Systemic absorption of sodium cromoglicate from a new cutaneous emulsion (Altoderm (R)) in children with atopic dermatitis

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CORRESPONDENCE

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Our objective was to determine the systemic absorption of sodium cromoglicate (SCG) in subjects with atopic dermatitis, being treated with a new cutaneous emulsion (Altoderm®). Altoderm is a 4% w/w concentration of (SCG) in a novel emollient base designed to enhance the skin penetration of SCG [1].

Nine subjects with atopic dermatitis, who had been using Altoderm for at least 3 months, were selected. Seven were aged 3 to 7 years, one 14 years and one aged 26. The protocol was approved by the Isle of Wight, Portsmouth & SE Hants Local Research Ethics Committee, UK. All parents or patients gave informed, written consent.

Subjects applying Altoderm twice daily to affected areas of skin collected a 24 hour specimen of urine during a 6 day period. They emptied their bladder in the morning, applied the cutaneous emulsion, and then collected all urine passed until before the application of emulsion the next morning. They weighed the Altoderm container before and after each application. The 24 hour collection was delivered to the clinic that day, total amount measured immediately and a 100 mL aliquot taken and stored at 4 °C. The determination of the amount of sodium cromoglicate in the aliquots was undertaken using a validated HPLC method.

Table 1. Subject details and results together with calculations of means and standard deviations

A)				
Subject No.	**Age (years)**	**Body Surface Area (BSA) (m^2)**	**SCG applied (mg/24 hrs)**	**Urine collected (mls/24 hrs)**
1	7	1.00	628	600
2	3	0.64	412	520
3	3	0.64	400	400
4	26	1.88	132	980
5	5	0.74	248	1,080
6	14	1.84	100	1,170
7	6	0.85	200	450
8	6	0.87	160	850
9	4	0.84	352	1,020
		Mean	*292.4*	*785.6*
		SD	*170.6*	*295.3*
B)				
Subject No.	**Concentration of SCG in aliquot (µg/L)**	**Urinary SCG (µg/24 hrs.)**	**SCG absorbed (%)**	**SCG absorbed BSA (mg/m^2)**
1	2.21	1,326	0.42	2.66
2	0.10	52	0.03	0.16
3	7.75	3,100	1.55	9.62
4	0.59	578	0.88	0.62
5	1.84	1,987	1.00	5.37
6	0.85	995	1.99	1.08
7	5.77	2,597	2.60	6.10
8	1.34	1,139	1.42	2.61
9	4.62	4,712	2.68	14.83
Mean	2.79	1,831.8	1.46	4.78
SD	2.65	1,444.2	0.91	4.85

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Table 1A shows age, body surface area, amount of SCG applied in mg/24 hours, and amount of urine collected over 24 hours. *Table 1B* shows the concentration of SCG in the aliquot sample, the amount of SCG excreted in the urine in μg/24 hours, the percentage systemic absorption of SCG and the amount absorbed based on body surface area. The mean amount of Altoderm applied each day was 7.78 ± 5.31 g (Range 3-20 g). The mean percentage of SCG absorbed was 1.46 ± 0.91% (Range 0.03-2.68%).

Systemic absorption of SCG is low. Absorbed drug is not metabolised and is eliminated within 24 hours. The amount of SCG excreted in the urine over 24 hours represents 50% of the amount absorbed [2]. A previous study in atopic dermatitis, using a 4% concentration of SCG in oil in water cream measured the amount of SCG in 24-hour urine specimens [3]. They reported absorption of 0.44 ± 0.02% (mean ± SE). The mean absorption from the 4% cutaneous emulsion we used was therefore 3 times greater than that from the 4% cream used in that study. This may have implications for both the efficacy and safety of the product used.

The safety of sodium cromoglicate in respect of systemic exposure was determined using the inhaled route in man. It is described in detail in a review by Cox *et al.* [4]. Pharmacokinetic studies that have been undertaken using this system, have shown that, on average, 12% of the inhaled dose is deposited in the respiratory tract, but it can be as high as 17.1%. That proportion of the drug reaching the respiratory tract is absorbed. The remainder is swallowed, of which up to 1% is absorbed [5]. The maximum approved dose via inhalation is 2 × 20 mg, four times daily or 160 mg/day. Assuming that up to 18% of this could be absorbed systemically; this would give an upper limit for daily systemic exposure of 28.8 mg/day. In our study, taking the maximum figures recorded, 20 g of Altoderm lotion (800 mg SCG) applied per day and 2.68% absorption, this would give a potential of 21 mg of SCG absorbed/day, below that approved for inhalation use.

We conclude that there are no safety implications in the clinical use of the new cutaneous emulsion in patients due to systemic exposure and that the enhanced absorption may improve clinical efficacy. ■

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1. Stainer R, Matthews S, Arshad SH, *et al.* Efficacy of a new topical skin lotion of sodium cromoglicate (Altoderm) in atopic dermatitis in children aged 2-12 years: a double-blind, randomized, placebo-controlled trial. *Br J Dermatol* 2005; 152: 334-41.

2. Moss GF, Jones KM, Ritchie JT, Cox JS. Plasma levels and urinary excretion of disodium cromoglycate after inhalation by human volunteers. *Toxicol Appl Pharmacol* 1971; 20: 147-56.

3. Ariyanayagam M, Barlow TJG, Graham P, Hall-Smith SP, Harris JM. Topical sodium cromoglycate in the management of atopic eczema - a controlled trial. *Br J Dermatol* 1985; 112: 343-8.

4. Cox JS, Beach JE, Blair AM, *et al.* Disodium cromoglycate (Intal). *Adv Drug Res* 1970; 5: 115-96.

5. Aswania OA, Corlett SA, Chrystyn H. Relative bioavailability of sodium cromoglicate to the lung following inhalation, using urinary excretion. *Br J Clin Pharmacol* 1999; 47: 613-8.