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Medication Desensitization: Single Intravenous Bag Method, in 3 Pediatric Patients

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Chemotherapies and biologic agents are known to cause hypersensitivity reactions (HSRs). It is imperative that pediatric patients receive these agents to treat their cancer or other rare condition, as oftentimes there are no available therapeutic alternatives. Successful medication desensitization has been described previously with a 12-step method using 3 intravenous (IV) infusion bags of varying concentrations. However, this 12-step process is time and resource intensive and increases the risk for medication errors. A recent study successfully used a simplified 12-step method with a single IV infusion bag for a paclitaxel desensitization. From the results of this study, our institution used this single IV infusion bag method for desensitization with 3 different medications. Two of these experiences were successful. We share those 3 experiences in this report.

ABBREVIATIONS COG, Children's Oncology Group; ERW, asparaginase *Erwinia chrysanthemi*; HSR, hypersensitivity reaction; IV, intravenous; PEG-ASP, pegaspargase

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Many chemotherapy and immunomodulatory biologic agents can cause hypersensitivity reactions (HSRs).[1,2] In many circumstances where pediatric patients require treatment with these agents, no second-line alternative therapeutic agents are available when these children develop HSRs. One published study of a medication desensitization method describes a 12-step process using 3 different intravenous (IV) infusion bags of varying concentrations to administer chemotherapeutic and biologic agents, including carboplatin and paclitaxel, to patients with previous HSRs.[3] Although apparently safe and effective, the method described is labor-intensive and inadequate for a variety of reasons. First, it requires preparation of 3 different IV infusion bags of varying medication concentrations, which can be burdensome from a compounding perspective. Second, administering nurses are required to make multiple adjustments to the rate of administration and must switch out the variably concentrated IV infusion bags 2 times during each administration, potentially increasing the risk for medication errors. Lastly, when the nurse switches the IV infusion bag to the next concentration, it is possible that a significant amount of medication remains in the bag that must be discarded and contributes to waste. A 2019 study compared a 12-step desensitization method using 1 IV infusion bag to the previously mentioned study.[4] Forty-nine adult patients were included in this study, 24 of whom underwent desensitization with a single IV infusion bag protocol, and 25 underwent desensitization with a multi–IV infusion bag protocol. The authors report a 98% success rate with the 12-step, single IV infusion bag desensitization method, citing significantly shorter administration times, and no difference in the rate of breakthrough reactions. Secondary to the success reported from this study and ongoing drug shortages, our institution implemented a 12-step, single IV infusion bag desensitization method for patients with previous HSRs to asparaginase *Erwinia chrysanthemi* (ERW), temsirolimus, and rituximab.[5] The details of these experiences are described below and in the Table.

Erwinia chrysanthemi

Our institution initially used the 12-step, single IV infusion bag desensitization method for a 17-year-old male with T-cell acute lymphoblastic leukemia treated per Children's Oncology Group (COG) protocol AALL0434.[5] He received 1 dose of pegaspargase (PEG-ASP) successfully, but 15 minutes after starting the infusion for his second dose he developed emesis, chest pain, diaphoresis, and hypotension despite premedication with IV famotidine and IV diphenhydramine. Because of this reaction to PEG-ASP and per COG recommendations, PEG-ASP was replaced by a course of ERW. Unfortunately, the patient developed lightheadedness, epigastric pain, and emesis during the initial dose of IV ERW. Although the infusion was paused, and resumed at only half of the initial infusion rate per institutional standards, the patient's reaction continued. A clinical decision was made to administer a 12-step medication desensitization for PEG-ASP, using 3 different IV infusion bags, which was ultimately successful as the

