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CONTRIBUTED REPORTS

Protocol for rapid increase of hemoglobin through high-dose IV iron dextran infusion

William Pogue, M.D.
Senior Attending Hematologist and Oncologist, Section of Hematology and Oncology (Retired)

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Protocol for rapid increase of hemoglobin through high-dose IV iron dextran infusion.

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Introduction

The following is the methodology I use for the administration of intravenous iron dextran, for total dose infusion. I have used this method for more than thirty-five years and it has worked quite well, with uniformly safe outcomes. During this time my patients have experienced allergic reactions far less often than one per hundred infusions, and none of these reactions has been a serious adverse event, and no instance of anaphylaxis has occurred. Attached to this memorandum is a copy of a package insert for iron dextran (Infed). A current package insert for the iron dextran product being used should always be reviewed, since these package inserts are periodically updated, and the product is currently made by more than one manufacturer.

The administration of iron dextran should always be done under controlled conditions, with frequent monitoring of the patient's vital signs, especially during the first ½ hour of administration, and every two hours or so after that. Resuscitative equipment and medication, particularly epinephrine, should be available at the time of infusion. I am, however, pleased to report that in my more than 35 years of clinical use, having administered iron dextran to more than 2,500 patients, none of my patients has ever had a serious adverse event, required epinephrine treatment, or required hospitalization or acute medical care following an iron dextran infusion.

I use a method called Total Dose Infusion (TDI), wherein the total calculated replacement dose of iron is administered in a single, 4-hour infusion. This method gives no more risk than giving a smaller dose of iron dextran (or any other intravenous iron salt), but neither does it confer more safety per dose. It does, however, allow the patient to receive a single dose of intravenous iron rather than multiple doses of iron, and thus the net risk for IV iron is vastly reduced. This is because anaphylaxis is not a dose related event, but rather a hypersensitivity phenomenon, and decreasing the number of antigenic exposures results in fewer risks of generating drug sensitization.

Although iron dextran is approved for intramuscular administration, there have been reports in the medical literature of development of sarcoma or other malignancy in the vicinity of such injections, so I do not use intramuscular iron dextran.
The FDA has approved iron dextran for a maximal amount of 100 mg daily. Thus, TDI is an off-label use of iron dextran.

Protocol and Technique for Total Dose Infusion of Iron Dextran

An intravenous line is started, using an intravenous catheter. A 20 gauge catheter or larger is preferred. The smallest size to be used should be 22 gauge. The intravenous solution to be used is normal saline.

Dextrose and water should never be used to administer Iron Dextran

The frequency of adverse reactions is substantially higher when D5W is used instead of normal saline. My volume of preference for the infusion is 500 cc. A large drip chamber (Buretrol brand) is connected to the IV bag and 100cc of saline is allowed into the drip

chamber and the IV flow is begun, at 125 cc/hr. An IV pump may be used here for convenience, but is not required. When it is clear that the IV line is functioning, the full dose of iron dextran is added to the IV bag via the medication addition port, and mixed with the saline. One to two drops of the diluted iron dextran is then allowed to enter the large drip chamber. For an iron dextran dose of 3000 mg, the resulting concentration of iron dextran in the drip chamber would now be <0.008mg/cc, but as yet no iron dextran will have reached the patient. The IV rate will carry some of the iron dextran to the patient within 2 to 5 minutes. This is effectively a "test dose." If no change in vital signs occurs then gradually add additional iron dextran solution to the drip chamber over 10 to 15 minutes. There will be a continuing increase in the concentration of the solution reaching the patient, until finally the patient is receiving the full strength of the preparation (which is approximately 6.0mg/cc). A recommendation from the literature for maximal safe rate of infusion is 12.5mg/minute, which would cap the administration rate at 2.08cc/min = 125cc/hr. No data for this recommendation are cited, and I frequently exceed this recommended maximum rate by administering the solution at a rate of 150 to 180 cc/hr. (=300 to 375mg/hr. = 15 to 18 mg/hr). If at anytime during the infusion the patient has any symptoms, I will slow the rate of infusion to a more tolerable rate, and proceed with the infusion. For the rare patient with nausea or any suggestion of sensitivity to the infusion, I will at this time treat with diphenhydramine and/or glucocorticosteroid. I do not routinely pretreat the patient with medications to prevent symptoms unless the patient has had symptoms from a previous iron dextran infusion.

The obvious benefit for this "test dose/rapid desensitization" method is to allow the patient to begin with a miniscule dose of iron dextran, rather than the package insert recommended 25mg, dose, which is sufficient to precipitate full-blown anaphylaxis if the patient is indeed sensitive. The tiny dose gives an opportunity for the patient to have a smaller reaction and for the medical personnel to stop the infusion quickly, before the adverse reaction can fully develop. On occasion, I have needed to slow an infusion, but none of my patients was unable to complete the full infusion, and no "medical resuscitation" beyond diphenhydramine and prednisone or dexamethasone has ever been required.

Care should be taken to avoid extravasation of the iron solution since it does stain tissue, although not permanently. To decrease the risk of tissue staining, I request that the IV line be flushed with 20 cc of normal saline at the end of the infusion in order to minimize the presence of any residual iron dextran in the iv catheter.

The patient should be forewarned of two other small concerns. Particularly with higher doses of iron dextran, perhaps as many as 1 in 3 patients may experience a few days of achiness after the infusion. This is self-limited, and rarely lasts beyond a few days. Fair-skinned patients may note the appearance of a mild "sun-tan" for a few weeks after the iron dextran, again, more so with higher doses, due to temporary localization of some of the iron dextran in the skin.

A brisk reticulocytosis often occurs starting a few days after the infusion. The rate of red cell production and hemoglobin rise is generally proportionate to the severity of the patient's anemia: most patients with severe iron deficiency will show a hemoglobin rise of approximately ½ gram/day for a week (i.e. 3 to 4 gram rise in hemoglobin in one week) if there are no other complicating medical problems. Patients with a lesser deficit, or with complicating illnesses will have a slower rate of rise.

Dose calculation for the iron dextran using the package insert is clumsy and requires that the physician use the supplied table. I find it much simpler to do the following dose calculation: simply multiply the deficit for the hemoglobin (in grams) by 250mg (amount needed to form a pint of blood), and add an additional 1000 mg to replace the normal reserve amount. Thus, a 17 year old girl with iron deficiency from menometrorrhagia, with a hgb of 5 and ferritin of 3, should receive 7 (hgb deficit in grams) X 250 mg of iron dextran = 1750 mg, for deficit replacement, plus 1000 mg for replenishment of normal iron reserves = 2750 mg for total dose. This would be given in 500 cc normal saline, IV over 4 hours.

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About the Author

William Pogue, M.D.

Senior Attending Hematologist and Oncologist, Section of Hematology and Oncology, The Hospital of Central Connecticut, New Britain, CT