Adverse Event Reporting

Dear Editor:

Accurate adverse event reporting in clinical trials is critical in assisting the medical community to evaluate the safety of pharmaceutical products. However, adverse event collection methods may influence the incidence of reported side effects.

Bent et al recently evaluated differences in reported systemic side effects when asking patients a general query such as "How are you doing?" versus giving them a specific symptom checklist.[1] The authors found that with a general question adverse events were reported in 11% of patients, but in 77% when using a specific checklist.

A similar difference might exist for ocular symptoms using general and specific queries for adverse events. Unfortunately, little information is available regarding response rate variation for adverse events in ophthalmic clinical trials based on general or specific queries.

We performed a meta-analysis of clinical trials managed by Pharmaceutical Research Corporation during the past 10 years that included a solicited ophthalmic symptom query checklist and also a general query, "How are you doing since your last visit?" All the included studies were conducted as double-masked, randomized, crossover comparisons of glaucoma medicines timolol, carteolol, dorzolamide, brinzolamide, bimatoprost, and dorzolamide/timolol or pilocarpine/timolol fixed combinations. One study included a placebo arm.[2]

The meta-analysis included data from 4 studies including 223 patients.[2–5] The results are shown in Table 1 (available at http://aaojournal.org). For 13 of 14 questions, there was a statistically greater positive response rate to a specific query than to a nonspecific one (chi-square or Fisher exact test, as appropriate). Only for photophobia, which had a low rate of positive responses generally, was a statistical difference not found.

This meta-analysis showed that a specific question about an ocular symptom more often provides a positive response than does a general query. Our findings helped confirm for ophthalmic symptoms what Bent et al found for systemic symptoms.[1] However, the prior trial differed from ours in that it was prospective, treatment was with a placebo, and patients were evaluated with a checklist of 53 symptoms. Our report represented a retrospective meta-analysis of comparative studies evaluating a variety of glaucoma medicines.

Nonetheless, statistical differences were found between general and specific ophthalmic queries in our analysis that may have importance to a physician in the following ways: (1) to assist in evaluating differences of adverse event rates between published studies, (2) to help to clarify why a published rate for a side effect might differ from that in their own clinical practice, and (3) to understand in clinical trial design that the chance of eliciting a specific symptom may differ based on the manner of query.

This study suggests that a specific ophthalmic symptom query will more often elicit a positive response than a general query.

This study did not evaluate differences in adverse event response rates in a prospective manner using the same glaucoma medications. Further research might further clarify differences in response rates between specific and general adverse event queries for ophthalmic products.

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References

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Table 1. Adverse Events

Symptom	% Unsolicited		% Solicited		*P* Value
	n/*n*	%	*n*/*n*	%	
Decreased/blurred vision	18/96	19	84/96	88	<0.0001
Red eye	0/60	9	33/60	55	<0.0001
Tearing	3/35	9	11/35	31	0.02
Crusting	0/35	9	11/35	31	0.0002
Sandy/gritty feeling	0/35	9	10/35	29	0.0005
Burning/stinging	12/223	5	59/223	27	<0.0001
Deep pain	0/35	9	6/35	17	0.01
Eye itching	9/198	5	31/198	16	0.0002
Dry eyes	0/223	0	26/223	12	<0.0001
Foreign body sensation	0/188	0	21/188	11	<0.0001
Ocular pain	5/223	2	14/223	6	0.03
Burning/not on instillation	0/163	0	8/163	5	0.004
Epiphora	0/163	0	7/163	4	0.007
Photophobia	0/163	0	1/163	1	0.32

Not every question was included in all 4 studies.