

Successful Desensitization To Infiximab In A Boy With Crohn's Disease

Background

Infiximab (IFX) is a chimeric mouse-human antibody, which targets tumor necrosis factor (TNF) alpha. IFX has proven to be highly effective in inducing and maintaining remission in moderate to severe Crohn's disease and ulcerative colitis. Despite its effectiveness, several adverse reactions to IFX have been identified, including infusion-related reactions (1).

Objective

To describe an accelerated desensitization protocol in a pediatric patient with severe infusion-related reaction to IFX.

Case report

A 10 years old boy with severe Crohn's disease refractory to the treatment with oral corticosteroids, was started in treatment with infliximab. During the first administration and with a short time to onset of the symptoms, the patient developed dyspnea, cough, chest pain and generalized urticaria. The infusion was stopped and treatment with hydrocortisone and clemastine was administered. One month later, a new dose was administered and the patient developed similar reaction. Four weeks later, we performed skin prick test and IDR at concentration of 1mg/ml, that were negative. We hospitalized the patient and after premedication with acetaminophen and loratadine, we performed a nine-hours desensitization protocol using three different concentrations (**Table 1A**) (total dose of 200 mg). In the next infusions, a progressive rate and/or a higher concentrations were used (**Tables 1B and 1C**).

Table 1 A.

Phase	Dilution	Infusion rate
1	Dilution # 1: 0,6 mg infliximab (3 cc from dilution # 2) + 30 ml DAD 5% (0.02 mg/ml)	6 ml/hr for 30 minutes
		15 ml/hr for 30 minutes
		30 ml/ hr for 30 minutes
		60 ml/hr until the end
2	Dilution # 2: 5 mg infliximab (0,5 cc from 200 mg / 20 ml dilution) + 25 ml DAD 5% (0,2 mg/ml)	5 ml/hr for 30 minutes
		10 ml/hr for 30 minutes
		20 ml/ hr for 30 minutes
		40 ml/hr until the end
3	Dilution #3: 195 mg infliximab (19,5 cc from 200 mg / 20 ml dilution) + 100 ml DAD 5% (1,95 mg/ml)	10 ml/hr for 30 minutes
		20 ml/hr for 30 minutes
		40 ml/ hr for 30 minutes
		80 ml/hr until the end

Protocol N° 1. Phases, dilutions and infusion rates used during the first day.

Table 1 B.

Phase	Dilution	Infusion rate
1	Dilution # 1: 0,6 mg infliximab (3 cc from dilution # 2) + 30 ml DAD 5% (0.02 mg/ml)	-----
		15 ml/hr for 15 minutes
		30 ml/ hr for 15 minutes
		60 ml/hr until the end
2	Dilution # 2: 5 mg infliximab (0,5 cc from 200 mg / 20 ml dilution) + 25 ml DAD 5% (0,2 mg/ml)	5 ml/hr for 15 minutes
		10 ml/hr for 15 minutes
		20 ml/ hr for 15 minutes
		40 ml/hr until the end

Methods (continuation...)

Table 1 B (continuation...)

Phase	Dilution	Infusion rate
3	Dilution #3: 195 mg infliximab (19,5 cc from 200 mg / 20 ml dilution) + 100 ml DAD 5% (1,95 mg/ml)	10 ml/hr for 15 minutes
		20 ml/hr for 15 minutes
		40 ml/ hr for 15 minutes
		80 ml/hr until the end

Protocol N° 2. Phases, dilutions and infusion rates used during the second day (one month after protocol N° 1).

Table 1 C.

Phase	Dilution	Infusion rate
1	Dilution # 1: 10 mg infliximab (1cc from 200 mg / 20 ml dilution) + 25 ml DAD 5% (0,4 mg/ml)	5 ml/hr for 10 minutes
		10 ml/hr for 10 minutes
		20 ml/ hr for 10 minutes
		40 ml/hr until the end
2	Dilution #2: 190 mg infliximab (19 cc from 200 mg / 20 ml dilution) + 100 ml DAD 5% (1,9 mg/ml)	10 ml/hr for 15 minutes
		20 ml/hr for 15 minutes
		40 ml/ hr for 15 minutes
		80 ml/hr until the end

Protocol N° 3. Phases, dilutions and infusion rates used during the third day (one month after protocol N° 2).

Discussion

There are no reports about the usefulness and security of desensitization protocols to infliximab in pediatric population. With our patient we started a 12 step protocol but with different concentration and volume than in other centers (2). In the second day, we remove the first step of the first dilution and increased the rate of infusion. By the third day, and because the previous one was well tolerated, we decided to start with an additional higher rate and concentration and the patient did not have any reaction. In the subsequent monthly administrations, the protocol N° 3 was used with good tolerance. It let us to think that in children with infusion-related reactions to infliximab, a progressive approach increasing both the infusion rate and concentration, could be safe and effective.

Conclusion

The proposed desensitization protocol was successful in a boy with infusion-related reaction to infliximab. Probably, the symptoms of the patient could be related to the infusion rate. To our knowledge, this is the first report of a successful desensitization to infliximab in children. More studies are needed to recommend the use of this protocol in the pediatric population.

References

1. Steenholdt C, Svenson M, Bendtzen K, Thomsen OØ, Brynskov J, Ainsworth MA. Severe infusion reactions to infliximab: aetiology, immunogenicity and risk factors in patients with inflammatory bowel disease. *Aliment Pharmacol Ther.* 2011; 34: 51–8.
2. Brennan PJ, Rodriguez Bouza T, Hsu FI, Sloane DE, Castells MC. Hypersensitivity reactions to mAbs: 105 desensitizations in 23 patients, from evaluation to treatment. *J Allergy Clin Immunol.* 2009;124:1259-66.