TREATMENT OPTIONS FOR AMBLYOPIA: SYSTEMATIC REVIEW OF VISUAL ACUITY IMPROVEMENTS

Catarina van der Elzen[1], Miguel Patrício[2], Miguel Castelo-Branco[3]

[1] Faculty of Medicine, University of Coimbra, Portugal

[2] Laboratory of Biostatistics and Medical Informatics, IBILI - Faculty of Medicine, University of Coimbra, Portugal

[3] IBILI – Faculty of Medicine, University of Coimbra, Portugal

Corresponding author:

Miguel Castelo-Branco

Address: IBILI, Azinhaga Santa Comba, Celas, 3000-548 Coimbra, Portugal

E-mail address: mcbranco@fmed.uc.pt

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ABSTRACT

The aim of the current systematic review is to establish a comparison between the two most widely used treatments for children with amblyopia. Occlusion and atropine are compared in terms of visual acuity (VA) improvement. **Methods:** The review was performed following the guidelines proposed in the PRISMA statement. Relevant studies assessing occlusion or atropine reporting acuity improvement measures were sought on PubMed and subsequently analysed and compared in terms of the age of participants, treatment duration, VA baseline measures and improvement. The VA measures reported in studies were converted to the Logarithm of the Minimum Angle of Resolution chart (LogMAR). **Results:** A statistically significant difference between the VA improvements associated to the two treatments was obtained, favouring occlusion. However, in terms of measures of dispersion, both the best and worst results were reported by articles performing this technique, with the range of improvement of atropine studies being narrower, possibly due, at least in part, to the fact that compliance issues were less present in this intervention type. **Conclusion:** On average, occlusion improved VA more than atropine, but with greater variability of results. Longer periods of treatment were more effective when analyzing subjects who underwent occlusion. Treating patients as early as possible leads to better results, though improvements were also reported for older patients. Future studies should include prolonged treatment in older individuals to correct sources of bias.

Key Words: amblyopia, treatment, occlusion, atropine, visual acuity, systematic review.

RESUMO

Esta revisão sistemática tem por objectivo estabelecer uma comparação entre os dois principais tratamentos usados actualmente em crianças amblíopes. Oclusão e atropina são comparados em termos de melhoria da acuidade visual (AV). **Métodos:** A revisão foi realizada aderindo às orientações propostas no PRISMA statement. Artigos relativos a tratamentos de oclusão e atropina que apresentam medidas de melhoria de acuidade visual, foram procurados na PubMed e, posteriormente, analisados e comparados em termos de idade dos participantes, duração do tratamento, as medidas iniciais de AV e de melhorias. As medidas de AV relatadas nos estudos foram convertidas para a escala do logaritmo do ângulo mínimo de resolução (LogMAR). **Resultados:** Quando associados a melhorias de AV, foi obtida uma diferença estatisticamente significativa entre os dois tratamentos, favorecendo o tratamento por oclusão. No entanto, em termos de medidas de dispersão, tanto os melhores como os piores resultados foram também relatados por artigos que executaram esta técnica, tendo a atropina, por sua vez, apresentado um intervalo de valores de melhoria mais estreito para o qual eventualmente terá contribuído o facto de problemas de adesão não terem estado tão presentes neste tipo de intervenção. **Conclusão:** Em média, a oclusão melhorou mais a acuidade visual do que a atropina, mas com uma maior variabilidade dos resultados. Períodos mais longos de tratamento demonstraram-se mais eficazes em doentes tratados com oclusão. Igualmente, verificamos que tratar pacientes o mais cedo possível leva a melhores resultados. Porém, verificou-se que crianças com mais idade também registaram melhorias. Estudos futuros deverão incluir tratamento prolongado em indivíduos mais velhos de forma a corrigir fontes de viés.

Palavras-Chave: ambliopia, tratamento, oclusão, atropina, acuidade visual, revisão sistemática.

