

Correspondence

Omalizumab anaphylaxis occurring outside the recommended observation times*To the Editor:*

In a case-control study in the September 2016 issue of the *Journal*, Lieberman et al¹ describe a series of 30 patients who had anaphylactic reactions associated with omalizumab administration, comparing them with 88 patients who received omalizumab without such reactions. Among their important findings is an increased risk for anaphylaxis to omalizumab in patients who have a history of anaphylaxis to food, medication, or other causes. Such a history would raise the overall 0.2% risk to 0.62%, but in those without such a history would lower the risk to 0.08%. The study also describes the time interval between omalizumab administration and the onset of anaphylaxis in the 30 cases, where in 21 (70%) symptoms began within 1 hour, in 8 (27%) within 2 hours, and in only 1 (3%) beyond 2 hours (3.5 hours). Finally, they describe the number of omalizumab doses received before the anaphylactic reactions in 28 of the cases where this had been recorded and found that the reactions occurred within the first 3 doses in 11 (39%), after 4 to 20 doses in 8 (29%), and after more than 20 doses in 9 (32%). In their concluding remarks, the authors state that “anaphylaxis occurred most frequently within the first 3 doses and within 1 hour of dosing.” It is certainly correct that the majority (70%) of anaphylactic events began within 1 hour of dosing and the vast majority (97%) within 2 hours. However, the statement that the reactions occurred most frequently within the first 3 doses does not appear to be supported by the data because 17 of 28 (61%) occurred after 4 or more doses (and in 1 case after more than 60 doses).

Current recommendations for mitigating the small risk of anaphylaxis associated with omalizumab administration include

“requiring a 2-hour observation period after the first 3 injections and a 30-minute observation period after subsequent injections.”² Application of these recommendations to a previous case series estimated that 77% of reactions would occur under observation.² It would be useful to be able to make such a calculation from the current case series, but we would need additional information such as how many of the 11 patients whose reactions occurred within the first 3 doses also began in less than 2 hours and how many of the 17 patients whose reactions occurred after 4 or more doses began in less than 30 minutes. Whatever the figure, it appears clear that a substantial minority of these rare reactions will occur outside the recommended observation periods, emphasizing the importance of the additional guidance given in the current recommendations, namely, “providing regular patient education about recognition of anaphylaxis symptoms and signs, and prescribing 1 or more epinephrine autoinjectors with training on proper use.”

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