CUTANEOUS ERUPTIONS AND LITHIUM

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A study was conducted to compare the incidence of cutaneous lesions in 126 patients treated with lithium carbonate and in 64 patients treated with minor tranquillizers or other antidepressant drugs. Cutaneous eruptions were seen in 78(61.90%) patients in the study group and in 18(28.12%) patients in the control group.

The commonest skin conditions in the lithium treated group were, acne and acneiform eruptions (15.1%), diffuse hyperpigmentation of face (9.5%), folliculitis of legs (4.1%), alopecia (4.0%) and tinea cruris (4.0%). In the control group acne and acneiform eruptions, diffuse hyperpigmentation of face and folliculitis of legs were seen in 6.2%, 3.1% and 1.6% patients respectively. The differences were statistically significant. Psoriasis with psoriatic arthropathy was observed in 2(1.58%) patients in the study group only. One striking observation in the study group was significant increase in the number of patients with diffuse facial pigmentation, progression of which was not affected by sunscreens.

Key words : Lithium carbonate, Cutaneous eruptions.

Cutaneous eruptions in the form of itchy maculo-papular lesions in patients taking lithium carbonate were first mentioned by Callaway et al.[1] Subsequently, symmetrical papular eruptions resembling dermatitis herpetiformis,[2] symptomatic hyperkeratotic follicular papules on extensors,[3] exfoliative dermatitis[4] and even precipitation and exacerbation of psoriasis[5] have been reported. Pustular lesions reported with lithium include folliculitis,[3] acneiform eruptions[6,7] and induction of pustular phase of psoriasis.[8] This group of pustular lesions is considered to be dose-dependent and may alert the clinician to a possible toxic state.[9] The present study was conducted to compare the incidence of cutaneous lesions in patients treated with lithium carbonate and others treated with minor tranquillizers or antidepressants.

Materials and Methods

Two groups of patients were selected. First group included 126 patients on lithium therapy for more than 4 weeks without additional psychoactive therapy. Second group of 64 patients were taking minor tranquillizer or antidepressant drugs for 4 weeks and acted as the control group. All patients were interrogated and examined only once during the course of therapy and subsequently if any cutaneous problem needed attention. None of the patients had any systemic disease requiring additional drugs. None had hypothyroidism. Correlation was attempted between the duration of therapy, serum levels of lithium and the type of cutaneous eruption.

A cutaneous condition was considered possibly secondary to lithium therapy if, (1) it appeared for the first time after initiation of therapy, and (2) if the already existing cutaneous condition exacerbated following therapy.

Results

Out of the 126 patients in the study group, 86 were males and 40 females. The age ranged from 13-70 years (mean 42.09 years). Duration of lithium therapy varied from 3-170 months (mean 59.60 months). The dose of lithium per day varied from 300-1200 mg. Serum lithium levels in the last 3 months of therapy varied from 0.19-2.00 mEq/L.

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In the control group, there were 37 males and 27 females. Their ages ranged from 10-60 years (mean 30.96 years). Duration of treatment varied from 62-66 months (mean 48.0 months).

Cutaneous eruptions were seen in 78 (61.9%) patients in the study group, 52 (66.6%) males and 26 (33.3%) females. In the control group, the cutaneous lesions were seen in 18 (28.1%) patients, 6 (33.3%) males and 12 (66.6%) females.

Commonest skin condition was acne and acneiform eruptions, seen in 19 (15.1%), followed by diffuse hyperpigmentation of the face in 12 (9.5%), folliculitis of legs in 8 (6.3%), and diffuse alopecia and tinea cruris in 5 (4.0%) patients each. Pityriasis versicolor was present in 4 (3.2%), and chronic generalised pruritus and dry ichthyotic skin of legs in 3 (2.4%) each. Psoriasis vulgaris with psoriatic arthropathy was observed in 2 (1.6%) males. In one patient psoriasis appeared for the first time and in the other it worsened and became un-responsive to conventional therapy. Lichen simplex chronicus, hyperkeratosis and fissuring of feet, contact dermatitis, monilial intertrigo and scabies were seen in 2 (1.6%) patients each. Ichthyosis vulgaris, chronic monilial paronychia, discoloration of nails of both hands, pigmented nevus, nummular eczema, keratolysis exfoliativa and pigmented purpuric dermatoses were seen in 1 (0.8%) patient each.

