Altered inflammatory responses in smokers

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Cigarette smoking has complex pharmacological and immunomodulatory effects on the expression of diseases such as inflammatory bowel disease and acne.[1,2] We investigated the effects of smoking on the inflammatory response to different stimuli by examining the microvascular and inflammatory components of the skin's response to injury.

Patients, methods, and results

We recruited 25 volunteers who smoked more than 20 cigarettes a day and 25 who were lifelong non-smokers. Volunteers were matched for age, sex, and skin type. Exclusion criteria included pregnancy, taking drugs likely to interfere with the study, and a history of skin disease, atopy, or allergy. Volunteers gave signed, informed consent and were told not to smoke for one hour before investigation. No other restrictions were imposed. Ethical approval was obtained from the Joint Ethics Committee of South Glamorgan Health Authority and the University of Wales College of Medicine.

Six tests were performed.

(1) Histamine acid phosphate solution (0·05 ml, 20 μg) was injected intradermally. After 15 minutes the responses were assessed by planimetry.

(2) Transvasin cream (Seton) (25 μl), which contains 2% hexyl nicotinate and 2% ethyl nicotinate, was applied to the forearm. Blood flow was continuously monitored with a laser Doppler flowmeter until the maximum flow was reached. Baseline and maximum blood flow were recorded.

(3) Three filter paper discs with solutions of 0·5%, 1%, and 2% sodium lauryl sulphate were applied to the forearm by using Finn chambers on Scanpor tape (Epitest, Hyrylä, Finland). The minimal irritancy dose was established as the concentration producing even erythema under the site of occlusion after 24 hours. Subjects were then challenged with twice the minimal irritancy dose, and the erythema was measured after 24 hours on a 10 cm visual analogue scale and with an erythema meter.[3]

(4) The minimal dose of ultraviolet B radiation required to produce uniform erythema with sharply defined borders after 24 hours was established by irradiating the back (650 μW/cm²). Twice this dose was given on the following day and the erythema measured as for the third test.

(5) Superficial microvascular blood flow in forearm skin was measured with a laser Doppler flowmeter before, during, and after occlusion of the brachial artery for two minutes. Baseline and peak flow were recorded.

(6) Skin prick tests were performed with three aqueous allergen extracts (house dust mite, cat fur, and grass pollen) and a glycerol control (Bencard).

Data were analysed with the Mann-Whitney U test, and the results are shown in the table. The response to histamine was no different in the two groups. Peak blood flow after hexyl and ethyl nicotinate was significantly reduced in the smokers, as were the irritant response to sodium lauryl sulphate and the erythema caused by ultraviolet B irradiation. Reactive hyperaemia after arterial occlusion was reduced in the smokers but not significantly so. The smokers were, however, significantly less reactive to common allergens.

Skin test results among smokers and non-smokers. Values are means (SD) unless otherwise stated

	Smokers	Non-smokers	p Value*
	Histamine		
Area (cm²):			
Weal	2·3 (0·8)	2·3 (1·3)	0·77
Flare	30·9 (9·7)	26·7 (11·3)	0·18
	Hexyl and ethyl nicotinate		
Blood flow (mV):			
Resting	33 (147)	37 (18)	0·51
Peak	326 (112)	424 (132)	0·04
	Sodium lauryl sulphate		
Erythema index	4·6 (0·9)	6·4 (1·2)	0·0003
	Ultraviolet radiation		
Erythema index	5·1 (1·2)	6·4 (0·8)	0·004
	Reactive hyperaemia		
Blood flow (mV):			
Resting	99 (32)	96 (23)	0·83
Peak	449 (180)	554 (161)	0·051
	Allergen testing		
No (%) of tests (n=75) with:			
No response	60 (80)	26 (35)	
Positive response	15 (20)	49 (65)	

*Mann-Whitney U test.

Comment

The evidence suggests that smoking alters the inflammatory response in the skin. Nicotine causes vasconstriction of peripheral blood vessels including those of the skin,[4] possibly by altering prostaglandin metabolism; prostacyclin production is reduced in smokers.[5]

We examined the responsiveness of the peripheral vasculature after arterial occlusion (independent of prostaglandins) and topically applied hexyl and ethyl nicotinate, which stimulate prostaglandin formation but not histamine release within the skin, causing vasodilatation. Both reactive hyperaemia and erythema in response to nicotinates were reduced in smokers, which suggests that more than one factor is operating.

The skin of smokers was also less reactive. Erythema in response to a direct irritant (sodium lauryl sulphate) and ultraviolet B irradiation (mediated by prostaglandins) was reduced in smokers, as were type 1 hypersensitivity reactions mediated by histamine.

Smoking clearly depresses cutaneous reactivity. Nicotine or another component of cigarette smoke may directly affect the cutaneous vasculature, prostaglandins, and immunological function. These effects may help to explain why smoking alters the course of diseases such as inflammatory bowel disease and acne.

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1 Motley RJ, Rhodes J, Ford GA, Wilkinson SP, Chesner IM, Asquith P, *et al.* Time relationship between cessation of smoking and onset of ulcerative colitis. *Digestion* 1987;37:125-7.
2 Mills CM, Finlay AY. Does smoking influence acne? *Clin Exp Dermatol* 1993;18:100-1.
3 Pearce AD, Edwards C, Hill S, Marks R. Portable erythema meter and its applications to use in human skin. *International Journal of Cosmetic Science* 1990;12:63-70.
4 Roth GJ, MacDonald JB, Sheard C. The effect of smoking cigarettes. *JAMA* 1944;125:761-7.
5 Nadler JL, Velasco JS, Horton R. Cigarette smoking inhibits prostacyclin formation. *Lancet* 1983;i:1248-50.

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