

# Factory packed and expired – about emergency insect sting kits

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## Keywords

- emergency kits
- allergy to insect venom
- compliance

## Summary

**Background:** Patients allergic to insect venom are instructed to always carry emergency medication – an emergency kit. According to the current guidelines, these emergency kits should contain a H1-receptor-blocking antihistamine and corticosteroid for oral use, as well as an epinephrine inhaler and in particular situations an epinephrine auto-injector.

**Patients and Methods:** For quality management reasons patients with wasp venom allergy who presented for sting challenge provocation test were told to demonstrate their emergency kits. Concomitantly, constituents of the patient's emergency kits were checked for date of expiry of the medication and the patients were interviewed on storage and use of the emergency kits.

**Results:** In total 42 patients with a median duration time of systemic immunotherapy of 2.5 year were evaluated. Medication post date of expiration was found in 54 % of the kits (n = 39). Only 31 % of the patients could demonstrate how to use the kits correctly. Problems were especially evident concerning for using the application of the inhaler and auto-injector. 50 % of the patients demonstrated using epinephrine auto-injectors in such way that an accidental injection into the fingers would have resulted.

**Conclusion:** To assure safe and effective handling of all components of the emergency kit, continuous training and repeated supervised practice is necessary.

## Background

Immediate hypersensitivity to insect venom is one of the most common and at the same time potentially most dangerous types of allergic reaction. Epidemiological studies report that 0.8–5 % of the general population experience systemic, anaphylactic reactions to insect stings [1]. In Germany, there are 10–20 fatalities resulting from insect stings according to the Federal Office of

Statistics [1]. People who are allergic to insect venom are thus instructed to always carry an anaphylactic kit ("emergency kit"). The German Society for Allergology and Clinical Immunology (DGAKI) recommends that emergency kits contain "...a rapid-acting H<sup>1</sup>-receptor-blocking antihistamine and corticosteroid (equivalent of 100 mg prednisolone) for oral use as well as preferably epinephrine (possibly beta-sympa-

thomimetic) for inhalation..." or, after excluding contraindications, possibly auto-injectable epinephrine [1].

The most commonly cited quick-acting antihistamines approved for use in Germany are cetirizine, clemastine, dimethindene, and fexofenadine [1, 2, 3, 4]. With the exception of fexofenadine, all are available in various galenical forms, usually as liquid. Only dimethindene (Fenistil®) and clemastine (Tavegil®)

are approved for intravenous use and for acute management of severe allergic reactions. In general, all oral preparations are approved only for treating urticaria and allergic rhinoconjunctivitis. In Germany, dimethindene, in the form of Fenistil® drops (N1, 20 ml), is probably the most common drug in emergency kits. The recommended dose of Fenistil® drops is derived from the approved intravenous dose of Fenistil® injection solution in anaphylactic reactions (0.1 mg/kg body weight) [5–8]. Dosage instructions are designed to be easily understood by patients, for instance drinking 1/3 of a bottle (6.6 mg = corresponding to a weight-adjusted dose for a person weighing 66 kg) or 1/2 of a bottle (10 mg = corresponding to a weight-adjusted dose for a person weighing 100 kg) of Fenistil® 20 ml N1 drops in the event of hymenoptera sting [4]. Betamethasone is usually prescribed as a liquid corticosteroid. Celestamine® N 0.5 liquid is a preparation that is available and approved for treating insect venom allergy. The contents of an entire bottle (N1, 30 ml) are equivalent to 110 mg prednisolone. Epinephrine inhalation aerosols are preferred over classic beta 2-sympathomimetics. Aerosols have an additional direct anti-swelling effect on the mucous membranes in patients experiencing an anaphylactic reaction with involvement of the upper respiratory tract. In 1996, the European-wide ban on Halon led to removal of the epinephrine Medihaler® from the German pharmaceutical market. The only currently available replacement is Primatene® Mist aerosol (Wyeth), which is approved in the USA as an over-the-counter asthma drug. The usual dose for bronchodilation is 2–4 puffs [7]. At this level, no stabilizing effect on the circulatory system is expected (Schlegel et al., submitted for publication). 15–45 puffs (0.22 mg epinephrine/spray), with optimal breathing technique, would be required to reach systemic adrenaline levels [9]. Thus Primatene® Mist aerosol is insufficient as the only epinephrine preparation in patients with circulatory symptoms and therefore should be supplemented by epinephrine autoinjection [1]. Two current products on the market in Germany are the Fastjekt® injector and Anapen®. The medication contained in the emergency kit should be taken immediately after every insect sting with the potential for an anaphy-