In the control group, cutaneous lesions seen were acne and acneiform eruptions in 4 (6.2%), diffuse alopecia and facial pigmentation in 2 (3.1%) patients each, chloasma, chronic pruritus, pityriasis versicolor, seborrhoeic capitis, nummular eczema, tinea cruris et corporis, verruca vulgaris, infectious eczematoid dermatitis, folliculitis of legs and plantar corn were seen in one (1.6%) patient each.

Statistically significant differences in the two groups in the incidence were observed for acneiform eruptions, diffuse hyperpigmentation of face, and folliculitis of legs (Table I).

Table I. Incidence of cutaneous lesions in the patients and controls.

	Number (percentage) of patients in the	
	Study group	Control group
Acneiform eruptions	19(15.1%)	4(6.2%)
Diffuse hyperpigmentation of face	12(9.5%)	2(3.1%)
Folliculitis	8(6.3%)	1(1.6%)
Diffuse alopecia	5(4.0%)	2(3.1) %
Mild ichthyotic change on legs	3(2.4%)	—
Chronic pruritus	3(2.4%)	1(1.6%)
Psoriasis	2(1.6%)	—

Comments

The efficacy of lithium carbonate in the treatment and prophylaxis of unipolar and bipolar affective disorders (manic depressive psychosis) has been well established.[10] The precise mechanism by which lithium compounds exert their therapeutic benefit and the precise site at which the action is exerted is yet to be defined.

Out of the various other toxic effects of lithium on many systems such as heart, parathyroid, thyroid, kidney and nervous system, skin lesions occur most frequently. Cutaneous side effects were first mentioned by Callaway et al.[1] Subsequently, folliculitis, acneiform eruptions and some other cutaneous side effects attributable to lithium have been shown to respond to a reduction in dosage,[3,7,11,12] but reappear on challenge.[12] Skin lesions in majority are reversible.

Acneiform eruption associated with lithium carbonate was first reported by Kusumi in 1971[6] and subsequently confirmed by others.[7,13] Exacerbation by lithium was also reported.[3]

Lithium has also been reported to exacerbate psoriasis[5,12,14] and to induce the pustular phase[8,15] with a latency period of one to 36 months. Psoriasis, resistant to conventional

therapy was also reported by other workers.[12,16] In the study of Skoven and Thormann,[12] psoriasis had appeared for the first time in 12, in 3 others pre-existing mild disease was aggravated and in many it was resistant. In 10 patients it improved on withdrawal of the drug and in the 2 challenged it reappeared after variable periods of time. We however feel that the incidence of psoriasis seen in lithium treated group (1.5%) does not differ much from the overall incidence of psoriasis in the general population varying from 0.25 to 1.5%.

Another important pustular lesion induced by lithium includes folliculitis,[3] which resembles keratosis pilaris. The gradual onset, frequent spontaneous remissions and high occurrence rates imply that it is physiologic rather than allergic and may be dose related (toxic levels more than 2 mEq/L).[9] In none of our patients the levels correlated with these lesions. The difference in the incidence in the study (6.3%) and the control groups (1.5%) was statistically significant. The folliculitis is of cosmetic significance only, the therapy can continue. The dermatologist should know that treatment of acneiform eruptions and folliculitis with tetracyclines can result in serious lithium toxicity, sometimes producing a nephrotoxic effect.[9]

Diffuse hair loss[17] and alopecia areata[16] have been reported in patients on lithium therapy. Diffuse loss of hair was found in 5 (3.9%) patients compared to 2 (3.1%) in the control group. Uncommon side effects included ulcers,[1] ichthyosis[15] and xerosis.[18] The last two side effects were seen in 2.4% and 1.6% of our study patients respectively.

