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BCG as a new therapeutic and prophylactic agent in patients with severe oral aphthosis

Sirs,

Recurrent aphthosis (RAU) is a major public health problem that has been considered as the most frequent oral mucosal disease in children and adults, affecting 20-25% of the world population (1). Its etiopathogenesis is obscure although immunodysregulation has been proposed by several investigators (2-4). The therapy of this medical problem remains an important dilemma. Many therapeutic trials that have shown benefit in the relief of oral aphthosis of antibiotics, anti-inflammatory, immunomodulators, anesthetics and alternative (herbal) remedies (4).

BCG was introduced as a vaccine against TB (7), but in recent years it has also been found to act as an immunomodulator in cases of leprosy, as the incidence of this disease was reduced tremendously after introduction of the BCG vaccine (7). BCG has been used successfully in the treatment of alopecia areata (6). In addition, the incidence of skin disorders has been reported to be low in BCG-vaccinated subjects (6).

Thirty-six patients (22 males and 14 females, age range 14-55 yrs, mean 25 yrs) with classic severe oral aphthosis, who presented to the multi-disciplinary Behçet's clinic, were enrolled in this study. Patients with features of Behçet's disease and other related problems were excluded. The selection of patients was limited to those with multiple lesions for at least 7 days each month during the 6-month period preceding the study. Patients were assessed using an oral clinical manifestation index which was designed by our clinic (Table I).

All those patients were vaccinated with 0.1 ml BCG vaccine in the deltoid area of the left arm 3 times at one month intervals. Patients were evaluated every month during the 6-month period of treatment (3 months) and follow-up (3 months) using the OCMI. The data were analyzed and the results were compared with each other before, after treatment and during follow-up using the ANOVA test.

Thirty-six patients (22 male and 14 female, whose age range 14-55 years, mean 25 years) were enrolled in this study. The results of OCMI before, every month (3 months) during BCG vaccinations and follow-up month (three) were summarized in Fig. 1. The result of BCG was very encouraging as the OCMI was reduced after the second month and reached minimum after the third vaccine (mean 7.55) which was statistically significant with the P value at 0.000001. During follow-up improvement was promising as during therapy and, when the result was compared after three months of follow-up with the OCMI before therapy, it was also statistically significant.

Many studies are encouraging an immunological dysfunction theory in attiopathogenesis of RAS as the analysis of the peripheral T-lymphocytes in patients with aphthae shows a decreased ratio of T-helper ($CD4^+$) cells to T-suppressor/cytotoxic ($CD8^+$) and, furthermore when aphthae have been investigated locally in oral mucosa, an increased percentage of ($CD8^+$) cytotoxic cells have been seen (3, 4). BCG has been used in the last years as an immunomodulatory agent and has been found to be effective in the treatment of alopecia areata (6), malignant melanoma (6), viral warts (7), and diffuse cutaneous leishmaniasis (6) etc. The present work showed that BCG is effective in controlling aphthosis. This has been shown clearly during the second month and improvement continued even during the 3-month follow-up. This supports the idea that BCG has a therapeutic and prophylactic role in the management of oral aphthosis. Further follow-up is needed for further evaluation of this therapy.

The mechanism of the action of BCG in the treatment of oral aphthosis cannot be clearly explained but most probably it is through its immunomodulatory effect.

This BCG immunotherapy also has been tried in Behçet's disease and the preliminary result is encouraging (Sharquie and Hayani 2004, unpublished data). In conclusion, the BCG vaccine is an effective new mode of therapy in patients with oral aphthosis and further evaluation through double-blinded studies is indicated to overcome the bias effect of spontaneous remission.

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Table I. Clinical oral manifestation index.

Type	
Minor ulcer	1
Herpetiform	2
Major ulcer	3
Number / attack	
1-3	1
4-6	2
7-9	3
9-12	4
More than 12	5
Duration of the attack	
1-4 day	1
5-8 days	2
9-12 days	3
More than 12 days	4
Frequency (attack/date)	
0-2 weeks	5
3-4 weeks	4
5-6 weeks	3
7-8 weeks	2
More than 8 weeks	1
SX	
Uncomfortable	1
Painful not interfere with eating or swallowing	2
Interfere with solid feeding	3
Interfere with liquid eating	4

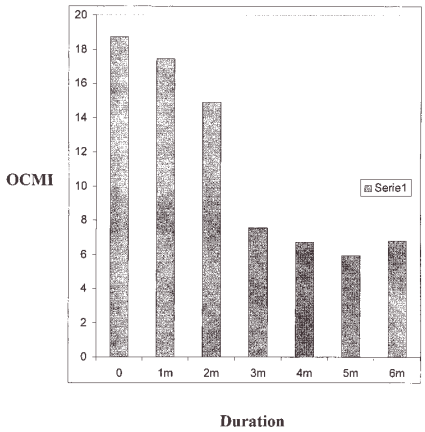

Fig. 1. Results.

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