

LONG-TERM TREATMENT WITH LOMUDAL

Bengt Arner: Dr Bertler and I felt that we were well-placed to carry out a long-term study of Lomudal because we had a large number of steroid-dependent patients with well-documented histories (1). We selected 60 patients, half of whom had previously-demonstrated hypersensitivities. Some of these hypersensitive patients were still undergoing hyposensitization treatment. The criterion for selection was that the patient was not free of symptoms, despite treatment with steroids (average dose 5 mg prednisolone/day). The details of the patient material are shown in Table 1. In collaboration with Johansson, we determined total IgE levels on two occasions, with an interval of 30 days between. There was very little variation between the two measurements and no obvious difference between the mean values for intrinsic and extrinsic asthmatics.

Careful consideration was given to the trial design. During an initial trial period we gradually reduced the dose of steroids to the minimum possible. The patient was then started on Lomudal. Initially, Lomudal with 0.1 mg isoprenaline added was used, as this was the only formulation then available. During Lomudal treatment, we further lowered the steroid dose as much as possible, while maintaining freedom from symptoms. Lomudal was then stopped and the steroid dose restored to the former level. The patient was then treated with a placebo containing as much isoprenaline as the Lomudal formulation, and attempts were again made to reduce the dose of steroids (Fig. 1).

In practice, it proved difficult to adhere rigidly to the trial design. Complications arose when patients developed infections and it became necessary to increase the dose of steroids and to use antibiotics. We found it was possible, however, to obtain information from periods of equal duration of Lomu-

TABLE 1
Patient Material for Trial of Steroid-sparing Effect of Lomudal.

Patient no.	Initials	Age and sex	Age at onset	Hyper-sensitivity	Hyposensitization performed	Steroid treatment (years)	Concentration of IgE in ng/ml	
							Sample I	Sample II
1	G.A.	55 F	42			6	120	125
2	A.J.	54 F	23			12	283	300
3	I.L.O.	37 F	23			11	89	95
4	G.O.	35 F	6			5	165	130
5	E.A.	49 F	47			1	47	39
6	S.O.	37 M	34			1	118	118
8	A.H.	53 F	16	+	1954-	6	215	208
9	J.D.	16 M	6	+	1963-	4	150	140
10	C.D.	10 M	8	+	1966-	1	665	530
11	Å.S.	53 M	45			6	120	130
13	A.G.	63 F	54			3	165	160
14	L.L.	32 F	13	+	1958-	5	1.150	1.350
16	M.U.	32 F	4	+	1960-1968	7	235	200
17	H.P.	47 M	36	+	1959-	8	685	560
18	L.A.	44 F	27	+	1963-	4	115	65
19	S.N.	46 M	44			1	2.450	2.325
20	S.P.	50 F	44	+	1963-	3	930	1.100
21	S.Å.	35 M	1	+	1966-	2	25	27
22	A.T.	62 F	50			12	18	19
23	B.N.	48 F	34	+	1965-	2	860	830
24	L.H.	56 M	49			5	760	830
25	V.B.	44 F	41			1	190	218
27	G.H.	36 F	20	+	1964-	3	81	74
28	G.L.	45 F	20			5	118	148
29	E.R.	35 F	22			1	303	255
30	J.S.	19 M	17			1	290	210
31	A.P.	24 F	1	+	1961-	4	415	415
32	G.P.	55 F	49			4	300	350
33	N.B.N.	60 M	54	+	1961-	6	400	310
34	T.T.	44 M	36			4	175	188
35	S.F.	51 F	43			8	440	455
37	V.H.	42 F	37	+	1964-	3	595	510
38	G.N.	19 F	1	+	1963-	4	62	88
39	S.H.	52 M	12	+	1954-1962	7	240	5
41	M.S.	45 F	40			1		
42	B.H.	28 F	1	+	1966-1969	2	67	3
43	A.B.A.	19 F	1			7	67	9

TABLE 1 (continued)

