Oxaliplatin Desensitization

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Has oxaliplatin desensitization shown success in preventing hypersensitivity reactions? If so, what is the proper oxaliplatin desensitization protocol?

Who asked the question? Medical doctor

List of drugs involved: Oxaliplatin, prophylactic antiemetics, corticosteroids, and antihistamines

Drug Information Response:
A research letter by Nozowa et al. outlines a case study of a patient who experienced a grade 3 hypersensitivity reaction (HSR) to FOLFOX chemotherapy regimen.[1] The patient was administered a series of diluted-oxaliplatin infusions, as well as a prophylactic antiemetic agent, corticosteroid, and antihistamine once prior to the diluted-oxaliplatin infusions and once during. The diluted-oxaliplatin protocol administered was as follows: 1:10000, 1:1000, 1/100, and 1/10 of oxaliplatin diluted in 100mL of D5W each given over 60 minutes, followed by the remaining 90% of the oxaliplatin dose diluted in 500mL of D5W given over 4 hours. The prophylactic agents were given just prior to the final 4 hour infusion. The patient was given 5 cycles of this protocol with a LV5FU2 chemotherapy regimen and it was successful in preventing HSRs. This research letter concludes that desensitization protocols seem to be determined empirically, but the majority follow the protocol as described in the above case study. The research letter notes that some sensitized patients who were given the final infusion (90% of remaining oxaliplatin dose) over 2 hours developed a macular rash, but when the final infusion was given over 4 hours instead, HSR prevention was successful. A comprehensive review by Hewitt et al. reiterates success with this same protocol in several case studies and also mentions success with a 12 step protocol.[2]

A retrospective study by Lee et al. further outlines this 12 step protocol as follows: initial 1:100 diluted-oxaliplatin solution administered at a rate of 2mL/hour, doubling the infusion rate every 15 minutes and increasing the solution concentration by tenfold every hour for a total of 12 steps of injections.[3] The study utilized both this 12 step protocol and the protocol mentioned above. In 38 patients, 89% were able to successfully undergo oxaliplatin-containing chemotherapy without HSR. Of these 38 patients, 20 had been previously treated with prophylactic medications to prevent HSR with oxaliplatin and were unsuccessful. The study indicates that since there are no standardized doses of prophylactic agents, desensitization should be the preferred first option in preventing HSR.

Final Recommendation: Oxaliplatin desensitization has shown success in preventing HSRs. There are two standard protocols utilized:

1.) 1:10000, 1:1000, 1/100, and 1/10 of oxaliplatin diluted in 100mL of D5W each given over 60 minutes, followed by the remaining 90% of the oxaliplatin dose diluted in 500mL of D5W given over 4 hours
2.) Initial 1:100 diluted-oxaliplatin solution administered at a rate of 2mL/hour, doubling the infusion rate every 15 minutes and increasing the solution concentration by tenfold every hour for a total of 12 steps of injections

References:

1. Nozawa H, Muto Y, Yamada Y. Desensitization to oxaliplatin with two stages of premedication in a patients with metasatic rectal cancer. *Clinical Therapeutics.* 2008 Jun;30(6):1160-5.

2. Hewitt M, Sun W. Oxaliplatin-Associated Hypersensitivity Reactions: Clinical Presentation and Management. *Clinical Colorectal Cancer.* 2006 Jul;6(2):114-7.

3. Lee S, Kang H, Song W, Lee K, Han S, Cho S. Overcoming oxaliplatin hypersensitivity: different strategies are needed according to the severity and previous exposure. *Cancer Chemotherapy & Pharmacology.* 2014 May;73(5):1021-9.