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SHORT PAPERS

Recurrent aphthous ulcers and nicotine

Renée Bittoun

Objective: **The aim of this study was to investigate the effect of nicotine, in the form of Nicorette tablets, on aphthous ulcers in non-smoking patients. The study was prompted by the observations that smokers are less likely to suffer from mouth ulcers, that some smokers on quitting develop them, and that patients on nicotine replacement therapy are less likely to develop ulcers than those having other types of smoking cessation therapy.**

Clinical features: **The three non-smoking patients who were selected for the study each had a long history of recurrent aphthous ulcers with no remissions.**

Intervention and outcome: **Each patient was given up to four 2 mg Nicorette chewing tablets per day. After one month of this regimen each patient was weaned off the tablets. In each case the ulcers healed and new ulcers did not appear during Nicorette therapy. Two of the patients relapsed when weaned off the tablets.**

Conclusions: **This preliminary trial shows that nicotine may have a beneficial effect on aphthous ulcers. Further studies are necessary to elucidate the mechanism.**

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Aphthous ulcers are common and occur in about 2% of the population at any given time.[1] It has been documented previously that cigarette smokers have a lower incidence of these ulcers[2] and we have recently reported very severe mouth ulcers of this type in smokers when they stop smoking. In that study we found that almost one-third (29%) of smokers attending our stop-smoking clinic had acute aphthous ulceration when they stopped smoking.[3] The ulcers developed within an average of nine days after quitting and lasted a mean of six days. Multiple ulcers were common with the sites most frequently involved being the tip of the tongue and the inside of the lower lip.

The aetiology of aphthous ulcers is unknown. Studies for possible viral, infectious[4] and immunological causes[5] or nutritional deficiencies[6] have been unhelpful. In a major review article on the aetiology and management of recurrent aphthous stomatitis, Scully and Porter reported that there was as yet no reliable preventive treatment available.[7]

It has been observed at our clinic that cigarette abstainers on nicotine replacement therapy (Nicorette, A B Leo, Sweden) are less likely to have ulcers than those undergoing other types of smoking cessation therapy. We have also observed that increasing the dose or number of Nicorette chewing tablets used greatly reduces the likelihood of ulcers developing and quickly eradicates those that do.

From these observations it was postulated that nicotine may play a role in the occurrence of some of these ulcers and that non-smokers who suffer from chronic recurrent aphthous ulcers may benefit from nicotine therapy. We wish to report three cases where this therapy was tried.

Case records

Case 1

A man aged 58 years was a smoker until 1975 when he developed coronary artery disease. After the death of his wife in 1984 he developed persistent aphthous ulceration in his mouth and since then had never had less than three ulcers at any time, most lasting four to six weeks. Immunological screening showed no abnor-

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mality and biopsies confirmed the presence of aphthous ulceration. Stress increased the number of ulcers and they had a marked effect on his eating habits and life-style. The patient presented with nine aphthous ulcers. He was given 2 mg Nicorette tablets and the dose was increased to a maximum of four tablets dispersed over the day. Urine assays for the concentration of cotinine (a metabolite of nicotine) showed none on initial presentation and a level of 79 nmol/L after three weeks of nicotine therapy. The ulcers began to disappear within three days of initiation of therapy and he then became ulcer free. After four weeks he gradually stopped using the Nicorette over a period of a week and 12 weeks after presentation he remained ulcer free.

