Glucoma experts debate merits of monocular trials

Cheryl Gutman
in Las Vegas

FO R years, glaucoma experts have recommended initiating medical therapy with a monocular trial. Recently, however, some specialists have questioned this fundamental practice based on studies examining IOP behaviour in treated and untreated glaucomatous eyes.

In a point-counterpoint presentation at the glaucoma subspecialty day meeting of the 2006 annual meeting of the American Academy of Ophthalmology, Tony Realini MD presented evidence to support his conclusion that a monocular drug trial is not a reliable approach.

Representing the opposing view and citing many of the same studies but with different interpretations, M Bruce Shields MD argued that the monocular trial has many advantages aside from establishing treatment efficacy and is still necessary and valid. However, he offered suggestions for a modified approach that would take into account the research findings of Dr Realini and others.

“A one-eye trial is important to confirm the efficacy of each glaucoma medication we prescribe, and considering that spontaneous IOP fluctuations occur and can confound our interpretation of a therapeutic response, it is helpful to have the fellow eye available as a control,” said Dr Shields.

He also proposed that a monocular trial has safety benefits, allowing better assessment of ocular adverse reactions by treating a single eye and exposing the system to adverse reaction risk with a lower medication dose. In addition, Dr Shields contended that patient acceptance might be higher for the monocular treatment trial.

“Patients seem to respond better psychologically to a strategy that aims to evaluate medication safety and efficacy in one eye before using it in both,” noted Dr Shields.

Dr Realini also reminded his colleagues that the monocular drug trial is not useful, Dr Realini put forth the concept that its value is predicated on four assumptions: 1) Fellow eyes exhibit symmetrical spontaneous IOP fluctuations over time; 2) There is no contralateral crossover effect from monocular treatment with a topical ocular hypotensive medication; 3) Fellow eyes respond symmetrically to a given medication, and 4) Patients take their medications as directed.

“These assumptions have not withstood critical scrutiny of scientific investigation. They are either patently false or open to serious debate, and while this story is probably not over and more research needs to be done, I would recommend abandoning the monocular treatment trial,” said Dr Realini.

Dr Realini also reminded his colleagues that glaucoma is a chronic disease and that few patients require intervention to produce an acute IOP drop. Dr Realini recommended obtaining several pre-treatment IOP measurements to establish the baseline along with multiple on-treatment measurements to evaluate efficacy.

“It’s a bad shot because the clinician does not know when patients will have fluctuation and when they will not,” he said.

Discussing the issue of a possible crossover effect, Dr Realini pointed out that 30 years ago, Thom Zimmerman described a noticeable IOP decrease in the untreated eyes of patients started on timolol in a single eye and postulated several mechanisms to explain that result. Further confirmation of a crossover effect of beta-blockers came more recently from the Ocular Hypertension Treatment Study (OHTS) in which IOP in contralateral untreated eyes fell by a mean of 1.5 mmHg with about one-third of patients experiencing an IOP decrease of at least 3 mmHg and 10 percent having a 6 mmHg or greater drop in the untreated fellow eye.

“Reflecting on these findings, the OHTS investigators stated that the true therapeutic effect of beta-blocker treatment may be underestimated by a one eye trial,” noted Dr Realini.

Dr Realini acknowledged that his own study examining IOP responses in fellow eyes starting treatment simultaneously supports the assumption that fellow eyes respond symmetrically. However, there are conflicting reports on this issue. In his earlier study of 52 patients who underwent monocular treatment in one eye and subsequently in the second, there was no correlation between right and left eye IOP reduction. In addition, Young et al. reported finding only a poor correlation in IOP lowering between fellow eyes before and after latanoprost (Xalatan, Pfizer) therapy.

“These latter investigators concluded a monocular therapy trial may not necessarily predict the response of the fellow eye to topical latanoprost,” Dr Realini said.

He suggested there was no need to present data to convince ophthalmologists about the falacy of assuming that patients take their medications as directed. As that issue applies to the monocular treatment trial, it creates situations for invalidating the results as patients may be noncompliant or put their medication in the wrong eye or both eyes, Dr Realini explained.

Dr Realini also reminded his colleagues that the results of the Hamilton Glaucoma Center study demonstrate that a significant proportion of patients experience periodic asymmetric IOP fluctuations and that fellow eye fluctuations occurred in both eyes 50 percent of the time in seven visits, Dr Realini said those results show the uncertainty of using the fellow eye as a control.