Table. Desensitization Information

	Asparaginase *Erwinia chrysanthemi*	Temsirolimus	Rituximab
Age, yr	17	19	2
Weight, kg	103.6	66.7	10.7
Diagnosis	T-Cell ALL	Mesenchymal chondrosarcoma	Opsoclonus/myoclonus syndrome
Dose	60,000 IU	35.8 mg	250 mg
Total volume	500 mL	895 mL	500 mL
Concentration	120 IU/mL	0.04 mg/mL	0.5 mg/mL
Administration rate	0.5 mL/hr for 15 min 1 mL/hr for 15 min 3 mL/hr for 15 min 6 mL/hr for 15 min 15 mL/hr for 15 min 37.5 mL/hr for 15 min 100 mL/hr for 15 min 200 mL/hr for 15 min 300 mL/hr for 15 min 400 mL/hr until complete	1 mL/hr for 15 min 2 mL/hr for 15 min 3 mL/hr for 15 min 4 mL/hr for 15 min 5 mL/hr for 15 min 6 mL/hr for 15 min 7 mL/hr for 15 min 14 mL/hr for 15 min 28 mL/hr for 15 min 56 mL/hr for 15 min 112 mL/hr for 15 min 224 mL/hr for 15 min 259.8 mL/hr until complete	1 mL/hr for 15 min 2 mL/hr for 15 min 4 mL/hr for 15 min 8 mL/hr for 15 min 15 mL/hr for 15 min 30 mL/hr for 15 min 45 mL/hr for 15 min 80 mL/hr until complete
Total infusion time, hr	3	6	8
Premedications	IV diphenhydramine IV famotidine IV methylprednisolone PO montelukast IV lorazepam	IV diphenhydramine IV famotidine IV methylprednisolone	PO acetaminophen IV diphenhydramine IV famotidine IV methylprednisolone
Number of successful doses	30	25	0

ALL, acute lymphoblastic leukemia; IV, intravenous

patient tolerated the total infusion. On day 7 after the infusion, the patient's serum asparaginase activity concentration was undetectable, indicating the presence of neutralizing antibodies to PEG-ASP.[6,7] The patient was no longer a candidate for subsequent doses of PEG-ASP and thus, he required an ERW desensitization.

Because ERW vials have a 4-hour stability, and have been on national shortage, it was prudent to develop a shorter desensitization protocol than the method using 3 different IV infusion bags. As shown in the Table, we developed a 12-step, single IV infusion bag desensitization method for ERW, which was administered over 3 hours in total. Premedications included IV diphenhydramine, IV famotidine, IV methylprednisolone, IV lorazepam, and oral montelukast. The desensitization was a success, and the patient has since tolerated 30 ERW administrations with this desensitization method while maintaining therapeutic serum asparaginase activity concentrations.

Temsirolimus

A 19-year-old female with recurrent mesenchymal chondrosarcoma received temsirolimus as part of her chemotherapy regimen. Shortly after the start of her first infusion, she experienced abdominal pain, rash, facial swelling, and throat tightness. The infusion was stopped, 1 dose of IV diphenhydramine was administered, and her symptoms resolved. Given the lack of alternative chemotherapy options, it was decided to proceed with a 12-step, single IV infusion bag desensitization. This was chosen over the 3 IV infusion bag method owing to the ease of administration and reduced risk of medication errors with the single IV infusion bag method. Because this medication has a 24-hour stability, we chose a longer infusion time of 6 hours. Additionally, the patient received premedication with IV methylprednisolone, IV famotidine (1 dose each), and IV diphenhydramine every 4 hours for 2 doses with first dose prior to infusion. She tolerated

the desensitization well and has since successfully received 25 doses of temsirolimus with this method.

Rituximab

A 2-year-old female with opsoclonus/myoclonus syndrome received her first dose of rituximab without complication. During her second infusion, she developed a rash and hives on her legs and face. The HSR was treated with IV diphenhydramine and IV methylprednisolone. The rash responded to treatment, but soon after, the patient began vomiting and was noted to have pallor, blue lips, and an oxygen saturation of 72% on room air. Epinephrine was administered intramuscularly, and the patient's symptoms resolved. Although corticosteroids, adrenocorticotropic hormone, and IV immune globulin are traditional treatment options for opsoclonus/myoclonus syndrome, the addition of rituximab has produced high success rates with tolerable side effects.[8] Given the lack of preferred treatment alternatives, the decision was made to proceed with a 12-step, single IV infusion bag desensitization. Similar to the temsirolimus desensitization, this was chosen over the 3 IV infusion bag method owing to the ease of administration and reduced risk of medication errors with the single IV infusion bag method. Premedications included oral acetaminophen, IV diphenhydramine, IV famotidine, and IV methylprednisolone. After receiving 2 hours of the rituximab desensitization, she developed a rash on her right cheek. The infusion was discontinued and additional doses of oral acetaminophen and oral diphenhydramine were administered. The rash continued to spread to her extremities and included an urticarial-like lesion on her left thigh. She did not have any respiratory symptoms. Given this subsequent reaction despite use of a desensitization protocol, the patient was deemed no longer able to receive rituximab.

Conclusion

This report describes 2 successful and 1 unsuccessful 12-step desensitization method using a single IV infusion bag in patients previously experiencing a HSR to chemotherapy or biologic agents. We hope that our experiences will provide other institutions with a simpler, less error-prone desensitization method to use for their patients experiencing HSRs who lack alternative treatment options.

Article Information

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