A PROSPECTIVE STUDY OF ALTERNATING OCCLUSION PRIOR TO SURGICAL ALIGNMENT FOR INFANTILE ESOTROPIA: ONE-YEAR POSTOPERATIVE MOTOR RESULTS

BY **Malcolm R. Ing MD,*** Anthony Norcia PhD, **David Stager Sr MD,** Bradley Black MD, Robert Hoffman MD, **Malcolm Mazow MD,** Sebastian Troia MD, William Scott MD, AND Scott Lambert MD

ABSTRACT

Purpose: Alternating occlusion prior to surgical alignment has been suggested by some strabismologists to possibly enhance the treatment of infantile esotropia. This report presents the data for 44 patients prospectively enrolled by random assignment to an alternating occlusion or no occlusion subgroup followed for 1 year postoperatively.

Methods: All patients were measured at entry into the study, at the time of surgery, and at 6 weeks and 1 year postoperatively. Alternating occlusion was full-time and symmetric for those with no amblyopia but asymmetric for those with amblyopia. The subgroup that did not receive alternating occlusion had occlusion for amblyopia only. Initial surgeries were performed between the ages of 6 and 13 months.

Results: The patients, as a whole, showed a significant increase of 9.14 prism diopters when followed for a mean of 4.2 months prior to initial surgery ($P < .00027$). Seventy-five percent of all patients were aligned by the initial surgery. Ninety-one percent of those patients aligned at 6 weeks were also aligned at the 1-year postoperative date. The results were similar for both the control group and the patients treated with alternating occlusion.

Conclusion: In our sample of patients, alternating occlusion does not detectably alter the increase in angle of deviation between the dates of entry and the date of the initial surgical alignment procedure, nor does it influence the postoperative alignment at 6 weeks or at 1 year.

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INTRODUCTION

Alternating occlusion prior to surgical alignment for infantile esotropia has been advocated by Jampolsky for many years.[1,2] Other practitioners use occlusion only part-time over the dominant eye to promote equal vision before alignment. A previous report on the outcome of surgery after alternating occlusion has indicated success rates comparable to studies in which no alternating occlusion was utilized.[3]

More recently, Jampolsky and associates[4] followed a group of patients with infantile esotropia who received alternating occlusion and observed that an index of abnormal binocularity—asymmetric monocular motion visual evoked potentials—declined during the course of alternating occlusion. From this finding, it was concluded that alternate occlusion was causing a significant and presumably positive alteration in an otherwise pathological system. These results suggested that alternating occlusion disrupted an active competitive interaction between the two eyes and that it had a beneficial effect. Nevertheless, no clinical prospective study has been reported to support this theory.

METHODS

Forty-four patients were enrolled in eight eye centers in a randomized, prospective study to examine the clinical efficacy of alternating occlusion versus a control group (ie, no occlusion except for amblyopia treatment). Inclusion criteria for patients consisted of constant esotropia of 15 prism diopters or more beginning before 6 months of age, confirmed by an ophthalmologist by 7 months of age. Patients who were more than 3 weeks premature or who had congenital nystagmus, central nervous system abnormality, developmental delay, retardation, dysmorphia, birth trauma, or hyperopia of 5 or more diopters in any meridian were excluded. Consecutive patients were assigned to the specific group by selection from a list of random numbers provided by the data coordination center at Smith-Kettlewell Eye Research Institute. Such patients, after the respective parents signed a permit to include their child in the study, received the random assignment in an envelope; the assignment was unknown to the investigator. Patching regimens were symmetric alternating occlusion for each eye during all waking hours in the alternating occlusion group if the eyes showed an equal alternating fixation on initial examination. All patients with strong monocular preference received asymmetric occlusion (2 or 3 days on the dominant eye and 1 day on the nondominant eye) until fixation was equalized. All patients in the control group received only part-time occlusion over the dominant eye until fixation was equalized.

Surgery was performed as close to 10 months of age as possible; the earliest surgery was performed at 6 months and the latest at 13 months of age.

Patients with any hyperopia in any meridian of greater than 2.75 diopters were given a 6-week trial of glasses before the surgery.