INTRODUCTION

Amblyopia is a common ocular disorder in children[1] and a cause of visual morbidity resulting from an abnormal visual input during the critical phase of early development.[2] Although it occurs in the absence of organic abnormalities,[3] being characterized by deficits in spatial vision,[4] it leads to visual deterioration affecting one or both eyes, the former situation being more common. Amblyopia has a prevalence of 1% to 3.2% [5] and it is classified into three main categories according to its etiology: strabismic, anisometropic and visual deprivation.[3]

Improvement of visual acuity is the primary objective of amblyopia therapy.[5] However, preferred treatment modalities vary a great deal among ophthalmologists. The most effective way of treating amblyopia is to intervene upon early detection, performing correction of any significant refractive error together with abnormal ocular alignment in addition to have periods where stimulation to the non-amblyopic eye is limited.[2,5]

Occlusion and atropine are the most commonly prescribed amblyopia treatments.[6] The former consists of patching the non-amblyopic eye, penalizing its visual stimulus and forcing fixation with the amblyopic eye. The latter consists of topically applying atropine to the non-amblyopic eye, blurring the vision, while also promoting stimulus fixation with the amblyopic eye.[6]

Articles directly comparing occlusion and atropine are scarce. The present work, structured according to the PRISMA Statement,[7] aims to review the common features and the most significant discrepancies between both treatments, focusing only on children up to 18 years of age. The treatments are compared in terms of the reported VA improvements. Other factors contributing to the reported outcomes are also taken into account, notably the age of the patients, the durations of the treatments in weeks and their frequencies.

MATERIAL AND METHODS

The protocol used for this systematic review was the PRISMA 2009 checklist,[7] which is available at www.prisma-statement.org. Studies reporting amblyopia treatments in human subjects were identified by searching the electronic database PubMed.[8] This search was run between September 2013 and July 2014. Other relevant records were retrieved by hand-searching the bibliographies of the articles meeting the inclusion criteria and contacting authors so that they could provide their publications. The following search string was used to identify full-text articles within the PubMed database: "amblyopia and (occlusion OR atropine) treatment". The subsequent filters were applied: human species, full-text article, English language and age up to 18 years. Only articles written in English reporting the visual accuracy improvement in children up to 18 years of age without any other stated medical condition (besides the aforementioned neuro-ophthalmic disorder) were considered.

To be included in the review, a study had to meet the following criteria besides those stated above: 1) it reported new results (case studies excluded); 2) it presents a measure of visual acuity improvement in Snellen, LogMAR or decimal chart; 3) the patients had not been subjected to prior treatments for amblyopia.

A preliminary screening from all articles was performed on the basis of their abstracts. Records retrieved on PubMed that did not meet the inclusion criteria were excluded. Afterwards the full texts of the remaining papers were thoroughly examined by a single observer, again taking the inclusion criteria into account.

The studies in the articles deemed eligible after this final stage of assessment were screened and the relevant information was inserted in an extraction sheet. The extraction sheet was pilot-tested on the first 15 articles that met inclusion criteria and then redefined to optimize

the data extraction for each item. The main outcome measure sought in the studies was the improvement in visual accuracy due to treatment. Additionally, the following topics were recorded for each eligible study: whether the treatment performed was occlusion or atropine; sample size; ages of the subjects; hours of occlusion a day or days of atropine per week; treatment duration; visual acuity before and after treatment in the amblyopic eye; and the visual acuity scale in which results are reported. The VA measures reported were converted to the LogMAR chart. This chart is often recommended for research settings.[9] A visual acuity conversion table can be found in **Appendix I**.

A meta-analysis was conducted where each variable was described in terms of frequencies or summary statistics and the normality of quantitative variables was assessed using Kolmogorov-Smirnov tests. A comparison between the visual acuity improvements reported in occlusion and atropine studies was performed resorting to a Mann-Whitney test. The same test was used to compare improvements of patients who underwent treatment of atropine 2 days per week and 7 days per week. Correlations between improvements and measures of frequency or duration of treatments were assessed with Spearman's rank correlation coefficients. All statistical analyses were performed using SPSS version 21, taking the number of patients into account and assuming a 0.05 level of significance.

