



Liquid Nitrogen Spray Cooling for Reducing Injection Pain: A Pilot Study

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Dear Editor:

Intralesional injection (ILI) represents one of the most common treatment modalities in dermatology due to its ability to deliver drugs directly into skin lesions with minimal systemic effects. Common indications for ILI include keloid, nail dystrophies, prurigo nodularis, alopecia areata and vitiligo¹. Triamcinolone is the most frequently injected drug, with bleomycin and 5-fluorouracil also administered for different purposes. However, a major inconvenience is the acute pain caused by injection. Liquid nitrogen (LN2) spray is also frequently used in dermatologic clinics. Thus, we conducted a preliminary study to determine the degree to which LN2 spray cooling reduced the injection pain associated with ILI.

A prospective, open trial was done with patients who visited our clinic between July and August, 2018. Patients who had two or more lesions requiring ILI of 0.4 mg/cc triamcinolone acetate mixed with lidocaine on their hands or feet were recruited. Two lesions positioned similarly on the left and right were selected and randomized to ILI with or without the LN2 spray cooling. For the LN2 spray cooling, LN2 was sprayed shortly before injection at a distance of 20 cm for 3~4 seconds until the skin surface turned a transient white color and appeared frost-like (Fig. 1). We received the patient's consent form about publishing all photographic materials. Then,

a questionnaire was given to each patient to identify their acute pain level using a numeric rating scale (NRS, 0 to 10). All participants provided written informed consent and this study was approved by our institutional review board (VC-18ZESI0117).

A total of 21 patients were enrolled in this study (Table 1). The mean (standard deviation [SD]) age was 54.7 years (12.7 years), with 15 patients being females. The most common diag-

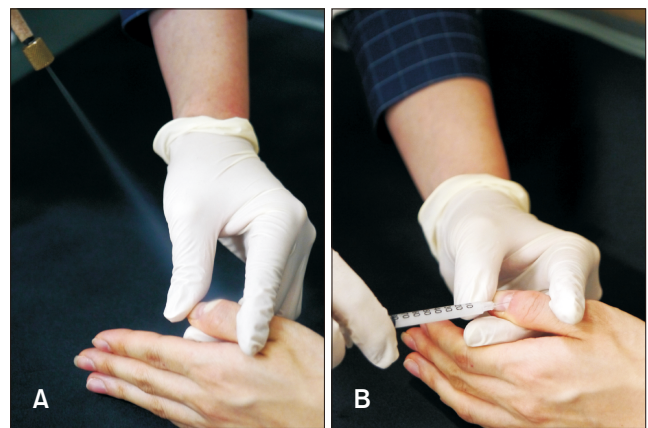


Fig. 1. (A) Liquid nitrogen spray cooling was done just before an intralesional injection to reduce injection pain. (B) Injection procedure followed subsequently.

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Table 1. Summary of the patients enrolled in this study

Patient no.	Sex/age (yr)	Diagnosis	Injection site	NRS score for control site	NRS score for cooling site	Reduction of NRS score	Adverse event
1	M/37	Vitiligo	Finger	10	5	5	None
2	M/66	Nail dystrophy	Proximal nailfold	7	4	3	None
3	F/71	Nail dystrophy	Proximal nailfold	10	6	4	None
4	F/65	Vitiligo	Dorsum of hand	8	4	4	None
5	F/57	Nail dystrophy	Proximal nailfold	5	3	2	None
6	F/53	Vitiligo	Dorsum of hand	9	6	3	None
7	M/61	Prurigo nodularis	Dorsum of hand	6	2	4	None
8	M/38	Nail dystrophy	Proximal nailfold	5	2	3	None
9	F/55	Nail dystrophy	Proximal nailfold	10	3	7	None
10	F/61	Nail psoriasis	Proximal nailfold	10	2	8	None
11	F/49	Nail dystrophy	Proximal nailfold	3	0	3	Burning sensation
12	M/43	Vitiligo	Finger	8	5	3	None
13	F/47	Nail dystrophy	Proximal nailfold	8	3	5	None
14	F/29	Nail psoriasis	Proximal nailfold	5	3	2	None
15	F/33	Vitiligo	Finger	6	4	2	None
16	F/67	Vitiligo	Dorsum of hand	3	2	1	None
17	M/69	Prurigo nodularis	Dorsum of hand	7	5	2	None
18	F/55	Vitiligo	Dorsum of hand	7	5	2	None
19	F/67	Vitiligo	Dorsum of foot	5	1	4	None
20	F/60	Nail dystrophy	Proximal nailfold	5	2	3	None
21	F/66	Nail dystrophy	Proximal nailfold	8	4	4	Burning sensation

M: male, F: female, NRS: numeric rating scale.

nosis was nail dystrophy (n=9), followed by vitiligo (n=8), nail psoriasis (n=2), and prurigo nodularis (n=2). The injected skin sites were proximal nailfold (n=11), dorsum of hands or feet (n=7) and fingers (n=3). The mean (SD) NRS score for the LN2 spray cooling sites was 3.4 (1.6) while that of the control sites was 6.9 (2.2). The pain reduction of the LN2 spray cooling was defined as 'NRS score for control site–NRS score for cooling site'. The mean pain reduction (SD) was 3.5 (1.6), and the difference was statistically significant ($p<0.001$, paired t-test). The LN2 spray was tolerable without apparent erythema or blister formation. Two patients experienced a transient burning sensation.

Cooling of the injection site produces instant anesthetic effects and has been proposed as a possible alternative for local anesthesia in dermatological procedures¹⁻⁴. One study reported that the anesthetic effects of skin cooling using ethyl chloride spray were comparable to those of a 45 minutes application of topical lidocaine-prilocaine cream (EMLA Cream[®]; Mitsubishi Tanabe Pharma Korea, Seoul, Korea) for pain relief⁵.

Our present study revealed that LN2 spray cooling effectively reduces the injection pain associated with ILI. As LN2 spray is a common dermatological supply, it has the advantage of easy and immediate application without additional cost. To avoid unwanted side effects like erythema or blistering, performers should be careful to keep a proper distance and maintain appropriate spray strength and duration. The conventional cryotherapy with LN2 can be toxic to melanocytes and is used as a depigmenting agent for remaining patches in universal vitiligo. However, if used at the proper intensity for a short time as used in our study, it can be safely applied to patients with vitiligo. Successful repigmentation of lesions by ILI rather than melanocyte toxicity was observed in 8 vitiligo patients of this study.

In conclusion, LN2 spray is a convenient, instant, and effective local anesthesia in patients who are anxious about ILI-associated injection pain. Further controlled trials with larger sample size are needed to confirm our observation.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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Squamous Cell Carcinoma at the Site of Cutaneous Lymphoid Hyperplasia

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Dear Editor:

An 82-year-old Japanese female noticed an erosive plaque on her lower lip in 2012. Although the plaque healed by itself, it

recurred after a month. She was referred to our hospital in 2014. She did not smoke or drink alcohol. Her past history was not in particular, and she had no experience of radiation therapy, burns, herpes zoster, and insect bite on her lip. She presented with partially erosive plaque with surrounding bulges measuring about 1.0 cm×2.0 cm on her lower lip (Fig. 1A). The serum level of zinc was within the normal limit (71.9 µg/dl). Histopathological examination of a biopsy specimen from the erosive plaque showed the elongation of rete ridges and parakeratosis, pseudocarcinomatous epithelial hyperplasia, superficial and deep infiltration of plasma cells, and small lymphocytes forming lymphoid follicles (Fig. 1B, C). Immunohistochemical staining showed CD20 was positive in folli-

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