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Short Desensitization In An Adolescent With Hydroxychloroquine Anaphylaxis

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To the Editor:

When patients present allergic reactions to the first line treatment for their disease, and when the use of alternative medication is not well tolerated or does not provide disease control, desensitization is indicated¹.

Hydroxychloroquine (HCQ) is the election drug for Systemic Lupus Erythematosus (SLE) treatment because of its efficacy and safety profile^{2,3}. We present an adolescent with a SLE who developed anaphylactic reactions to HCQ and in whom this drug was successfully reintroduced after a short desensitization procedure.

A 17 year-old African non-atopic girl diagnosed of SLE, Antiphospholipid Syndrome (AphS), Raynaud's phenomenon, Nephrotic Syndrome secondary to Lupus Glomerulonephritis grade II/III and Hyporeninemic Hypoaldosteronism was referred to our Allergy department for 2 episodes of anaphylaxis due to HCQ. The patient was hospitalized in the Pediatrics Department when she received the second dose of HCQ 200 mg and 60 minutes later she developed hives in face and neck with generalized pruritus and dyspnea which resolved with dexchlorpheniramine administration. Two days later she was given HCQ at the same dose and within a few minutes she developed facial edema, hypotension and tachycardia that resolved with hydrocortisone and dexchlorpheniramine. After these anaphylactic reactions, she was treated with other drugs (cyclophosphamide, mycophenolic acid, azathioprine, systemic corticosteroids and rituximab³), that were used to control her lupic nephropathy, with poor tolerance. Also, at this moment, the patient continued with high risk of developing thromboembolic events (high titers of Anticardiolipin/Antiphospholipid antibodies). For all the above reasons HCQ was the best drug to benefit this patient. She was therefore referred to our Allergy Department for desensitization to HCQ.

Before desensitization, written consent by the patient and her mother was obtained. Skin prick test (SPT) and intradermal test (IDT) were performed with HCQ serial 10 fold dilutions from 2 µg/ml to 20 mg/ml prepared in a saline solution at the Pharmacy

Department. SPT were negative to all the concentrations tested. IDT with HCQ 2 mg/ml elicited a 6 mm erythema, and at 20 mg/ml a 10 mm wheal. No reaction was observed in SPT nor IDT at the same concentrations in 5 control subjects. Total IgE was 359 kU_A/L and baseline serum tryptase was 1.81 µg/L. The patient was premedicated with dexchlorpheniramine 5 mg, methylprednisolone 100 mg, acetylsalicylic acid (ASA) 300 mg and montelukast 10 mg according to the standard premedication of rapid drug desensitization procedures^{1,4}. Additionally, a single dose of omalizumab 300 mg was administered 3 days before (there are some case reports of successful desensitization to drugs like insulin, deferoxamine and meropenem with omalizumab as premedication⁵). Corticosteroids and antihistamine (dexchlorpheniramine 5 mg intravenously in the first 2 days of desensitization, and ebastine 10 mg orally until the end of the desensitization) were administered one hour before the procedure daily. Montelukast and ASA were given daily during the desensitization procedure.

The desensitization schedule was planned to be done in 7 days. It was started at the Pediatrics Intensive Care Unit (PICU), where the patient received increasing doses of HCQ every 30 minutes during the first 3 days (Table 1) reaching a cumulative dose of 63.5, 164 and 150 mg during the first, second and third day respectively. On the 4th day the patient received a single dose of 150 mg at the PICU and since it was well tolerated she was discharged. She was advised to take 150 mg at home on the 5th and 6th days (weekend). Finally on the 7th day, the patient was given a single dose of 200 mg at the day care facility of the Allergy Department. No adverse reactions were observed during the desensitization procedure. Afterwards the patient took HCQ 200 mg daily at home together with ASA as part of her usual treatment. Ebastine and montelukast were stopped 10 days after reaching the HCQ 200 mg therapeutic dose. See table 1.

Eight months after desensitization, HCQ tolerance is maintained and the patient has achieved a good disease control.

There are only 2 reports of HCQ desensitization, but to the best of our knowledge, our patient is the first documented case of successful desensitization to HCQ in an adolescent. Mates⁶ in 2006 reported desensitization to HCQ in 36 days in four adult patients with SLE or Rheumatoid Arthritis. Díaz and Maquiera⁷ in 2010 reported a desensitization to HCQ in 28 days in a 48 year-old man with SLE and HCQ anaphylaxis. Due to the severe and poorly controlled SLE in our patient, these previously described procedures with a 4 to 5 weeks length were considered too long, and therefore a shorter schedule with a cluster up dosing on the first 3 days was designed. This allowed us to reach therapeutic doses of HCQ in just one week time without any safety concern, and achieved quicker disease control.

Day	Dose (mg)	Interval (minutes)	Cumulative dose (mg)	Location
1	0.5	30	63.5	PICU
	1	30		
	2	30		
	4	30		
	8	30		
	16	30		
	32			
2	32	30	164	PICU
	32	30		
	50	30		
	50			
3	50	30	150	PICU
	50	30		
	50			
4	150		150	PICU
5	150		150	At home
6	150		150	At home
7	200		200	Allergy Dept.