lactic reaction. This should help stop or prevent the allergic reaction from becoming more severe in patients who have not yet been treated for insect venom allergy as well as those in whom specific immunotherapy has failed. Based on current data, after 3–5 years of specific immunotherapy with bee or wasp venom there are at least 6–7 years of protection [16]. Yet after therapy, a small number of patients develop anaphylaxis again after being stung, and it is thus recommended that an emergency kit be carried even after completing immunotherapy. Ultimately, emergency kits are a lifelong preventive measure and should continue to be carried.

### Patients and methods

Patients undergoing ongoing specific immunotherapy (SIT) with wasp venom, who volunteered for a sting challenge test with a live wasp at the Department of Allergology of the University Hospital of Tübingen, Germany were asked to present their emergency kits. The vast majority of these patients had received their kits from out clinic a number of years before and had been instructed in its use. Patients were given individual instruction from a physician using a demo set as well as detailed information for reference (Table 1). The components of the emergency kit for insect venom allergy were: Fenistil® drops 20 ml (N1), Celestamine® N 0.5 liquid 30 ml (N1), Primatene® Mist aerosol and/or a Fastjekt® injector. Patients were told that immediately after a hymenoptera sting, regardless of whether they had any symptoms, they should drink “1/3 of the bottle of Fenistil® drops and the entire bottle of Celestamine® N 0.5 liquid.” If the patient had “shortness of breath or difficulty swallowing, 2–4 puffs every 10–15 minutes” of Primatene® Mist aerosol should be taken. The Fastjekt® injector should be used in the event of “shortness of breath and/or signs of circulatory compromise.” The expiration dates of the drugs contained in the emergency set was checked. Patients were asked “Let us assume that you have just been stung by a wasp. When and how would you use your emergency kit?” In a semi-structured interview, patients were instructed to demonstrate how to use the kit in front of a physician using their own kit or a demo kit. For demonstration of the Fastjekt® injector, a safe

Fastjekt®-trainer, made by the same manufacturer, was used. Knowledge of correct dosage and handling of the medications was evaluated according to standardized measures by the physician. The expected ranges for the indications and dosages of individual drugs are shown in Table 1. After the demonstration, semi-structured interview was conducted. The interview consisted of open questions and also asked about the supervising physician for systemic immunotherapy, whether the patient had experienced an accidental sting since SIT, and if so whether an emergency kit was available and was actually used, as well as how often in daily life or in which actual situations they actually carried the emergency kit with them.

### Results

Forty-two patients with wasp venom allergy were evaluated in preparation for sting challenge. Twenty-seven women (64 %) and 15 men (36 %) participated. The median age was 42 years (range: 8–72 years). Median length of known wasp allergy was 3 years (range: 2–15 years) and median duration of specific immunotherapy (SIT) was 2.5 years (range: 1–6.5 years). The median severity of anaphylactic reactions (after Ring & Messmer) at the time of the first event was grade II (range: grade I–III). After starting SIT on an inpatient basis, 20/42 (48 %) patients were under the outpatient care of a dermatologist specializing in allergology and 22/42 (52 %) of a general practitioner/general internist.

During SIT, 10/42 patients (24 %) were stung accidentally by a wasp or an unknown insect. All of these patients (10/10) reported that the emergency kit was available at the time of the event. Only 4/10 (40 %) used the set as instructed immediately after being stung. Afterward, three of these patients did not experience a generalized reaction. One patient had a grade III anaphylactic reaction despite having used the kit. One patient (1/10 patients) took only Fenistil® drops after being stung and did not experience a generalized reaction. Half of the patients (5/10) waited to see what happened rather than using the emergency kit immediately. None of them experienced a generalized reaction.

During the semi-structured interview, 14/42 patients (33 %) reported always having their emergency kits with them.

