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AN ATTEMPT TO IMPROVE PERCEPTION OF THE TEMPERATURE SENSATION IN HYPOAESTHETIC AREAS IN LEPROSY PATIENTS

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To prevent deformities in the leprosy patients caused by burns, an attempt has been made to improve perception of the temperature sensation in the hypoaesthetic skin areas. The sensory loss in each lesion was first graded by determining the minimum temperature felt as hot (MTH) at the affected skin area in comparison with the MTH at the corresponding unaffected skin area by means of a specially designed device named temperature-sensation-testing-and-grading device. An intradermal injection containing 3.2 μg of histamine acid phosphate at the centre of the lesion led to a decrease in the MTH by 3 to 9°C in 8 out of 12 patients including one who had a complete loss earlier. This decrease in the MTH was maintained for 15 minutes in 6 patients. A repeat study in 10 of these patients gave similar findings. In another 40 patients, a histamine-DMSO solution prepared by mixing 1 mg histamine acid phosphate with 1 ml of DMSO applied at the centre of the leprosy lesion led to a decrease in the value of MTH by 1-11°C in 14, including 3 patients who could not perceive even 50°C as hot before the application. Fifteen minutes after the application, only 3 of these patients had a decreased value of MTH. Repetition of the experiment in 18 of these patients revealed similar results.

With this limited success, it is considered worthwhile to undertake further experiments to develop suitable means under which a leprosy patient with impaired perception of the temperature sensation can be made to feel almost normal sensation and thus protect his skin from burns.

Key words : Leprosy, Sensation, Temperature, Improvement.

One of the major causes of deformities in leprosy patients is the trophic/traumatic ulcers developing due to the impaired perception of the sensations of temperature and pain.[1] In the past, patients had been advised to use protective prosthetic devices to prevent direct contact with hot objects,[2] but these mechanical devices are generally cumbersome and inconvenient, especially when the patient is involved in manual work. It is considered that a system which acts from within the body to improve the perception of sensation will be more acceptable.

It is a common observation that an area of inflamed skin is generally hyperaesthetic. It was therefore, considered worthwhile to try an agent which will induce a limited degree of inflammation in the skin area, to see if this would increase the perception of heat stimuli. Since histamine is one of the important mediators during inflammatory reactions,[3] it was considered worth checking if histamine injected intradermally or applied locally along with dimethylsulphoxide (DMSO) would increase the sensory perception. Histamine is a very potent

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drug but in controlled doses it can be given intravenously as well as subcutaneously[4] without producing any untoward effects. Moreover, histamine reactions in skin resolve without leaving behind any sequelae.

Materials and Methods

Patients included in this study had tuberculoid or borderline-tuberculoid leprosy having anaesthetic or hypoaesthetic patches. The sensory loss in each lesion was graded by determining the minimum temperature felt as hot (MTH) at the affected skin area and comparing it with the MTH at the unaffected skin area either in the adjoining skin or on the corresponding opposite site of the body. The MTH was determined by the method already described by us[5] using a special device named *temperature-sensation-testing-and-grading device.*[6]

Histamine solution for injection was prepared by dissolving histamine acid phosphate (Sigma Chemicals, USA) in double distilled water to obtain a concentration of 16 μg/ml. The solution was tested for sterility and then stored in an appropriate bottle.

After determining the MTH at the centre of a leprosy lesion, 0.2 ml of the histamine solution was injected intradermally at that site. The MTH was determined again immediately after the injection and also 15 and 25 minutes after the injection.

To test the reproducibility of the system, double blind determinations were carried out in three patients. For this purpose, two sites in the same lesion were marked and evaluated for the MTH. At one site, 0.2 ml of normal saline and at the other 0.2 ml of the histamine solution were injected intradermally by one investigator, while variation in the MTH at both the sites was evaluated by the other investigator without knowing which of the sites had been injected with normal saline and which site with histamine. The MTH determinations were done immediately and also at 15 and 25 minutes after the injection. In all the three patients, there was a reduction in the MTH at the site injected with histamine, but not at the site injected with normal saline.

Histamine-DMSO solution for external application was prepared by mixing 1 mg of histamine acid phosphate with 1 ml of dimethylsulphoxide. One drop of this solution was applied externally at the centre of a leprosy lesion after determining the MTH. The solution was massaged into the skin area and the MTH was determined again immediately and also 15 and 25 minutes after the application.

Double blind determinations were carried out for these tests also in three patients by applying the histamine-DMSO solution at one site and only DMSO solution at the other. The MTH at both these sites was determined by the other investigator without knowing what has been applied at each site. In all the cases, reduction in the MTH was observed only at the sites where histamine-DMSO solution had been applied. The site where only DMSO had been applied did not show any reduction in the MTH.

