

Non-specific reactions caused by diluents containing glycerol in nasal and bronchial challenge tests

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Summary

Sixty-one patients hospitalized because of asthma and/or allergic rhinitis were given nasal and bronchial challenge tests with diluents containing glycerol. 62% of the patients with rhinitis and 37% of those with asthma gave positive reactions. Glycerol should therefore not be used in allergen extracts which are meant for challenge tests. The non-specific effect of glycerol seems to be cumulative with increasing dose.

Introduction

Challenge tests are needed in the diagnosis of respiratory allergies to reveal the specific sensitization of the target organ to environmental allergens. The allergen extracts for challenge tests used in clinical practice have not been properly standardized. The extracts, their contents, stability and potency vary from one manufacturer to another, and different batches from the same manufacturer may even vary widely when the allergens are tested using the RAST technique (Björkstén, 1977). Glycerol is generally added to allergen solutions to improve their stability. The allergen extracts for challenge tests and the control solution manufactured by Bencard (Brentford, England) contain 50% glycerol, 0.5% phenol and 6% sodium chloride. The allergen extracts (excluding pollens and house dust) made by Dome Laboratories (England) contain 50% glycerol, 0.5% phenol and 0.9% sodium chloride. We report our observations on the effect of diluents containing glycerol on nasal and bronchial challenge tests.

Patients, methods and results

Sixty-one patients hospitalized because of asthma and/or allergic rhinitis were given a challenge test using the control solution supplied by Bencard. The nasal challenge test was administered to thirty-four patients (mean age 35 years) and the bronchial challenge test to twenty-seven patients (mean age 54 years). On the morning of the challenge test the patient had to be asymptomatic and the respiratory performance of

the asthmatics had to exceed 70% of their predicted values of FEV_1 . No medication was allowed for 12 hr before the challenge.

In the nasal challenge test the glycerol solution was administered by dropping 0.05 ml of the solution into each nostril after the control test with physiological saline. A 5% solution was tested first and then a 50% solution if no reaction ensued. The reaction was regarded as positive if two of the subjective symptoms (sneezing, itching, rhinorrhea, obstruction or eye irritation) were clearly detected. The degree of nasal blockage was verified by measuring the nasal peak expiratory flow rate with a Wright's peak flow meter (Taylor, Macneil & Freed, 1973; Lahdensuo & Haahtela, 1977).

The bronchial challenge test was made with a DeVilbiss No. 40 nebulizer with a constant air flow of 5 l/min. After the physiological saline control the patient inhaled 1.0 ml of 0.5% glycerol solution. If there was no reaction, the test was repeated with 5% and finally 50% glycerol solution. The bronchial reaction was regarded as positive if there was a fall of 15% or more in FEV_1 within 15 min and the patient experienced dyspnoea and/or definite bronchial wheezing was heard on auscultation.

Twenty-one of the thirty-four patients (62%) gave a positive reaction within 15 min to the nasal test (Table 1). In five the 5% glycerol solution was strong enough to cause a reaction. Some of the patients who reacted positively experienced a prolonged reaction which lasted for hours and was quite unpleasant, involving severe rhinitis and headache. In the bronchial challenge tests ten of the twenty-seven patients (37%) developed significant bronchial obstruction (Table 1). Two of these patients gave positive reactions when 5% glycerol solution was inhaled. Seven had such strong reactions that they were given two puffs of an isoprenaline aerosol. In three further patients bronchial obstruction was prolonged and detected 3–6 hr after the challenge.

Table 1. The results of the nasal and bronchial challenge tests with Bencard's control solution containing glycerol

Tests	Number	Percentage
Nasal tests ($n = 34$)		
No reaction	13	38
Positive reaction	21*	62
A fall in $PEFR_n > 15\%$	12	57
and symptoms		
Only symptoms	9	43
Bronchial tests ($n = 27$)		
No reaction	17	63
Positive reaction	10*	37
A fall in $FEV_1 < 15\%$	0	0
A fall in FEV_1 15–25%	5	50
A fall in FEV_1 26–40%	3	30
A fall in $FEV_1 > 40\%$	2	20

*15 min after challenge.

Discussion

The reactions seen in our challenge tests were obviously caused by the glycerol. We did not observe any significant reactions to the small amounts of phenol used in the

extracts. Even minute amounts of glycerol can cause significant nasal and bronchial reactions in patients with chronic respiratory allergy. Glycerol is the simplest tribasic alcohol. Because of its sweet taste and preservative capacity it is widely used in the food industry. Glycerol is known to induce false positive reactions in intracutaneous tests (Slavin, 1974). The respiratory reactions seen in our series are undoubtedly non-specific in nature.

We conclude that glycerol should not be used in allergen extracts which are meant for use in challenge tests. If, however, a glycerol-based extract must be used in a bronchial challenge, a control test should be carried out on a different day using the same amount of glycerol which the patient inhales during the true challenge. The non-specific effect of glycerol seems to be cumulative with increasing doses.

It is important for specific challenge tests to be reliable. It is deplorable if the treatment strategy—elimination, medication, hyposensitization and in some cases even a change of profession—is based on untenable facts derived from poorly controlled testing.

The stability of the allergen extracts is a problem, but as far as the extracts for challenge testing are concerned this could be resolved by using freeze-dried material prepared for testing just before the challenge and destroyed afterwards. In any event manufacturers must be required to give the exact contents of their products on vial labels.

Acknowledgments

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