

Anaphylactic shock after subcutaneous injection of mandragora D3, a homeopathic drug

To the Editor:

Mandrake (*Mandragora officinarum*) is a plant of the nightshade family, Solanaceae. Extracts of its roots containing tropane alkaloids such as atropine and scopolamine are used in homeopathy.¹ A stem solution for homeopathic use (D1) consists of approximately 0.3 mg/mL of these alkaloids. However, for injections the stem solution is diluted up to 100,000-fold (D6).

The patient described is a 32-year-old woman without previous history of atopy or food hypersensitivity. Because of annoying shoulder pain, she started a homeopathic self-care treatment prescribed by her family physician. Twice a week she injected 0.3 mL of mandragora D6 and, on the recommendation of her family physician, successively increased the dose and potency up to D3.

Although she reported recurrent local swellings after the self-injections 4 months later, the family physician himself gave several small injections of a 2-mL solution of mandragora D3 into shoulder and elbow tissue. Approximately 5 minutes later tingling in palms and scalp, nausea, and swelling of lips and eyelids arose. Severe dyspnea developed accompanied by lower abdominal cramping. Within the next minutes the patient collapsed and loss of consciousness associated with stool incontinence occurred. After initial emergency treatment, the patient was referred to the intensive-care unit of a nearby hospital and was discharged 24 hours later.

Skin prick tests were performed with a panel of common inhalant allergens (Allergopharma, Hamburg, Germany) as well as with mandragora D3 and crude root powder. A positive wheal-and-flare reaction was demonstrated to mandragora D3 and to the root powder but not to the inhalant allergens. Ten atopic control subjects did not reveal positive skin prick tests to mandragora D2, a 10-fold higher concentration than D3. Mandragora-specific IgE antibodies could not be detected in the patient's serum by the experimental ImmunoCAP FEIA system 3 and 4 months after the severe reaction (Pharmacia Diagnostics, Uppsala, Sweden). Patch tests with mandragora root powder showed a typical delayed-type reaction with erythema, infiltration, and aggregated vesicles consistent with an acute dermatitis. In vitro test for lymphocyte proliferation to mandragora (D3) resulted in an unusually strong proliferation of T lymphocytes (Table I).² T cells of four controls including two subjects exposed to subcutaneously applied mandragora were not proliferating to this substance.

Table I. Comparison of in vivo and in vitro tests in the study and control subjects

Method	Study subject	Controls (n = 10)
Skin prick tests (wheal diameter, mm)		
Mandragora root powder	3	Negative
D2	ND	Negative
D3	6	
D6	2.5	
Potato	5	
Tomato	3	
Red pepper	2.5	
ImmunoCAP FEIA (kU/L) (RAST class)		
Mandragora root powder	0	ND
Potato	0.67 (1)	
Tomato	2.49 (2)	
Red pepper	0.42 (1)	
Patch test at 48 h (mandragora root powder)	Consistent with acute dermatitis	Negative in 3 controls
Lymphocyte proliferation (SI) (concentrate of mandragora root powder)		(mean value of 4 controls)
0.10 µg/mL	36.8	1.4
1.00 µg/mL	70.5	1.2
10.0 µg/mL	93.4	1.2

ND, Not done; SI, lymphocyte stimulation index (counts/min + antigen/counts/min – antigen; control 357 counts/min [mean of triplicate]).

Homeopathy is regaining popularity around the world.³ Relying on concepts first set by Hahnemann in 1810, homeopathy is often used in cases where conventional therapy is not considered effective or if patients desire an unconventional “biologic” remedy. Homeopathic medications generally depend on products with an old tradition in herbal medicine. Although phytoproducts are known to cause various side effects, some homeopathically prepared mixtures are thought to be too diluted to induce side effects, and hypersensitivity reactions are rare.⁴ This case report demonstrates that homeopathic treatment can elicit severe allergic symptoms with in vivo and in vitro evidence for sensitization to this substance. Thus plant extracts used for homeopathy may still contain antigenic determinants that are recognized by T cells (as revealed by positive patch and lymphocyte proliferation test) and IgE antibodies (positive skin prick test). These components may induce sensitization by repetitive subcutaneous injections of small doses, as shown for the mandragora extract, resulting finally in a specific IgE response. These IgE antibodies seem to be cross-reactive with other proteins of the Solanaceae because our patient demonstrated positive skin prick test and ImmunoCAP FEIA results to potato, tomato, and red pepper. Because the patient repeatedly developed abdominal

cramps after eating tomatoes after the anaphylactic reaction to the mandragora treatment, this cross-reactivity could be of clinical relevance.

In conclusion, homeopathic remedies containing plant extracts may still have sufficient sensitizing potency that can elicit severe allergic reactions. The development of local reactions after injections with mandragora and other phytotherapeutics labeled as either phytomedicine or homeopathy has to be managed like with other drugs and should be considered as a warning signal to stop treatment because continuation may lead to potentially life-threatening allergic reactions.

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Arthur Helbling, MD

Karl A. Brander, PhD

Werner J. Pichler, MD

Division of Allergology, Department of Rheumatology and Clinical Immunology/Allergology, University Hospital 3010 Bern, Switzerland

Ulrich B. Müller, MD

Department of Internal Medicine, Zieglerspital Bern, Switzerland

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