From the University of Hawaii, Honolulu, Hawaii (Dr Ing); Smith-Kettlewell Eye Research Institute, San Francisco, California (Dr Norcia); University of Texas Southwest, Dallas, Texas (Dr Stager); Louisiana State University, Baton Rouge, Louisiana (Dr Black); University of Utah, Salt Lake City, Utah (Dr Hoffman); Baylor University, Houston, Texas (Dr Mazow); University of Iowa, Iowa City, Iowa (Dr Scott); and Emory University, Atlanta, Georgia (Dr Lambert). Supported by grants from the Smith-Kettlewell Eye Research Institute and the Children's Eye Foundation, San Francisco, California.

*Presenter.

Bold type indicates ~~ASOS~~ member.

The mean refractive errors in the alternate occlusion and control groups were 1.75 ± 0.20 and 1.77 ± 0.26 diopters, respectively. If the strabismus declined to less than 15 prism diopters after spectacle correction, the patient was excluded from the study.

Measurements of the deviation on entry into the study and just prior to surgery were recorded for all patients. Postoperative measurements were made at 6 weeks following surgery, and any deviations greater than 15 prism diopters were treated by additional surgery. If the defect was greater than 15 prism diopters in two postoperative visits, the original pattern of alternating occlusion or no occlusion was utilized until the patient received second surgery. Misalignment at entry was compared with misalignment just prior to surgery to investigate any possible difference during the preoperative period for the two groups of patients. Postoperative alignment results at 6 weeks and 1 year were recorded for each patient.

The protocol of the study was reviewed by each investigator's human subjects review committee. Data collected throughout the study were examined periodically by the data coordinating center at Smith-Kettlewell to determine if one or the other treatment regimens produced significantly poorer results in postoperative alignment outcome measures, number of surgeries, or depth of amblyopia.

The eye occluders (coverlet) were provided by Biersdorf, Inc (Wilton, Connecticut).

RESULTS

Measurements of the deviation on entry into the study and just prior to surgery are shown for all patients in Table 1. There was a significant increase in the angle of deviation of 9.14 prism diopters overall when patients were followed for a mean of 4.2 months (P = .00027). Also notable, there was no significant difference in the increase in deviation in patients followed with alternating occlusion compared with the control group (Table 2).

The age at initial surgery was similar for both groups (mean age, 9.6 months) (Table 3). The motor alignment results showed no significant difference in the initial alignment to within 10 prism diopters at 6 weeks between the two groups. Both groups did equally well with 75% of patients aligned at 6 weeks postoperatively (Table 4). Ninety-one percent of the patients who were aligned at 6weeks maintained their alignment at the 1-year postoperative measurements, and there was no significant difference between the two groups (Table 5). Secondary surgery was necessary for 4 of 19 in the alternating occlusion group and for 5 of 25 in the control group. Of these second surgeries, two patients in the alternate occlusion group received surgery for overcorrection and two for undercorrection. All of the control group had surgery for undercorrection. The second surgery was successful in four of four patients with alternating occlusion and four of five subjects in the control group. Therefore, postoperatively, eight of nine patients were aligned by the second surgery.

TABLE 1. MEASUREMENTS OF THE ANGLE OF DEVIATION ON ENTRY INTO STUDY, AT PREOPERATIVE VISIT, AND AFTER SURGERY

PATIENT NO.	INVESTIG-ATOR	GROUP	NEAR HORIZONTAL DEVIATION (PD)					MONTHS BETWEEN ENTRY AND PREOP	NO. OF SURGERIES
			Entry	Preop	Change From Entry to Preop	Postop 6 wk	Postop 1 yr		
1	1	Alt occl*	30	45	15	0	0	4.8	1
2	1	Control	45	30	–15	6	4	5.0	1
3	1	Control	45	40	–5	10	6	4.7	1
4	1	Control	35	45	10	0	2	6.1	1
5	1	Alt occl	40	45	5	4	2	4.8	1
6	1	Alt occl	35	50	15	30	0	5.4	2
8	1	Control	45	50	5	0	0	5.4	1
7	1	Alt occl	38	40	2	0	0	3.3	1
9	1	Control	40	45	5	0	0	3.3	1
10	1	Control	40	50	10	25	0	5.6	2
11	1	Control	45	60	15	0	0	5.6	1
12	1	Control	20	30	10	0	0	3.7	1
13	1	Alt occl	25	50	25	0	0	6.0	1
14	1	Alt occl	40	50	10	–30	0	5.4	2
15	2	Control	75	50	–25	0	0	1.6	1
16	2	Control	70	45	–25	8	0	1.9	1
17	2	Alt occl	60	70	10	0	4	5.3	1
18	2	Control	50	45	–5	4	0	4.7	1
19	2	Alt occl	40	50	10	0	0	1.0	1

