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Prevention of Dextran Anaphylaxis

Ten Years Experience with Hapten Dextran

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Key Words

Dextran-induced anaphylactoid/anaphylactic reactions · IgG antibodies ·
Dextran-reactive antibodies · Immune complexes

Introduction

Dextran-induced anaphylactoid/anaphylactic reactions (DIAR) were described already in the 1950s. The pathomechanism was explained during the 70s as being either non-immunologic, usually mild anaphylactoid reactions, or mostly severe immunologic immune-complex-mediated anaphylactic reactions [1]. The latter are caused by naturally occurring predominantly IgG class dextran-reactive antibodies (DRA) [2]. No IgE class DRA have been demonstrated. The infusion of clinical dextran into a predisposed patient with a high titer of DRA generates large noxious immune complexes, leading to release of vasoactive mediators that cause the clinical symptoms.

Hapten Inhibition

Since severe DIAR is classified as immune complex anaphylaxis, specific hapten inhibition can be used for prevention. If a monovalent hapten (e.g. dextran I) is injected first, the combining sites of the specific antibodies are blocked. When polyvalent antigen (e.g. clinical dextran) is subsequently injected, the formation of immune complexes is inhibited.

Hapten inhibition with a monovalent hapten dextran (dextran I, MW 1,000 D; Promit®) has proven to be an effective prophylactic measure in clinical trials performed from 1978 to 1982 on 130,000 patients [3].

Postmarketing Surveillance

We have evaluated all spontaneous reports to the manufacturer and to the WHO database INTDIS regarding adverse reactions to clinical dextran after preinjection of Promit and to Promit alone during 10 years, 1983-1992. The sales figure for Promit was 5.1 million doses distributed to 15 countries during this period, each dose corresponding to one subsequent exposure to clinical dextran.

Results

The worldwide incidence of severe grade III-V DIAR to clinical dextran after the prophylactic use of hapten inhibition was approximately 1/200,000 doses of Promit. In Sweden, where reporting of severe adverse drug reactions is mandatory, the incidence was approximately 1/70,000. This indicates a 35-fold reduction of the incidence of severe DIAR compared to the use of clinical dextran without Promit (table 1) [4]. Only two fatal reactions were reported, i.e. an incidence of 1/2.5 million doses, indicating a 90-fold reduction. Both reactions occurred in patients with extremely high titers of DRA. Mostly mild, side effects to Promit were reported in approximately 1/100,000 doses. These reactions are not antibody mediated.

Conclusion

The introduction of hapten inhibition with Promit has greatly reduced the risk of serious side effects to dextran, making dextran one of the safest colloids in use.

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Table 1. DIAR in Sweden in 1975-1979 [4] and 1983-1992

Grades of severity	Characteristic symptoms	DIAR, n	
		1975-1979 (without dextran I)	1983-1992 (with dextran I)
I	Skin manifestations (flush, erythema, urticaria) Lumbar pain	61	78
II	Mild to moderate hypotension (blood pressure 40-60 mm Hg depending on duration) Gastrointestinal disturbances Respiratory distress	94	44
III	Severe hypotension, shock (blood pressure 40-60 mm Hg) Bronchospasm	78 } 44 } $\approx 1/2,000^1$ 23 }	12 } 4 } $\approx 1/70,000^1$ 1 }
IV	Cardiac and/or respiratory arrest		
V	Fatal reaction		
Total		300	139

¹ During 1975-79, 647,756 units of clinical dextrans (Macrodex®/Rheomacrodex®) were sold to hospital clinics in Sweden, corresponding to 0.3 million dextran-treated patients [4]. During 1983-92, 1.2 million doses of dextran I were sold, which is assumed to correspond to the same number of patients since dextran I is given only before the first infusion of clinical dextran.

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