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### **Anaphylaxis to Polyvinylpyrrolidone in Eye Drops Administered to an Adolescent**

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Polyvinylpyrrolidone (PVP) is a polymer derived from the monomer N-vinylpyrrolidone, an organic compound consisting of a 5-membered lactam linked to a vinyl group. It is widely used in medical products as an excipient, especially in tablet formulations, and in ophthalmic solutions as a lubricant. When linked to iodine, it is called povidone-iodine, which is used as an antiseptic agent.

Even though PVP has been considered safe to date, cases of adverse reactions have been reported. While skin reactions to PVP from cutaneous exposure, such as contact dermatitis, are frequent, only a few cases of anaphylaxis from various administration routes have been described in the literature [1-5].

Few cases of anaphylaxis to eye drops have been reported; some involved reactions to the active ingredient [6,7] and only 1 to the preservative, benzalkonium chloride [8].

We report the first case of anaphylaxis to PVP as an excipient in an ophthalmic preparation.

A 15-year-old girl was referred to the Allergy Unit of the Anna Meyer Children's Hospital, Florence, Italy because of suspected anaphylaxis to eye drops.

The only relevant information in her clinical history was a previous reaction following exposure to a hairspray at the hairdresser's some months earlier. At that time, the patient experienced cutaneous itching of the scalp, tearing, and cough. The symptoms cleared up spontaneously in a few minutes.

Two months before our evaluation, she had conjunctivitis and was treated with topical tobramycin and dexamethasone eye drops, with no reaction. A month and half later, owing to recurrent conjunctivitis, the ophthalmologist prescribed another type of corticosteroid eye drops, which contained loteprednol. Immediately after the administration of one drop in both eyes, she developed anaphylaxis (periorbital swelling, angioedema of the tongue and lips, dyspnea with a sensation of nasal obstruction, and throat constriction). At the emergency department, she was given epinephrine, antihistamines, and oral corticosteroids, and her symptoms resolved progressively. A blood analysis during the episode revealed total IgE of 3850 kU/L (normal range, 0-100 kU/L).

Two weeks after being discharged, the patient was admitted to our Allergy Unit. Prick-by-prick testing with the culprit eye drops containing loteprednol 0.5% yielded a positive result after 10 minutes (Table). Histamine (ALK-Abelló; 10 mg/mL)

Table. Allergy Work-up

Drug/Excipient	Prick-by-Prick
Eye drops with loteprednol 0.5 %	13 mm (18 × 8 mm)
Tobramycin 0.3% and dexamethasone 0.1%	Negative
Povidone-iodine	13 mm (20 × 6 mm)
Polyvinylpyrrolidone	12 mm (18 × 8 mm)
Iodinated contrast agent	Negative

was used as a positive control. Skin prick tests with common inhalants (commercial extracts of pollens, mites, molds, cat and dog epithelia, and latex [0.1 mg/mL, ALK Abelló]) proved positive to mites.

In the search for a possible allergy to one of the excipients contained in the eye drop formulations, we checked the ingredients of both ophthalmological products (ie, the culprit product and the previously tolerated eye drops), which proved to be the same except for 1 excipient (ie, povidone). In order to exclude possible sensitization to most of the excipients contained in both eye drops, the tolerated product was also tested using the prick-by-prick approach, and the results were negative. The only remaining suspect excipient was povidone, which was present in the culprit eye drops, but not in the tobramycin and dexamethasone eye drops. We then performed prick-by-prick testing with povidone iodine 7.5% antiseptic solution, which is routinely used as a disinfectant in the hospital. The result was positive (Table). Given that many drugs contain povidone and PVP as excipients, we searched for the most frequently used drugs containing one of these substances. The search revealed a paracetamol tablet formulation with PVP; therefore, we performed prick-by-prick testing with the powder of a crushed tablet, and the result was positive (Table). In the past, the patient had always used PVP-free acetaminophen suppositories. Lastly, in order to exclude an iodine allergy (since adverse reactions to iodinated contrast media are not uncommon [9]), we also tested an intravenous iodinated contrast agent using prick-by-prick testing, which was negative.

In conclusion, we advised the patient and her parents to avoid preparations, cosmetic products, and food containing PVP. We prescribed self-injectable epinephrine for immediate management of anaphylaxis and trained the patient in how to use it.

PVP is widely used in many products. It can be found in personal care items such as hair styling products, as was the case of the previous cutaneous and respiratory reaction that the patient experienced on exposure to hairspray.

In pharmacology, PVP is used as a binder, especially in tablets, and as a lubricant in eye drops, as well as an antiseptic agent when linked with iodine. PVP is also used as a food additive, with E number E1201.

Although the possibility of povidone anaphylaxis is known in literature, this is the first pediatric case of anaphylaxis to PVP in eye drops. In the case we report, it

was easy to show that the agent causing the adverse reaction was the excipient and not the active ingredient, thanks to the availability of the formulation of both the ophthalmic preparations. It was very important for the patient to discover that she was allergic to such a frequently used substance. In our opinion, if a single intraocular drop triggered a medium-severity adverse reaction, then accidental oral ingestion of PVP in a drug or in food could have caused much more severe anaphylaxis.

Even though self-injectable epinephrine prescription is not recommended in the case of anaphylaxis to drugs [10], we provided the patient with this life-saving drug, as povidone/PVP/E1201 is so widespread and found in many brands of medications containing the same active ingredient. Moreover, we took into account the possible risk of recurrence or accidental contact (ie, at the hairdresser's).

In summary, the case we report stresses the need for an accurate allergy work-up in order to reach a confident diagnosis and give advice to the patient on which drugs can or cannot be used in order to avoid life-threatening reactions.

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#### Conflicts of Interest

The authors declare that they have no conflicts of interest.

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