Clinical Experience With Timolol in Childhood Glaucoma

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We studied 67 patients (100 eyes) with childhood glaucoma who were treated with timolol maleate. Thirty of these patients (40 eyes) did not require additional surgery or medications after being treated with timolol (follow-up, from six to 60 months). Thirty-one eyes (78%) in this group had a pressure drop; 18 eyes (45%) had a pressure drop of greater than 10 mm Hg. We conclude that timolol is effective in the treatment of pediatric glaucoma, although there is a need to be aware of its potential complications.

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The use of timolol maleate in the treatment of glaucoma in adults has been the subject of many studies. These studies have shown that timolol is an effective and safe medication in adults. The efficacy and safety of timolol in children, however, is not well established.

Olson et al and Williams and Ginther described severe side effects in children treated with timolol. Boger and Walton also described complications in a young patient. Zimmerman et al and McMahon et al each observed complications in five children after the use of timolol. With the exception of the review of Zimmerman et al, in which four patients (eight eyes) had more than 40 months of follow-up, all these studies have had follow-up periods of six weeks to 14 months. Passo et al reported that plasma levels of timolol after patients received timolol drops were considerably higher in children than in adults.

MATERIALS AND METHODS

The original study population of McMahon et al was resurveyed four years later to look for additional complications and to assess the long-term efficacy of timolol treatment in pediatric glaucoma. Additional patients who had started timolol treatment since the 1981 study were added after review of medical records from the files of Shaffer Associates Medical Group, San Francisco. Patients were included in the study if they started timolol therapy before their 18th birthday.

From patient records, we noted birthdate, ocular diagnosis, glaucoma medications, and initial timolol dosage. We also obtained the most recent intraocular pressure (IOP) before stopping timolol therapy, final or most recent timolol dosage, number of glaucoma medications, and reason for stopping timolol therapy.

Results

We studied 67 patients (100 eyes) who started topical timolol therapy...
before the age of 18 (Table 1). Fifty-five of these patients (87 eyes) had failed glaucoma surgery before beginning timolol therapy.

Table 2 compared the diagnosis of our group with those of previously reported studies.

Our follow-up period ranged from five days to 5 ½ years, with a mean length of 1 ½ years. Table 3 compares this with those of the other authors.

Of the 67 patients, seven experienced an adverse reaction to timolol. Only two of these patients were advised to stop the medication because of side effects. A 10-year-old boy had a severe asthma attack immediately after starting timolol therapy, and a 17-year-old boy had a marked reduction in pulse rate. The remaining five patients suffered transitory reactions from timolol therapy. These included two cases in which the patient complained of dizziness, and one case each of asthma, drowsiness, and hyperactivity. These and previously reported side effects from the studies of McMahon, Boger, Zimmerman, and their colleagues, are summarized in Table 4.

Seventeen patients (31 eyes) required surgery due to inadequate reduction of IOP (Table 5). Of those, 15 patients (27 eyes) were restarted on timolol.

In eight patients (13 eyes), timolol therapy was discontinued because of successful surgery (four eyes of two patients), noncompliance (two eyes of one patient), complications (two eyes of two patients), or lack of apparent effect (five eyes of three patients).

Fifty-nine patients (87 eyes) remained on timolol therapy at the end of the study. Fourteen of these 59 patients (20 eyes) not requiring glaucoma surgery after timolol therapy did require additional medications to control their IOP.

The 30 patients (40 eyes) who had no eye surgery or additional medical therapy after initiating timolol were used to evaluate the efficacy of timolol in lowering IOP. Of these eyes, 78% had at least 1 mm Hg lowering of IOP; 58% had a pressure drop greater than 20%; 45% had a decrease in IOP in excess of 10 mm Hg. The average pretimolol IOP in these 40 eyes was 30.1 mm Hg (SD, 9.5) with final IOP of 22.7 mm Hg (SD, 8.5; < .001) (Figure). The follow-up period for this subgroup was 2.7 years (SD, 2.4). Table 6 summarizes the effectiveness of timolol in lowering IOP in these 40 eyes as well as results reported by other authors.

**COMMENT**

Timolol therapy was discontinued because of side effects or complications in two of our patients. It is interesting that these two patients were those we previously described in 1981. We have not seen serious complications of timolol therapy in children in our practice since that report. This may be due to our exclusion from timolol therapy of any children who have a history of cardiac arrhythmias or bronchospasm.

Zimmerman et al reported three...
cases of ocular complications, whereas we found none. That report includes many patients who started timolol in their late teens and 20s. These older patients are probably more apt to report side effects, such as tearing and itching, than is our younger glaucoma population.

Twenty-eight of our 67 patients (43 of 100 eyes) have used timolol for more than three years. We have not recognized any increase in side effects in these children after long-term use. Compliance with timolol therapy appears good. As far as we are aware, only one of the children failed to follow the prescribed timolol regimen. This high level of compliance is indicative of the generally well-tolerated nature of the drug.

It is difficult to assess efficacy in the pediatric age group. Intraocular pressure measurements are often hard to obtain and, in very young children, must often be measured under general anesthesia. Often these patients are receiving multiple medications and have undergone surgery. In the group who needed no further pressure lowering maneuver after starting timolol, there was a substantial mean IOP drop of 7 mm Hg. This is an encouraging result in these difficult glaucomas.

Our data indicate that timolol may be effective in lowering IOP in childhood glaucomas. Since developmental glaucoma patients often have severe glaucoma, additional medication and surgery may be required to achieve adequate IOP control.

Our results compare favorably with those of Zimmerman et al and Boger and Walton.7,8 Boger and Walton reported a higher incidence of surgery after timolol use, but their study population was considerably older than ours. Over a follow-up period of six months, McMahon and colleagues10 reported only seven eyes that needed surgery after timolol treatment.

Although we cannot state on the basis of our study that 0.25% timolol is as effective as 0.5% timolol, the majority of patients who achieved stability with timolol did so with the 0.25% solution. More importantly, all of the patients with complications were using the 0.5% solution. Our current strategy in children is to initiate therapy with the 0.25% solution and increase to the 0.5% preparation only if the effect with the lower dosage is not adequate. One should then re-evaluate the IOP level to be sure that better control has been obtained with the stronger dosage.

Passo and colleagues11 have described high plasma levels of timolol after receiving one drop of 0.5% timolol. These plasma timolol levels were considerably higher than in the adult population they tested. As recommended by Zimmerman and Passo, utilization of a single drop and obstruction of the nasolacrimal passage may help reduce systemic absorption up to 40%.

The usual precautions of excluding patients with systemic contraindications and using the lowest effective dosage are particularly important in the use of this drug in childhood. It is also important to notify the parents of potential side effects so they can immediately discontinue the drug therapy.

The Food and Drug Administration has not ruled on the safety or efficacy of this drug in children, and it is wise to make parents aware of this. However, the sequelae of uncontrolled glaucoma are such that the advantages of this therapy, when it is effective, warrant its use.

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