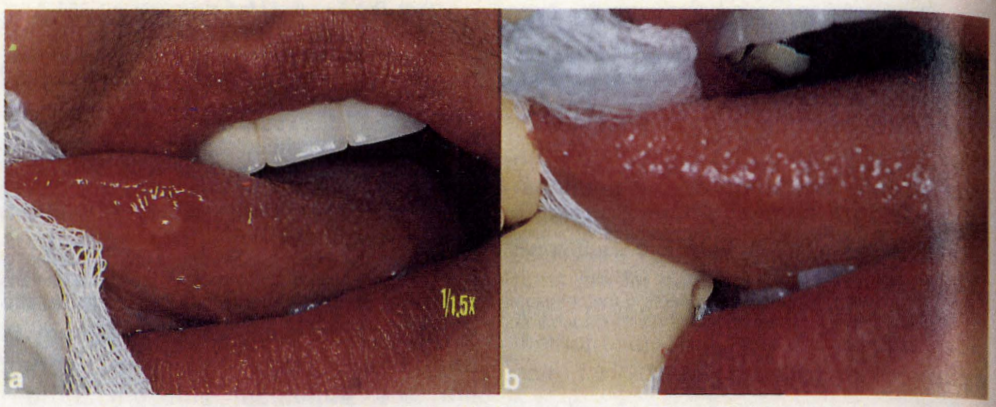

*FIGURE: Aphthous ulcer in a woman which had been present for four weeks; (**a**) on presentation and (**b**) seven days later after therapy with 4 × 2 mg Nicorette daily.*

Case 2

A 40-year-old woman had never smoked and had been fit and well apart from multiple aphthous ulcers that she had had continuously since puberty. A biopsy confirmed the presence of aphthous ulceration and immunological screening tests showed no abnormalities. She reported that the ulcers increased in number and severity before menstruation and diminished during pregnancy but that she had never been ulcer free. Most of the ulcers lasted for seven to eight days and she had never had less than three at any one time. On presentation she had four large aphthous ulcers. She was given 2 mg Nicorette tablets and the number was increased until she was taking 4 × 2 mg tablets per day. Six days after starting treatment she was ulcer free. She continued with this dose of Nicorette for one month and was free of ulcers. She was then weaned off the Nicorette. Two days after ceasing Nicorette altogether she developed a large ulcer on her tongue. She continued to abstain from the gum for one month and during that time returned to her usual condition of continuous ulceration. When the Nicorette regimen was reinstated she again went into remission. She has remained ulcer free for three months on this regimen. Regular measurement of urine cotinine levels shows low values (average 138 nmol/L) when taking Nicorette.

Case 3

A 22-year-old man who had never smoked and who reported he was in good health presented with a history of recurrent mouth ulceration since puberty. He usually had four to five ulcers at a time. On presentation, he had four large ulcers which had been present for several weeks. He noted that stress increased the duration and number of ulcers and that he was never ulcer free. Recent orthodontic treatment had greatly exacerbated the condition. Biopsy of his previous ulcers showed no other abnormality. He commenced the 2 mg Nicorette regimen and the number was increased daily until he was using 4 × 2 mg tablets per day. His ulcers began healing within a few days of starting therapy. Within one week he was ulcer free. He reported an anaesthetic effect of the Nicorette gum on the ulcers. Attempts to wean him off the Nicorette resulted in a recurrence of the ulcers within a few days of cessation of therapy. He has now been ulcer free for three months taking a maintenance dose of 4 × 2 mg Nicorette per day. Regular urinalysis shows low levels of cotinine averaging 200 nmol/L.

Comments

There have now been 10 patients whose aphthous ulcers have been successfully treated at this unit (Figure). The use of nicotine as a medication is controversial as the addictive nature of the substance is well known. However, most active smokers show high urine cotinine levels (many thousands of nmol/L) whereas the levels of cotinine in the urine of our patients were very low, approximately equivalent to the nicotine blood level resulting from one cigarette per day.

The low levels of nicotine suggest that the action is local and not systemic. Further studies delivering topical nicotine to the oral mucosa and systemic nicotine via nicotine patches may help to elucidate the mechanism of the effect of Nicorette on aphthous ulcers.

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Clearly Australia's recent performance in drug evaluation has provoked attack from across the community. The long lead time for drug evaluation is a major problem, but idiosyncrasies in our marketing requirements may also deter companies from prompt submission of marketing applications. As a result Australians have been one of the two last to benefit from new drug developments. Granted Australians want the protection given by our high standard of drug evaluation but they also want access to the best drugs on the marketplace. One hopes the future will find Australia collaborating extensively with other countries on safety and efficacy evaluations, perhaps eventually using the findings of designated agencies.

— Finkel E. Australia's system of drug evaluation — protection or pedantry? *Today's Life Sci* 1991; 3(1): 4-10.