Patient no.	Initials	Age and sex	Age at onset	Hypersensitivity	Hyposensitization performed	Steroid treatment (years)	Concentration of IgE in ng/ml	
							Sample I	Sample II
44	J.H.	47 F	1			3	130	125
45	L.O.S.	21 M	1	+	1963~	3	160	125
46	G.S.	55 M	46	+	1960~	6	1.600	11.700
47	T.P.	25 M	1	+	1957-1963	1	380	460
48	A.L.B.	36 F	23			1	325	370
49	G.S.	41 M	38			1	305	300
50	N.S.	61 M	53			7	455	285
51	M.L.O.	49 F	32			4	140	153
52	A.G.W.	49 F	1			10	99	135
53	A.B.	16 F	1	+	1959-1967	8	155	130
54	E.A.	41 F	27	+	1967~	1	240	250
55	N.E.N.	48 M	7			1	66	295
58	L.L.	33 M	29			2	56	59
59	B.P.	20 F	19			1	49	37
60	E.K.	22 F	4			1	425	460

dal and placebo treatment. The mean steroid doses and the numbers of patients are shown in Fig. 2. Using a variety of statistical tests, it can be shown that the reduction in steroid dose due to Lomudal is significant. Similarly, there was a statistically significant reduction in steroid dosage when the follow-up period of Lomudal treatment was compared to the control period (Fig. 3). The mean overall reduction when the Lomudal period was compared with the placebo period was only 0.6 mg/day (Table 2). Although this reduction may seem small, it should be pointed out that it is a mean, and in many patients we were able, with the use of Lomudal, to withdraw steroids completely or in large measure. We were unable to distinguish between the responses of the extrinsic and intrinsic group.

In the treatment of on-going asthma, I think the first concern of the clinician should be to treat the acute symptoms with β_2 -stimulants, orally or by inhalation. Expectorants are

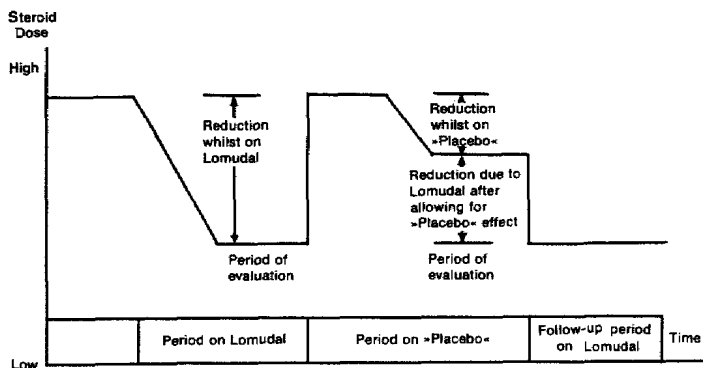


Fig. 1.
Trial design.

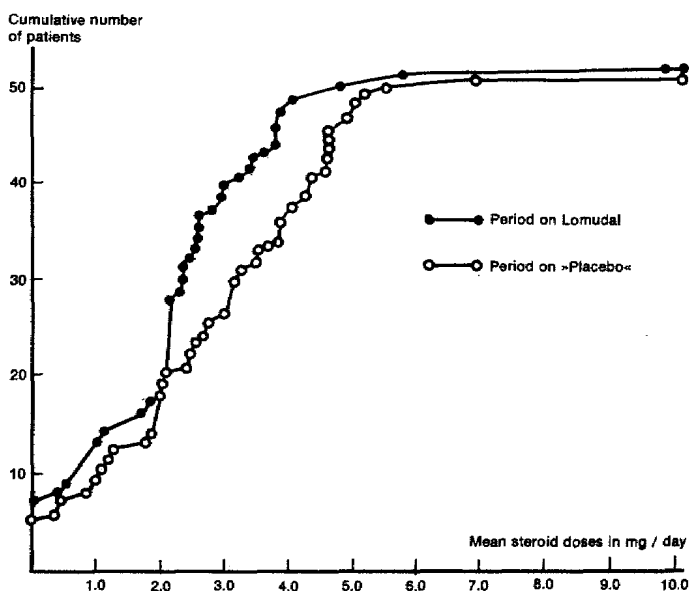


Fig. 2.

Mean steroid doses in 52 patients during Lomudal and placebo treatment.