In 3 patients, histamine-DMSO solution was applied at the same site, twice, at an approximate interval of one hour. The MTH was determined both the times immediately after the application. In all the three cases, there was reduction in the values of MTH on both the occasions.

Results

The effect of injecting histamine intradermally was studied in 12 leprosy patients, age range 17-48 years, having the disease for 1-17 years. Ten of these patients were evaluated again at a later date.

At the leprosy lesions, the MTH varied between 37 and 50°C in 8 patients. The remaining 4 could not appreciate even 50°C as hot. Immediately after the histamine injection, 8 patients showed a decrease in the MTH by 3-9°C. In 3 of these patients, the MTH came

down to almost the level of the unaffected skin. Six patients showed a decreased value of the MTH even after 15 minutes. One patient did not show any reduction in the MTH immediately after the injection but showed reduction by 9°C after 15 minutes and 7°C after 25 minutes(Table I).

Table I. MTH at the unaffected and the affected skin areas in leprosy patients before and after an intradermal injection of histamine.

Number of the patient	Minimum temperature felt as hot (MTH) in °C				
	Unaffected contralateral skin	Leprosy lesion			
		Before histamine injection	After histamine injection		
			Immediate	15 minutes	25 minutes
1	33	48	45	48	48
2	34	48	43	43	48
3	32	41	37	41	41
4	34	37	37	37	37
5	39	49	40	43	49
6	37	42	38	38	42
7	39	46	39	42	46
8	35	48	42	42	48
9	34	>50	>50	41	43
10	34	>50	41	43	>50
11	34	>50	>50	>50	>50
12	36	>50	>50	>50	>50

Out of the 10 patients evaluated at their second visit, 7 patients showed reduction in the MTH by 2-8°C immediately after the injection and this reduction was maintained at 15 minutes also. In one patient reduction in the MTH was observed even 25 minutes after the injection.

The effect of applying histamine-DMSO solution was studied in 40 patients in the age range 12-80 years, having the disease for 3 months to 7 years. At the leprosy lesions, in 18 patients the MTH varied between 32 and 49°C compared to 30 and 39°C at the corresponding unaffected sites, in 6 patients the MTH at the affected and the unaffected skin areas were the same, while 16 patients could not perceive even 50°C as hot. Immediately after application of the histamine-DMSO solution, 14 patients showed a decrease in the MTH by 1-11°C. After 15 minutes, only 3 patients had decreased values of MTH, this decrease varying between 2 and 11°C. Out of the 16 patients who did not perceive even 50°C as hot, in 3 patients the MTH values decreased below 50°C after application of the histamine-DMSO solution (Table II).

Out of the 18 patients evaluated at their second visit, 6 patients showed reduction in the MTH by 3-7°C immediately after the application and in 4 patients this reduction was maintained at 15 minutes also, but by 1-5°C. After 25 minutes none, of the patients showed any reduction.

Comments

Comparison of the values of MTH at the affected and the unaffected skin areas provides a good tool for evaluating the degree of sensory impairment in a leprosy lesion. The present study has shown that an intradermal injection of histamine acid phosphate leads to a significant decrease in the values of MTH in most of the leprosy patients and one of the patients who

Table II. MTH at the unaffected and the affected skin areas in leprosy patients before and after application of histamine-DMSO solution.

Number of the patient	Minimum Temperature Felt as Hot (MTH) in °C				
	Unaffected skin	Leprosy lesion			
		Before application	After application of solution		
			Immediate	15 minutes	25 minutes
1	34	42	37	40	42
2	34	40	38	40	40
3	34	43	37	43	43
4	39	49	44	49	49
5	34	42	38	42	42
6	35	39	35	39	39
7	35	41	39	41	41
8	34	48	37	37	48
9	34	42	38	38	42
10	32	47	39	47	47
11	39	47	46	47	47
12	37	>50	49	49	>50
13	38	>50	43	47	>50
14	35	>50	46	47	>50

could not appreciate even 50°C as hot before the histamine injection could perceive a much lower temperature after the injection. This shows that histamine can indeed lower the MTH and thus improve perception of the sensation of heat. Histamine-DMSO solution was used to avoid the necessity of repeatedly injecting histamine into the affected skin areas. The results corroborated the observations made with intradermal injections of histamine in that the MTH values were significantly lowered even in some of the patients who earlier had a complete sensory loss, but prolongation of the duration of effect was not achieved.

These two experiments provide evidence that it is possible to improve sensory perception by producing a subclinical inflammatory reaction in the affected skin area, even though the success so far has been limited and transient. To convert these observations into practically useful measures, it will be necessary to try other compounds which would be safer and have a prolonged effect. Such an agent could either be incorporated into an ointment with compounds like DMSO for local application, or enclosed into micro-capsules to be transplanted/injected under the skin; a slow release of the agent would maintain the area in an improved state of sensory perception for a prolonged period.

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