RESULTS

A total of 46 studies in 28 articles meeting the inclusion criteria and the relevant features were recorded on an extraction table, see **Appendix II**. The process of identification and selection of the articles is as described above and illustrated in **Figure 1**. Initially, searching the PubMed database for the predefined search terms retrieved a total of 493 records. The corresponding abstracts were reviewed and 342 were discarded taking the eligibility criteria into account. Five out of the remaining 151 articles were duplicates. After removing these, 118 papers were further rejected after an analysis of their full text revealed the eligibility criteria not being met. A total of 46 studies included in the eligible 28 articles were then included in the qualitative and quantitative analysis presented below.

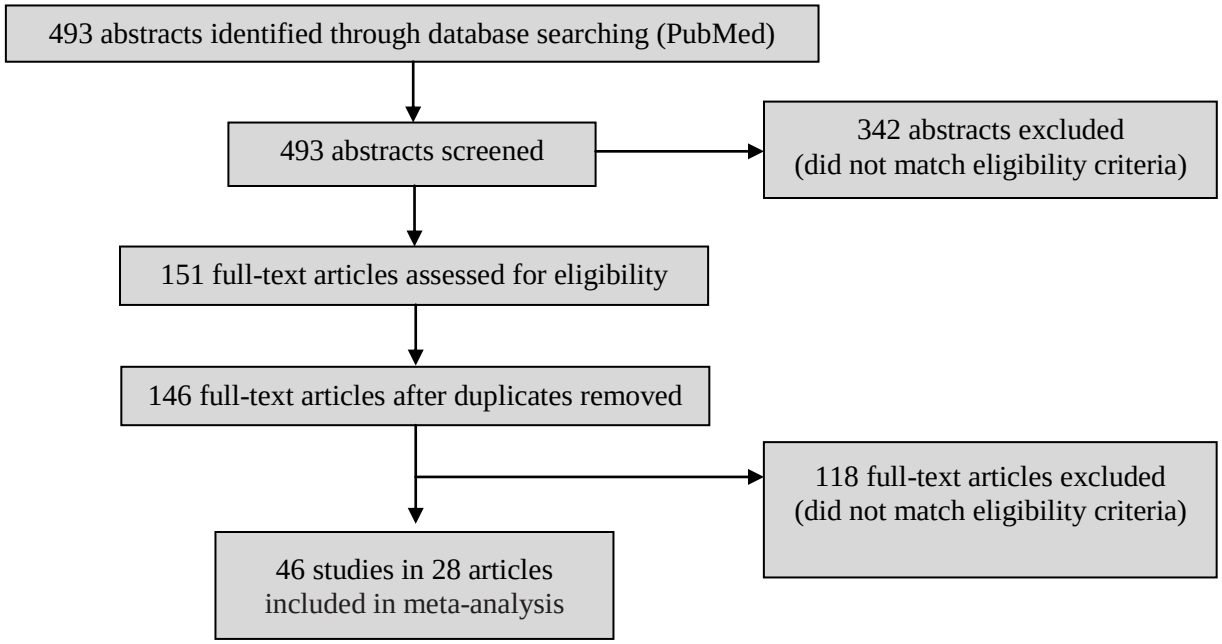

FIGURE 1. Flow chart diagram of the study selection process.

Out of the 46 studies, 30 report performing occlusion and 16 atropine. However, studies assessing the latter typically include a larger number of participants: the total number of subjects in studies of occlusion and atropine is 1127 and 933, respectively. In occlusion studies the average number of participants is 37.6, with the median being 27, the minimum 7 and the maximum 104. In atropine studies the average is 58.3, the median 57.5, the minimum 8 and the maximum 103. In what follows, we start by describing the studies in terms of the age of participants, the frequency and duration of treatment and the visual acuity improvements achieved.

The ages of the subjects of the occlusion and atropine studies ranged from 2 to 18 and from 1 to 12 respectively, averaging 7.09 and 5.93, see **Figure 2**.

