. RMS episodes were noted along with increased histamine in plasma; particularly so, during episodes marked as severe [6].The red-man syndrome occurs frequently in normal adults who receive 1000 mg of vancomycin over 1 h, that vancomycin causes an infusion rate-dependent increase in plasma histamine concentration, and that the increase in plasma histamine concentration is correlated with the severity of the reaction[7]. The local intra-wound application of vancomycin powder has been found effective in controlling the rates of surgical site infections, and it has gained popularity for use in many surgical specialities, notably neurosurgery. RMS is a well-known histamine-mediated hypersensitivity reaction classically caused by intravenous administration of vancomycin , although there have been very rare reports of RMS associated with oral or intraperitoneal administration of vancomycin[8]. The intensity of the response to the reaction may not be unchanging. It has been observed in patients who have received vancomycin treatment for more than a week without any adverse effects, during a 90 minutes or 120 minutes infusion, last few minutes, there are delayed reaction. Most of the hospital protocols require vancomycin to be infused over 60 minutes, as a minimum[9].Although modern preparations of vancomycin are associated with a lower incidence of adverse events than the early preparations, a number of clinically significant problems remain. Consequently monitoring of serum concentrations is required. In a meta-analysis of comparative trials adverse events were significantly less likely to occur with teicoplanin (13.9%) than with vancomycin (21.9%) (P = 0.0003). This was particularly significant when nephrotoxicity was considered: 4.8% vs. 10.7%, for teicoplanin and vancomycin, respectively (P = 0.0005). The syndrome of red man, which is probably related to the release of histamines, appears after the quick administration of vancomycin however, it is very rare after teicoplanin use. In USA trials, thrombocytopenia was more commonly seen with teicoplanin administration but this was almost exclusively in patients receiving much larger doses than are now recommended. The lower rate of adverse events supports the choice of teicoplanin over vancomycin in treating infections where the two antibiotics have similar efficacy[10].

CONCLUSION:-

To prevent future occurrences of red man syndrome, it is crucial to meticulously evaluate the administration of vancomycin and consider alternative antibiotics for individuals at heightened risk. Supportive care measures are imperative during treatment to enhance patient comfort and monitor for potential complications. Ensuring adequate hydration is vital for the patient's overall well-being and aids in flushing out any residual drugs or byproducts from the system. Rigorous monitoring of vital signs—such as blood pressure, heart rate, and respiratory status—is essential for promptly identifying any deterioration in symptoms or complications. Equipping patients with comprehensive information and clear instructions regarding red man syndrome can significantly reduce the likelihood of recurrence and foster greater involvement in their own care.

REFERENCES:-

1. Sivagnanam, S., & Deleu, D. (2003). Red man syndrome. *Critical care (London,*

England), *7*(2), 119–120. https://doi.org/10.1186/cc1871
2. Martel, T. J., Jamil, R. T., & King, K. C. (2023, January 25). *Vancomycin flushing Syndrome*. StatPearls - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK482506/
3. Chen, C., Ng, K., Lin, Y., & Kao, M. (2018). Red man syndrome following the use of vancomycin-loaded bone cement in the primary total knee replacement. *Medicine*, *97*(51), e13371. https://doi.org/10.1097/md.0000000000013371
4. *UpToDate*. (n.d.). UpToDate. https://www.uptodate.com/contents/vancomycin-hypersensitivity/print
5. Myers, A. L., Gaedigk, A., Dai, H., James, L. P., Jones, B. L., & Neville, K. A. (2012). Defining risk factors for red man syndrome in children and adults. *The Pediatric infectious disease journal*, *31*(5), 464–468. https://doi.org/10.1097/INF.0b013e31824e10d7
6. Mark R. Wallace, John R. Mascola, Edward C. Oldfield, Red Man Syndrome: Incidence, Etiology, and Prophylaxis, *The Journal of Infectious Diseases*, Volume 164, Issue 6, December 1991, Pages 1180–1185, https://doi.org/10.1093/infdis/164.6.1180
7. Polk RE, Healy DP, Schwartz LB, Rock DT, Garson ML, Roller K. *Vancomycin and the red-man syndrome: pharmacodynamics of histamine release*. J Infect Dis. 1988 Mar;157(3):502-7. doi: 10.1093/infdis/157.3.502. PMID: 2449506.
8. Nagahama, Yasunori *Red man syndrome caused by vancomycin powder* Journal of Clinical Neuroscience, Volume 50, 149 - 150
9. Upendrababu, V. (2018). Red man syndrome. *International Journal of Current Research*, *10–12*, 76485–76487.
10. Wood M. J. (2000). Comparative safety of teicoplanin and vancomycin. *Journal of chemotherapy (Florence, Italy)*, *12 Suppl 5*, 21–25. https://doi.org/10.1080/1120009x.2000.11782314