TABLE 1. (CONTINUED) MEASUREMENTS OF THE ANGLE OF DEVIATION ON ENTRY INTO STUDY, AT PREOPERATIVE VISIT, AND AFTER SURGERY

PATIENT NO.	INVESTIG-ATOR	GROUP	NEAR HORIZONTAL DEVIATION (PD)					MONTHS BETWEEN ENTRY AND PREOP	NO. OF SURGERIES
			Entry	Preop	Change From Entry to Preop	Postop 6 wk	Postop 1 yr		
20	2	Alt occl	40	40	0	0	8	1.8	1
21	2	Control	40	45	5	0	0	2.6	1
22	3	Control	40	45	5	0	0	3.8	1
23	3	Alt occl	50	50	0	6	0	5.0	1
24	3	Control	40	75	35	20	0	4.3	2
25	3	Control	30	65	35	8	2	7.4	1
26	3	Control	50	50	0	2	0	9.8	1
27	3	Alt occl	45	75	30	–15	4	4.5	2
28	3	Control	40	60	20	4	0	4.1	2
29	4	Alt occl	40	40	0	0	0	3.3	1
30	5	Control	30	65	35	12	10	1.9	1
31	5	Alt occl	45	50	5	25	10	3.7	2
32	5	Alt occl	50	50	0	0	0	2.5	1
33	5	Control	35	50	15	25	25	3.3	1
34	5	Control	80	90	10	10	30	3.2	3
35	6	Control	35	30	–5	0	12	10.1	1
36	6	Control	25	45	20	25	6	2.8	3
37	6	Alt occl	30	65	35	–10	12	3.7	1
38	6	Alt occl	55	65	10	0	–30	3.5	1
39	6	Control	45	95	50	0	0	2.7	1
40	6	Alt occl	25	25	0	8	4	2.4	1
41	6	Control	95	85	–10	0	0	2.4	1
42	7	Alt occl	25	40	15	15	0	6.0	1
43	7	Alt occl	40	55	15	10	0	6.0	1
44	8	Control	70	75	5	14	3	1.2	1
		Average increase		9.1		Average duration		4.2	
		± SE		2.33					
		P value		.00027					

Alt occl = alternating occlusion; PD, prism diopter; SE = standard error.
*Patients in "Alt occl" group received constant alternating occlusion.

TABLE 2. NEAR HORIZONTAL DEVIATIONS IN PRISM DIOPTERS AT ENTRY INTO STUDY AND AT TIME OF SURGERY (PREOPERATIVE)*

GROUP		ENTRY			PREOPERATIVE		
	n	Min	Max	Mean	Min	Max	Mean
Alternating occlusion	19	25	60	39.6	25	75	50.3
Control	25	20	95	46.6	30	95	54.6
Total	44	20	95	43.6	25	95	52.7

*No significant difference between groups: entry, $P = .11$; preoperative, $P = .34$

TABLE 3. AGE IN MONTHS AT INITIAL SURGERY FOR PATIENTS IN EACH GROUP*

GROUP	N	MIN	MAX	MEAN
Alternating occlusion	19	6.8	12.7	9.6
Control	25	6.3	13.1	9.5
Total	44	6.3	13.1	9.6

*No significant difference between groups: $P = .82$.

TABLE 4. ALIGNMENT TO WITHIN 10 PRISM DIOPTERS AT 6-WEEK POSTOPERATIVE VISIT AFTER SURGERY*

GROUP	SUCCESS RATE
Alternating occlusion	74% (14/19)
Control	76% (19/25)
Total	75% (33/44)

*No significant difference between groups: $P = .70$.

TABLE 5. INITIAL ALIGNMENT TO WITHIN 10 PRISM DIOPTERS OF ORTHOPHORIA AT 6 WEEKS COMPARED WITH 1-YEAR ALIGNMENT FOR EACH GROUP*

GROUP	6 WEEKS	1 YEAR	%
Alternating occlusion	14	13	93
Control	19	17	89
All	31	28	91

*No significant difference between groups: $P = .62$.