**Table 1:** Components of emergency kits prescribed by the Department of Allergy of the University Hospital Tübingen, trained instructions on use depending on symptoms, and dosages of drugs. Incorrect dosage and use of the kit observed in patient demonstrations.

| Original instructions for use<br>(based on practical and written instruction) |                                                                    |                                                                                                                            | Evaluation of patient demonstrations<br>of emergency kit use                                                                                          |                        |
|-------------------------------------------------------------------------------|--------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|
| Medication                                                                    | Indication                                                         | Correct dosage/use                                                                                                         | Incorrect dosage/use                                                                                                                                  | Practical component    |
| <b>Fenistil® drops<br/>N1 (20 ml)</b>                                         | Always,<br>immediately                                             | Drink 1/3 of the bottle<br>(remove droplet tip of<br>the bottle when creating<br>your emergency kit)                       | Dosage too low, according<br>to package insert<br>(20–40 drops = 1–2 mg)<br>Overdose due to confusion<br>with Celestamine®<br>(= drink entire bottle) | Not evaluated          |
| <b>Celestamine® N 0.5<br/>liquid<br/>N1 (30 ml)</b>                           | Always,<br>immediately                                             | Drink entire bottle                                                                                                        | Dosage too low due to<br>confusion with Fenistil®<br>(= drink 1/3 bottle)                                                                             | Not evaluated          |
| <b>Primatene® Mist<br/>aerosol</b>                                            | Shortness of<br>breath                                             | 2–4 puffs, repeat as<br>needed after 5 minutes,<br>turn mouthpiece around<br>and replace on bottle<br>before use           | 1 puff, did not repeat,<br>attempt to use spray in the<br>“off” position                                                                              | Similarly<br>evaluated |
| <b>Fastjekt® -injector</b>                                                    | Circulatory<br>symptoms<br>and/or severe<br>shortness of<br>breath | Place the black cap on<br>the lateral thigh, remove<br>the gray safety cap, press<br>firmly against the thigh<br>to inject | Pressing the<br>(needle-containing) black<br>cap to perform the injection                                                                             | Similarly<br>evaluated |

These patients had also found convenient ways of organizing the contents of the kit. Another 8/42 patients (19 %) reported regularly carrying the emergency set, although there were certain activities or situations in which they did not have it or when it would be forgotten. Their emergency kits were noticeably less well-organized, and often the drugs were in their original packages. There was less of a perceived need to carry the emergency kit with them at all times, and carrying the kit “on yourself” was sometimes equated with storing it in the glove compartment or trunk of a car, or keeping it in a closet or kitchen drawer. Fifteen of 42 (36 %) patients reported carrying the kit only occasionally, during certain leisure activities or on vacation, but not for daily activities or at work. Three patients out of 42 (7 %) reported that they did not keep the emergency kit with them, but stored it in a central location such as in the car or at home. At follow-up, it was discovered that 2 of 42 patients (5 %) had no emergency kit. In an analysis of the factors influencing whether the patient carried

the kit with them, it was noted that compliance was high in 7/11 patients (64 %) with a history of a grade III anaphylactic reaction as well as 8/10 patients (80 %) with self-reported accidental stings.

Thirty-nine emergency kits were checked. Of these, only 18/39 (46 %) contained no expired drugs. At least one expired drug was found in 20/39 kits (51 %) (Figure 1). In 16 of 39 kits (41 %) the antihistamine Fenistil® drops was past the expiration date, and in 8/39 (21 %) the corticosteroid Celestamine® N 0.5 liquid had expired. Celestamine® N 0.5 liquid keeps the longest, so if it was past the expiration date, usually other drugs in the kit were as well, some by more than a year. 31/39 emergency kits (79 %) contained Primatene® Mist aerosol and one contained an Infectokrupp® inhaler. Beta 2-sympathomimetic agents were not contained in any emergency kit. 7/39 kits (18 %) did not contain any inhalable epinephrine preparation or beta 2-sympathomimetic drug. Of the 31 Primatene® Mist aerosols that were checked, 17

(55 %) were past the expiration date. A Fastjekt® injector was part of 10/39 emergency kits (26 %). In 5/10 (50 %) it was the only epinephrine preparation and in another 5/10 kits (50 %) it supplemented the kit. Six of the 10 Fastjekt® injectors (60 %) that were checked had already expired.

