

the cause, as demonstrated in this case.⁵ Invasive procedures can be avoided if proper serologic tests are performed by an accurate and reliable reference laboratory.

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Systemic reactions to immunotherapy: Comparisons between two large allergy practices

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In the January 1995 issue of the *JOURNAL*, Tinkelman et al.¹ reported on the incidence and severity of systemic reactions to immunotherapy injections in the offices of their Atlanta allergy practice during 1991. In this report we compare 12 months of similar data from our Oklahoma City practice during 1994 with the Atlanta findings.

Although there are some differences in procedures, both practices use mixtures of aqueous allergenic extracts for the treatment of inhalant allergies and venom sensitivity. However, the practices differ in observed frequency and severity of reactions. As in the Atlanta report,¹ we did not study efficacy, just risk.

We suggest that these differences in immunotherapy reactions are due to differences in injection schedules and dosages.

METHODS

As in the Atlanta report,¹ patients in Oklahoma were skin tested with aqueous extracts of individual aeroallergens and venoms (not mixes).

Study subject coordination

The protocol for this study was inspected by the University of Oklahoma Health Sciences Center Institutional Review Board and exempted from further review.

Our 1:100 (wt/vol) maintenance immunotherapy extracts are prepared with 1:100 concentrations of individual allergen solutions. Thus the 1:100 Atlanta extracts, which are prepared with 1:10 individual ingredients, would be 1:10 according to our nomenclature.

We, like the Atlanta group, operate a pollen and mold counting station, which is certified by the Academy of Allergy Asthma and Immunology.

Throughout 1994, an incident report was filled out by the nurse involved whenever a patient reported symptoms that might indicate development of a systemic allergic reaction during the 20-minute postinjection observation period in our clinic or when a patient returned for evaluation or treatment later that day because of subsequent development of such symptoms. These incident reports along with chart reviews furnish the information for this study.

Our injection clinic experience with systemic reactions is compared with that reported by Tinkelman et al.¹ in Atlanta. Also, comparisons of some possible risk factors were made between our reactor group and a random sample of 100 of our injection clinic patients who were tolerating their injections.

Statistical methods included the chi square test and testing the difference of proportions by using the Z statistic based on the normal distribution.

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TABLE I. Injection clinic patient data

Usual injection procedures	Oklahoma	Atlanta ¹	
Starting concentration (wt/vol)	1:62,500 (48%)* More dilute (44%)*	1:100,000	
Buildup concentration increases	Five-fold	10-fold	
Buildup injection frequency	Weekly	Twice weekly	
Maintenance concentration	1:100 (43%)* 1:250 (37%)* 1:500 (12%)*	1:100 (actually 1:10)†	
Maintenance injection frequency	Weekly	Less frequent than weekly	
Visits for injections	104,101	162,436	
Reactions (number)	22 (in 18 patients)	98 (in 96 patients)	$p < 0.0001$
Overall reaction rate per visit	1/4700	1/1600	$p < 0.001$
Respiratory reaction rate	19/22	72/98	NS
Hypotension rate	0/22	7/98	—
Reactions during buildup	17	36	NS
Reactions during maintenance	5	62	$p < 0.01$
Patients with previous reactions	9/18		
Reactors with starting concentration more dilute than 1:62,500	14/18 (78%)		
Interval between injection and reaction			
Median	20 min		
Range	2-38 min		
>20 min	4 patients		

*Data from injection clinic random sample ($n = 100$).

†See text.

RESULTS

Our observations are described and contrasted with those of the Atlanta group in Table I.

The systemic reaction rate in our series was about one third of that reported by Tinkelman et al.¹ Systemic reactions to allergy injections in our clinic occurred most often early in the buildup phase. Although such reactions could occur at any time, there was much less risk at high doses in Oklahoma City than in Atlanta. Also, reactions in Oklahoma appeared less severe, as evidenced by lack of hypotension, although the number of patients with hypotension in Atlanta was small.

One risk factor for an injection reaction in Oklahoma patients was strong allergic sensitivity, as reflected by weaker starting concentrations for reactors than for a random sample of 100 patients from our general population ($p < 0.05$). A diagnosis of asthma was related to a slight but statistically insignificant increased reaction rate. Also, one half of our reactors had previously experienced some systemic symptoms from allergy injections. A history of preceding local reactions was generally not

present and hence not helpful in predicting increased risk.

Reactions occurred most often in May and June (4 each); otherwise, no indication of seasonality was evident. We could not identify any particular sensitivity or atmospheric allergen level in relation to increased risk.

DISCUSSION

In our experience the patient most likely to react anaphylactically to immunotherapy is the highly allergic one. Buildup and maintenance dose schedules appear to be important risk and safety factors.

The reduced frequency and severity of systemic immunotherapy reactions in the Oklahoma patients compared with the Atlanta patients are probably not due to major differences in patient populations. They are more likely related to a lower starting dose, more gradual buildup, more frequent maintenance injections, a lower but more frequent maintenance dose, or some combination of these factors.

The average maintenance dose reached in Atlanta appears to have been greater than that in

Oklahoma City and was given less frequently. These factors probably explain the lower incidence of reactions during maintenance treatment and perhaps also the lack of hypotension in our patients. Total cumulative maintenance doses from the Oklahoma and Atlanta reports cannot be compared.

As reviewed by Creticos,² there is convincing evidence that favorable responses to a single allergen (ragweed) are dose-related. If both toxicity and favorable clinical response to immunotherapy are dose-related, then what doses, schedules, and mixtures will minimize reactions and maximize improvement? Combined studies of both safety and efficacy are needed to answer these questions.

I compliment the Atlanta group for providing benchmark data.

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