Successful Desensitization to Rituximab in Four Patients with Autoimmune Diseases

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Background

Rituximab is a chimeric monoclonal anti-CD20 antibody used frequently in the treatment of hematologic malignances and autoimmune diseases. Infusion-related reactions are common (1, 2), and no standardized strategy is approved to the treatment of them, apart of premedication, although its efficacy is controversial (3). Underlying mechanism of reactions include massive cytokine release, hypersensitivity, immune imbalance, cross reactivity, and symptoms not directly affecting the immune system. In the case of rituximab, massive citokyne release seems to be the most common. Our aims were to describe a new short desensitization protocol to rituximab and to establish if IgE is involved in these reactions.

Methods

Patients with autoimmune diseases in which rituximab had induced hypersensitivity reactions were prospectively included. A six hours intravenous (continuous infusion)desensitization protocol was used **(Table 1)**. Prick and intradermal (IDR) skin tests (1 mg/ml) were made to each patient previous to the onset of the first desensitization protocol. Premedication with hydrocortisone, loratadine and acetaminophen were given one hour before the onset of the infusions.

Dilution	Concentration	Infusion rate	Dose (mg)*
# 1	50 mg /250 ml (0,2 mg/ml)	25 ml/h for 30 min	2,5
		50 ml/h for 30 min	5,0
		100 ml/h for 30 min	10
		150 ml/h for 30 min	32,5
# 2	250 mg /250 ml (1 mg/ml)	25 ml/h for 30 min	25
		50 ml/h for 30 min	50
		100 ml/h for 30 min	75
		150 ml/h for 30 min	100
# 3	700 mg /500 ml (1,4 mg/ml)	25 ml/h for 30 min	70
		50 ml/h for 30 min	105
		100 ml/h for 30 min	140
		150 ml/h for 30 min	385

Table 1.
Proposed desensitization protocol with rituximab. *The total cumulative dose was 1000 mg for all the patients.

Results

Four patients (three women and one man) were prospectively included. Previous reactions included skin manifestations (urticaria and/or angioedema) in all of them and dyspnea in one (patient # 3). None of the reactions were presented with the first cycle of rituximab and occurred between few minutes and three hours of the onset of the infusion. Prick test and IDR were negative in all the patients. A total of seven desensitizations were made in the four patients **(Table 2)**. All patients tolerated them. Minor side effects were present in four of the seven protocols (three patients), but none of the infusions had to be stopped at any time.

Patient	Age	Sex	Diagnoses	Type of reaction and cycle (*)	TOTR	# D
# 1	11	M	SLE	Urticaria, dyspnea, angioedema (2)	30 min	1
# 2	27	F	SLE	Erythema, oedema (3)	180 min	2
# 3	39	F	RA and SS	Urticaria, dyspnea (5)	90 min	2
# 4	31	F	RA	Angioedema, erythema, pruritus (14)	90 min	2

Table 2.
Main characteristics of the four patients. M: male; F: female; SLE: systemic lupus erythematosus; RA: rheumatoid arthritis; SS: Sjögren syndrome; (*): cycle of rituximab during which reaction was presented; TOTR: time to onset of the reaction; # D: number of desensitizations made in each patient.

Conclusions

In these patients, infusion-related reactions to rituximab seem to be not related to IgE sensitization. However, a short desensitization protocol was successful in them. Large scale studies are needed to recommend the use of desensitization in patients with non allergic hypersensitivity to rituximab.

References

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