The striking observation in the patient group was diffuse facial pigmentation. It started in the peri-orbital region spreading gradually to involve the cheeks and forehead. It was seen in all patients and was often the first to appear. Colour of pigmentation varied from light to dark brown mixed with slaty shade in some. Progress of the pigmentation was not altered by sunscreens.

In the present study more males (66.6%) in the lithium treated group developed cutaneous lesions as compared to the females. This is in contrast to an earlier study[16] where more females developed cutaneous side effects.

The incidence (62%) of cutaneous eruptions compared to 28.1% in the controls is much higher than that (3.4%) reported by Vester gaard et al[19] and 7.2% reported by Bone et al.[20] However, the data in these studies was based on the information volunteered by the patients which will mostly include symptomatic lesions, compared to total body examination by a dermatologist. Sarantidis and Waters[16] in a detailed study on 91 lithium treated patients found the incidence of cutaneous reactions possibly due to lithium in 34%.

References

1. Callaway CL, Hendric HC and Luby ED. : Cutaneous conditions observed in patients during treatment with lithium, Amer J Psychiat, 1968; 124 : 1124-1125.
2. Posey R : Lithium carbonate dermatitis, JAMA, 1972; 221 : 1517.
3. Rifkin A, Kurtin BB, Quitkin F et al : Lithium induced folliculitis, Amer J Psychiat, 1973; 130 : 1018-1019.
4. Kuhnley EJ and Granoff AL : Exfoliative dermatitis during lithium treatment, Amer J Psychiat, 1979; 136 : 1340-1341.
5. Skott A, Mobacken H and Starmark Jr : Exacerbation of psoriasis during lithium treatment, Brit J Dermatol, 1977; 96: 445-448.
6. Kusumi Y : A cutaneous side effect of lithium : report of two cases, Dis Neru Syst, 1971; 32 : 853-854.
7. Yorder FW : Acneiform eruption due to lithium carbonate, Arch Dermatol, 1975; 11 : 396-397.
8. Evans DL and Martin W : Lithium carbonate and psoriasis, Amer J Psychiat, 1979; 136 : 1326-1327.
9. Heng M : Cutaneous manifestations of lithium toxicity, Brit J Dermatol, 1982; 106 :107-109.

10. Baker JB and Pepplinkhuizen L : More about the relationship of lithium to psoriasis, Psychosomatics, 1976; 17 : 143-146.
11. Okrasinski H : Lithium acne, Dermatologica, 1977; 154 : 251-253.
12. Skoven I and Thormann J : Lithium compound treatment and psoriasis, Arch Dermatol, 1979; 115 : 1185-1187.
13. Rhiz-Maldonaldo RR, Fransisco C and Taunayo L : Lithium dermatitis, JAMA, 1973; 224 : 1534.
14. Carter TN : The relation of lithium carbonate to psoriasis, Psychosomatics, 1972; 13 : 325-327.
15. Reiffers J and Dick P : Cutaneous side effects of treatment with lithium, Dermatologica, 1977; 155 : 155-163.
16. Sarantidis D and Waters B : A controlled study of cutaneous conditions associated with lithium carbonate, Brit Med J, 1983; 143 : 42-44.
17. Peter SM and Rodney PRD : Hair loss and lithium, Internat J Dermatol, 1984; 23 : 603-604.
18. Hoxtell E and Dahl M : Xerosis from lithium carbonate, Arch Dermatol, 1975; 111 : 1073-1074.
19. Vestergaard P, Arndisen A and Schou M : Clinically significant side-effects of lithium treatment, Acta Psych, (Scand), 1980; 62 : 193-200.
20. Bone S, Roose PS, Dunner LD et al : Incidence of side effects in patients on long term lithium therapy, Amer J Psychiat, 1980; 137 : 103-104.