

Sublingual swallow or spit?

G. Passalacqua*, G. Villa, V. Altrineti, P. Falagiani, G. W. Canonica, G. Mariani, M. Bagnasco

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• THE sublingual route of administration of immunotherapy has been approved for clinical use on the basis of several controlled trials (1, 2). Usually, the vaccine is kept under the tongue for 1–2 min and then swallowed (sublingual/swallow). Nevertheless, in some of the earliest studies, the vaccine was kept in the mouth and then spat out (sublingual/spit route), and this modality also achieved a measurable clinical effectiveness. The rationale of the latter procedure implied the concept of direct and rapid absorption of the vaccine through the mucosa. In recent pharmacokinetic studies in man employing the radiolabeled major *Parietaria judaica* allergen (Par j 1), we showed that indeed no direct absorption could be detected (3, 4), but a long-lasting persistence of the Par j 1 allergen on the mucosal surface was observed. By the procedure previously described (3), involving the administration of a radiolabeled allergen, we investigated the pharmacokinetics of the sublingual/spit route. Two healthy volunteers underwent this procedure after providing informed consent.

Briefly, the purified Par j 1 (MW = 12 500 kDa) was radiolabeled with carrier-free ¹²³I to yield a specific radioactivity of about 100 µCi/µg (3.7 MBq/µg). About 15 µg of

the radiolabeled Par j 1 allergen (corresponding to about 1.5 mCi [55 MBq]) was administered sublingually to two nonallergic volunteers. The allergen had to be kept sublingually for 3 min without swallowing and then spat into a proper container for subsequent radioactivity counting; afterward, the subjects were allowed to swallow and rinse their mouths. During the first 3 min, dynamic scintigraphy (1 frame/10 s) of the head and neck was recorded; static scans of the head, chest, and abdomen were also recorded 15, 30, and 60 min after spitting. Heparinized blood samples were collected at 5, 10, 15, 30, and 60 min for plasma radioactivity count. The results were compared with those obtained in three volunteers who had swallowed the entire dose after retaining it under the tongue for 20 min.

About 30% and 26%, respectively, of the dose administered could be recovered in the saliva spat out by the two volunteers. After spitting, the subjects were permitted to swallow normally; therefore, the progression of the radiolabeled allergen along the gastrointestinal tract could be observed. Plasma radioactivity began to increase only after swallowing (thus confirming the absence of any direct sublingual absorption), and with a peak attained about 2 h after swallowing. The plasma radioactivity pattern following sublingual/spit administration did not differ from that of the volunteers who swallowed.

These data suggest that the more appropriate and advantageous way to administer the allergen sublingually is the sublingual/swallow procedure. In fact, after spitting, most of the protein remains in the mouth; thus, the spitting method does not

differ from the sublingual/swallow procedure. On the other hand, the sublingual/spit procedure leads to a certain loss of the allergen administered. The observation that the sublingual/spit procedure also achieves favorable clinical results indirectly confirms that, although brief, the contact of the allergen with the oral mucosa is a crucial step in the mechanisms of action of this desensitizing treatment.

*Allergy and Respiratory Diseases
Pad. Maragliano
L.go R. Benzi 10
16132 Genoa
Italy
Tel. +390103538908
Fax: +390103538904
E-mail gpass@smartino.ge.it

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