DISCUSSION

Ing[5] first reported a progressive increase in misalignment in infantile esotropia in 1994. This observation was also reported by Biglan.[6] Since that study, there have been no reports prospectively examining this observation of increasing misalignment in infantile esotropia, except for the present study. Overall, the mean increase in the angle of deviation of 9.14 prism diopters was significant in this group of patients followed for a mean of 4.2 months prior to the initial surgery ($P = .00027$). The increase in misalignment was found to be 15 or more prism diopters in 15 (34%) of 44 of these patients, emphasizing the need to measure the angle of deviation just prior to surgery to reduce the risk of undercorrection by using a lesser degree of esotropia as a guide for surgery. Stabilization of the motor misalignment was initially speculated to be a possible beneficial effect of alternate occlusion, but this effect was not evident.

Successful alignment was achieved in about 75% of cases in both treatment groups (Table 4). Whereas the difference between the groups was not statistically significant ($P = .70$, Fisher's exact test), we cannot necessarily conclude that alternate occlusion has no effect. We must remember that, by chance, our small random sample might obscure a real discrepancy between the treatment groups. Thus, we need to estimate our test's ability to detect small treatment effects—in statistical parlance, the *power* of our test. In general, the power of a test depends on the sample size: increasing the number of patients in a study will increase our confidence that small differences between treatment groups reflect a true discrepancy. Given our overall rate of postoperative alignment (75%) and our sample size of 44 patients, success rates in the two treatment groups would have to differ by 25% to reach a significance level of 5%. Put another way, even if we observed 89% success with alternate occlusion and 64% success with no occlusion, we still could not reject the null hypothesis that alternate occlusion has no effect on postsurgical alignment. This lack of power due to insufficient sample size could easily conceal a clinically relevant treatment effect. For example, more than 130 patients would need to be tested to be confident that a 15% difference in treatment groups was significant. Similar considerations also apply to the stability of alignment between 6 weeks and 1 year after successful surgery (Table 5).

The postoperative alignment at 6 weeks has been reported to be the most important predictive factor in the long-term functional results by Bateman and associates.[7] In our study, a high percentage (91%) of patients aligned at the 6-week postoperative examination maintained that successful alignment at 1 year. Although the long term (4-year postoperative) results were not yet available for these groups of patients, the correlation of the 6-week and 1-year postoperative results at least partially supports the concept of the 6-week postoperative examination being of prime importance in determining the motor alignment in the future.

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PEER DISCUSSION

DR IRENE H. LUDWIG. To answer the question whether alternate occlusion prior to surgery for congenital esotropia improves the outcome, Dr Ing has undertaken the most difficult and highest-level study possible—the prospective, randomized, masked, and controlled clinical trial. This is the gold standard for clinical studies, but is very time and resource consuming. To have organized and seen this ambitious project through to completion is an amazing accomplishment for a clinician.

The paper is a concise and well-written description of the study's findings, namely the lack of finding a difference in outcome for the patching vs. the no patching groups, as well as the significant finding of a progressive increase in the angle of esodeviation over the several months prior to surgery. The section in which Dr Ing carefully explains the meaning of a study in which no statistical difference was found impressed me. Many physicians incorrectly equate lack of a statistically significant difference between two groups as proof of no difference. This paper discusses the effect of sample size and magnitude of treatment effect on the chance of proving a statistically significant difference between two groups. It makes no claim to have proven that alternate occlusion has no effect on outcome, only that a treatment effect of 25% or more should have been demonstrated by this study's sample size with 95% certainty. One can therefore assume that alternate occlusion does not improve outcome by more than 25%.

The highly statistically significant finding of a progressive increase in the angle of deviation between the initial visit and the time of surgery was proven by this study. It is interesting to me how closely this number agrees with the findings presented by Dr Ing in his 1994 AOS paper, which was a review of his own retrospective clinical data. Some of the criticism of that study was the use of retrospective data, but the numbers came out the same anyway.

In order to improve the quality of clinical studies of medical interventions, the clinical trials community has pushed to educate physicians about the need for randomized controlled clinical trials. Some of the message, especially the need for prospective data collection, has gotten across, but few clinicians understand the fundamental principles of these studies. Reviewers automatically criticize the use of retrospective data. Without proper randomization, masking, and use of controls, collecting data prospectively confers no improvement to a study, and may actually increase bias, as the investigators have already thought about outcome before beginning to amass data. We may be disregarding useful retrospective data by our insistence on prospective clinical trials.