All 42 patients were asked to demonstrate their current or original emergency set in theory and practice. Only 13/42 (31 %) were able to do so correctly (Figure 2). Eighteen of 42 patients (43 %) knew the correct dose of Fenistil® drops from memory. Another 8/42 patients (19 %) arrived at the correct dosage using markings that had been placed on the bottle or a note previously made on the package. The remaining 16/42 patients (38 %) gave either an incorrect or no answer (Table 1). Not included in the analysis was the fact that in none of the 39 kits that we checked had the droplet tip of Fenistil® drops been removed in advance; this would have allowed it to be quickly swallowed in an emergency. Nineteen of 42 patients (43 %) knew the correct dose of

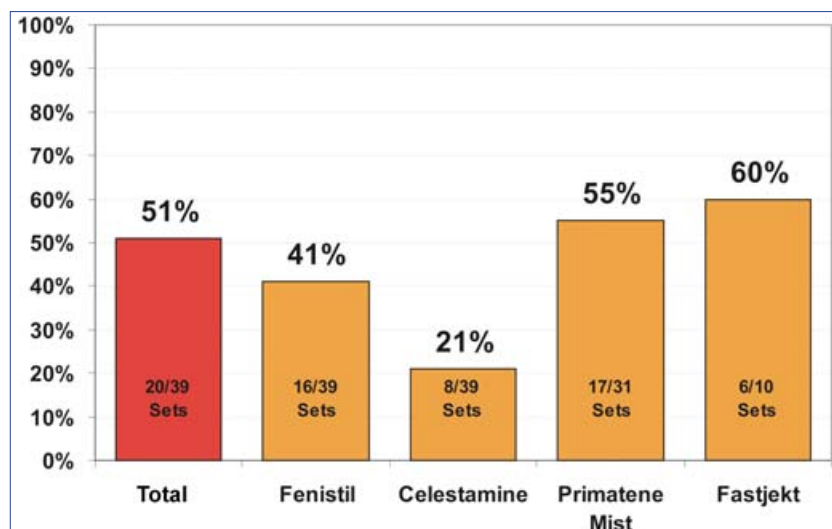


**Figure 1:** Expired medications (red) in the emergency kits and of the components Fenistil®, Celestamine®, Primatene® Mist inhaler (n = 31) and Fastjekt® Injectors respectively.

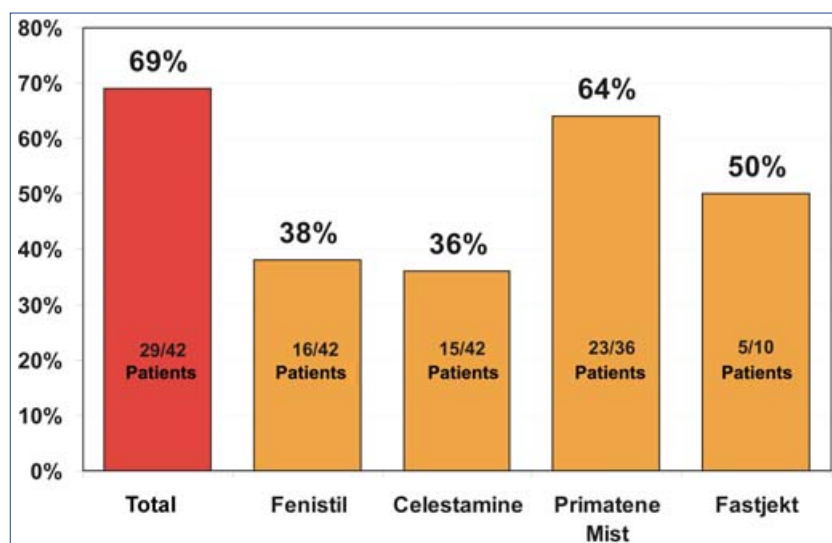


**Figure 2:** Percentage of patients whose use of at least one emergency medication was incorrect (red) as well as incorrect use of Fenistil®, Celestamine®, Primatene® Mist inhaler and Fastjekt® injectors respectively.