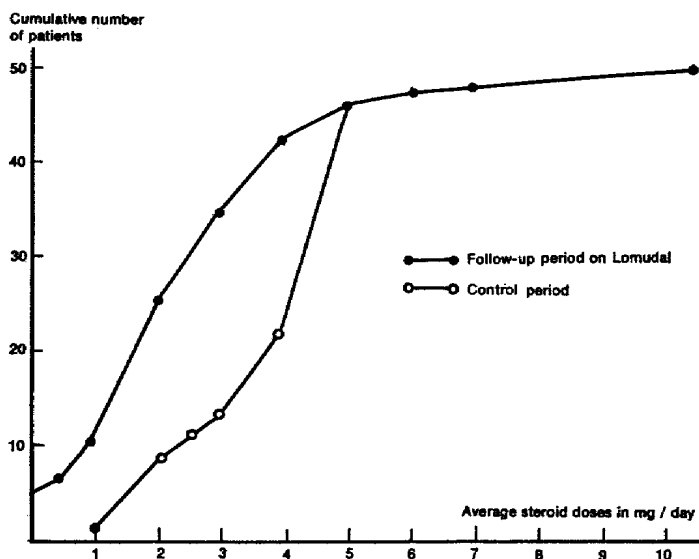


Fig. 3.

Mean steroid doses in 50 patients during control period and during Lomudal treatment.

TABLE 2
Mean Steroid Doses during Different Periods of Treatment.

Periods of treatment	Number of patients	Steroid dosage (mg/day) Mean $\pm$ s.d.
Control period	52	1.1 $\pm$ 1.7
Period on Lomudal	52	2.3 $\pm$ 1.8
Period on "placebo"	52	2.9 $\pm$ 2.0
Follow-up period on Lomudal	50	3.0 $\pm$ 2.2

often useful. Where acute symptoms are severe and infection may be present, tetracyclines and prednisolone may be used over a short period to obtain a remission. When the patient is symptom-free, tetracycline and if possible prednisolone can be

withdrawn and the patient maintained on sympathomimetics. I think the time to start Lomudal treatment is when the patient is in a reasonable condition. During our trial, the formulation of Lomudal with isoprenaline was well-liked by patients. This was probably due at least in part to the effect of the isoprenaline and we now recommend our patients to inhale either salbutamol or terbutaline a few minutes before inhaling Lomudal. This will, hopefully, aid the penetration of the Lomudal powder into the smaller airways.

REFERENCES

1. Arner, B., Berg, B., Bertler, A. & Johansson, S. G. O. (1971): Steroid sparing effect of disodium cromoglycate in chronic bronchial asthma. *Acta allergol.* 26, 383-389.

Discussion

F. Lange-Nielsen: I would like to ask Bengt Arner if he can divide his big material into sub-groups. Probably some groups of asthmatics get a good steroid-sparing effect, while other groups get no effect at all.

B. Arner: Our material included patients who had required 5 mg/day of prednisolone for prolonged periods. I remember that with one particular patient, we were able to discontinue steroids with Lomudal treatment, but his allergic rhinitis then became more troublesome. Hopefully, the drug will be made available as a nasal spray for cases such as this. It indicates that the drug exerts its action only on the organ to which it is applied.

During our steroid reduction trial, we found that the steroid consumption was related to some extent to how often we saw the patients and the amount of encouragement they received from us. Even allowing for this variable we felt that during comparable periods the use of Lomudal allowed a reduction in steroids.

J. Havnen: The work of Aas & Fjulsrud in Oslo is relevant to this discussion of the steroid-sparing effect of Lomudal (3). They studied 18 children with perennial asthma who were receiving up to 10 mg of prednisolone/day and found that with Lomudal they could reduce steroids by an average of 40 per cent. There was a wide variation—some children could not reduce their dosage at all, while others could reduce very significantly.

We had a case last year which highlights the need for care in patients treated with Lomudal who have been on long-term steroids. A 14-year-old girl with severe extrinsic allergic asthma was able to reduce and eventually to stop her doses of steroids in hospital. While at home, after discharge, she consumed an amount of uncooked cake dough, developed an allergic reaction together with bronchial asthma to the raw egg in the dough and was dead within half an hour. One must be aware of these potential hazards. Now we would probably switch patients from oral steroids to beclomethasone aerosol as a first step.

I. Engström: We have studied a group of 44 children who were treated with Lomudal for 6 months or more (2). Their steroid dosage had been reduced to the minimum possible before starting on Lomudal. We found a great variation in the reductions obtained during Lomudal treatment. In one group of 26, no reduction was possible; in the other, of 18, it was possible to reduce the dose and, in 11 of these patients, to withdraw steroids completely. In this group, there was a significant predominance of atopic children with positive skin and provocation tests and high serum IgE levels.

REFERENCES

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2. Havnen, J. (1973): Dinatrium-Kromoglykat (Lomudal). Klinisk virkning, indikasjoner og praktisk anvendelse ved astmatiske lungesykdommer. *T. Norske Laegeforen.* 1740.

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