An improperly designed clinical trial may unintentionally squash a therapeutically useful treatment by showing a negative result due to insufficient sample size. In some long-term conditions, such as childhood strabismus, it may be impossible to ever answer our questions with clinical trials. Surgery cannot be delivered in a masked fashion, as sham surgery is unethical. Some disorders do not fit the clinical trial model of a single, defined intervention, with an easily measured short-term outcome. We should all understand the principles of clinical trials and statistics in order to evaluate the studies that appear in our literature. We should also look into ways to make better use of the large quantities of retrospective data readily available. New data mining algorithms are able to deal with bias in large data sets, and could be used to improve the reliability of retrospective information.

Dr Ing's well-done, classical clinical trial provided us with two very useful points of information about the management of congenital esotropia. The close agreement of today's findings with his 1994 retrospective study is fascinating, and supports the value of well-designed retrospective studies.

DR GUNTER K. VON NOORDEN. To the my best of my knowledge it was Dr Jampolsky who proposed alternating occlusion, not to improve the motor results of strabismus surgery as investigated in this study, but to prevent the development of sensorial adaptations as a result of incongruous visual input to the visual system (Jampolsky A, Scott SB: Ocular deviations, Int Ophthalmol Clin. 1964;4:567-701). Have you looked into differences in the sensory results between these two groups to determine whether alternating occlusion is an effective therapy?

DR EDWARD L. RAAB. Was there something purposeful about the delay between entry into the study and when the surgery was done, or was that just a logistic necessity based on individual scheduling? Your control group was not a no-occlusion group. It was either no-occlusion or something other than alternating occlusion, and I'm wondering whether those are really not two different groups, because the patients requiring monocular occlusion from amblyopia could have been different in other respects, which bears on Dr von Noorden's question concerning your outcome.

DR PAUL R. MITCHELL. If you had a significant change in degree of esotropia between the first visit and the pre-op, would you ever cancel the surgery and re-measure again, or just go ahead and operate for that new deviation?

DR EVELYN A. PAYSSE. In the long-term follow up of these patients, were the other problems that develop in infantile esotropia lessened by alternating occlusion, such as inferior oblique overaction and DVD?

DR MALCOLM R. ING. I thank Dr Irene Ludwig for reviewing the paper so carefully and also for going back into the TRANSACTIONS to find that 1994 paper, because it was actually one of the ideas that resulted from that investigation and was not our original intent; the original intent was to find out if there was an effect. With regard to Dr von Noorden's question, Dr Arthur Jampolsky did feel that there was a sensory effect that you were going to improve in the long run. These patients are going to be followed longer and at the end of the 4-year study there will be a sensory analysis. This present report is only the motor results. Why did we do the motor exam? We wanted to determine if there was some adverse effect in the early stages.

Dr Raab, the delay only existed because the patients were going to be measured more than once prior to surgery. The original thought was that if the patients came in very young, like at 2-3 months of age, that perhaps when you instituted alternating occlusion, you might indeed preserve a 2-3 month sensorial benefit and that you might get a more beneficial effect later on. We were not going to rush every patient that came in the next day for surgery, because we did want to see if there was an effect of the alternating occlusion. It just fell out in the analysis that these patients were followed for a mean of 4.2 months. Why most of the investigators operated at 9 months is not really known but this is what the data revealed.

Regarding the occlusion for amblyopia question, the congenital or infantile esotropic patient who does not have amblyopia, i.e. a true alternator, may indeed have a different matrix, and may have a better chance at binocularity than the one that you have to intervene with and do some kind of occlusion to equalize fixation prior to surgery. We do not have enough patients, I think, if we eliminate all those that had to have amblyopic treatment vs. non-amblyopic treatment. Therefore we lumped them together into what we called the "standard treatment," which is equalizing fixation by whatever means, by patching, prior to surgery.

Regarding Dr Paysse's question, we will evaluate these patients in the long term to determine if, indeed, overaction of the inferior obliques and secondary hyperopia will be effected. We do know that many of these patients require glasses even though they don't start off in glasses.