Celestamine® N 0.5 liquid from memory. Another 8/42 patients (19 %) were able to ascertain the dose using markings on the bottle. Fifteen of 42 patients (36 %) could not answer or would have taken too small a dose. In 36 patients we evaluated the use of Primatene® Mist aerosol. Along with theoretical knowledge (Table 1), we evaluated whether they were able to correctly prepare the spray bottle for actual use by taking off the mouthpiece, turning it around, and replacing it. Only 13/36 patients (36 %) could do so correctly while 23 of 36 patients (64 %) could not. It was noted that most patients who had difficulty demonstrating the use of their emergency kits had sets that contained drugs

which were still in their original, unopened packages. These patients had never removed the spray from its package to become more familiar with it. The indications for using the Fastjekt® injector were correctly cited by 8/10 patients (80 %). Nevertheless, they had significant difficulty when it came to actually using the Fastjekt® trainer. Based on patient demonstrations, it can be assumed that had they been using an actual Fastjekt® injector, 5/10 (50 %) would have injected a finger (usually the thumb) with epinephrine rather than the thigh, as a result of pressing the black tip containing the needle after removing the gray safety cap (aiming the injector in the wrong direction or “experimenting” with the unlocked injector).

## Discussion

The notion of the use of emergency kits for self-medication by anaphylactic patients was developed in the mid-1970s using the insect venom allergy as model [11–16]. Although such kits have been used worldwide for more than 30 years as an integral part of managing insect venom allergy and other forms of anaphylaxis, they still involve certain fundamental problems. First, the recommendations on the contents of such kits and the administration of the medications vary noticeably since they have not been supported by studies on contents, recommendations for use, and effectiveness, but ultimately are based on experimentation or consensus recommendations [1, 17–19]. The problem of lacking evidence of effectiveness of a drug in an anaphylactic reaction was recently shown by Sheikh and colleagues. An attempted Cochrane analysis on the effectiveness of antihistamines in anaphylaxis could not be completed given lacking data [20]. A guideline by the German Society for Allergology and Clinical Immunology (DGAKI) for insect venom allergy (Level S1) and a recently published guideline drawn up by all German-speaking allergological societies on acute therapy of anaphylactic reactions (Level S2) may serve as a basis for determining the contents of an emergency kits [1, 19]. Yet these guidelines also lack binding recommendations on kit contents, galenic form of the drugs they contain, when and in what order to use the drugs according to symptoms, and individual drug dosages. The underlying reasons for this are lacking data and legal issues surrounding recommendations for off-label use. For example, the use of antihistamines in emergency kits is already considered off-label use, since it is beyond the scope of approved indications and dosages. The guideline on acute therapy of anaphylactic reactions addresses this point directly: “When administering antihistamines, only the maximum approved dose may be officially recommended. Yet the expert group agrees that, owing to the critical nature of the situation, in some circumstances dosage levels may be administered that exceed official recommendations [19].” A guideline for doctors and patients that focuses on patient management and self-medication in an anaphylactic reaction is currently being

developed by the “anaphylaxis” working group of the DGAKI [19]. In German-speaking countries, an estimated 2 million people have emergency kits for insect venom allergy. Based on the results of our small study, 1 million of them would only carry their kit some of the time or not even use it all. 30 % would not be able to use their emergency kit as instructed. Even under the comparatively stress-free conditions described here, many patients were unable correctly work the aerosol canister or epinephrine autoinjector. The potential rate of injury resulting from use of an epinephrine autoinjector is also a concern. In an actual emergency, incorrect use of the drugs in the emergency kit is liable to be even higher. These results correspond to the experience with epinephrine autoinjectors in other studies on anaphylactic patients which have noted a high reluctance to use the autoinjector and a relatively high rate of error [21, 22]. It is worth noting that the experience of an actual emergency situation, i.e., having an anaphylactic reaction or experiencing an accidental sting, significantly increases patient acceptance of the emergency kit and thus the willingness to carry it on a daily basis. Comparable observations have been made by Rohrer and colleagues in a retrospective analysis of anaphylactic patients in the Dermatology Clinic of Bern [23]. In the present study, higher compliance is especially reflected in prompt use of medications and knowledge of their use. Nevertheless, the rate of error was high even among the latter group of patients. This shows that a one-time demonstration and receipt of informational material is not enough. When demonstrating an emergency kit, special attention should be given to allowing the patient adequate time to try out all components of the kit several times under guidance. It cannot be expected that patients will use the kit with confidence in a potentially life-threatening situation after only a single training session. Rather regular follow-up courses and practice are needed. It is thus advisable that at least once a year, for instance in the spring before the hymenoptera season, patients should be asked about their emergency kits, the kit should be checked, and its use practiced again during a visit to the doctor. <<<

### Conflict of interest

None.

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