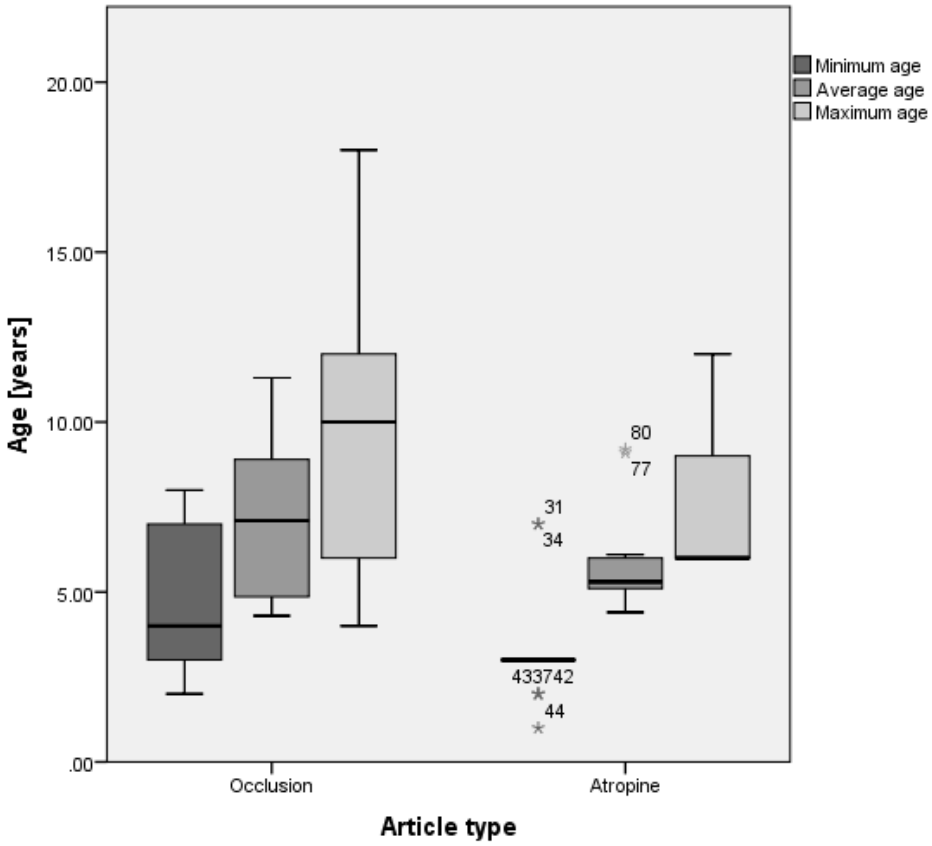

FIGURE 2. Minimum, average and maximum ages reported in occlusion and atropine studies.

A total of 6 occlusion studies state having assessed "full time occlusion" or "24 hours occlusion". These were excluded from analyses where this variable comes into play, as they do not state a quantitative measure of effective treatment duration comparable with the remaining articles. Out of the remaining studies, 16 report the number of hours of occlusion. On average, patients underwent occlusion treatment 4.71 hours, the minimum hours of treatment being 0.5 hours, the maximum 7 hours and the median 6 hours. In turn, 7 atropine studies performed treatment daily and 8 twice a week (in separate days or over the weekend). The total number of people who had 2 days of treatment per week was 477, while the total number of people with daily treatment was 383. One atropine study, which mentions one to two weeks per month as the frequency of treatment, was excluded from analyses where the atropine treatment frequency is a variable.

One occlusion study did not report the number of weeks during which the treatment took place. For the patients of the remaining 29 occlusion studies, the average treatment duration was 43.5 weeks, the median being 26, the minimum 7 and the maximum 325. Patients underwent atropine treatment for an average of 24.6 weeks, the median being 18, the minimum 10 and the maximum 73. The occlusion study reporting the treatment lasting 325 weeks was excluded from analyses where the treatment duration is taken as a variable, as it lasted much longer than all other studies. Indeed, the maximum duration of occlusion studies after exclusion of the aforementioned study is 52 weeks.

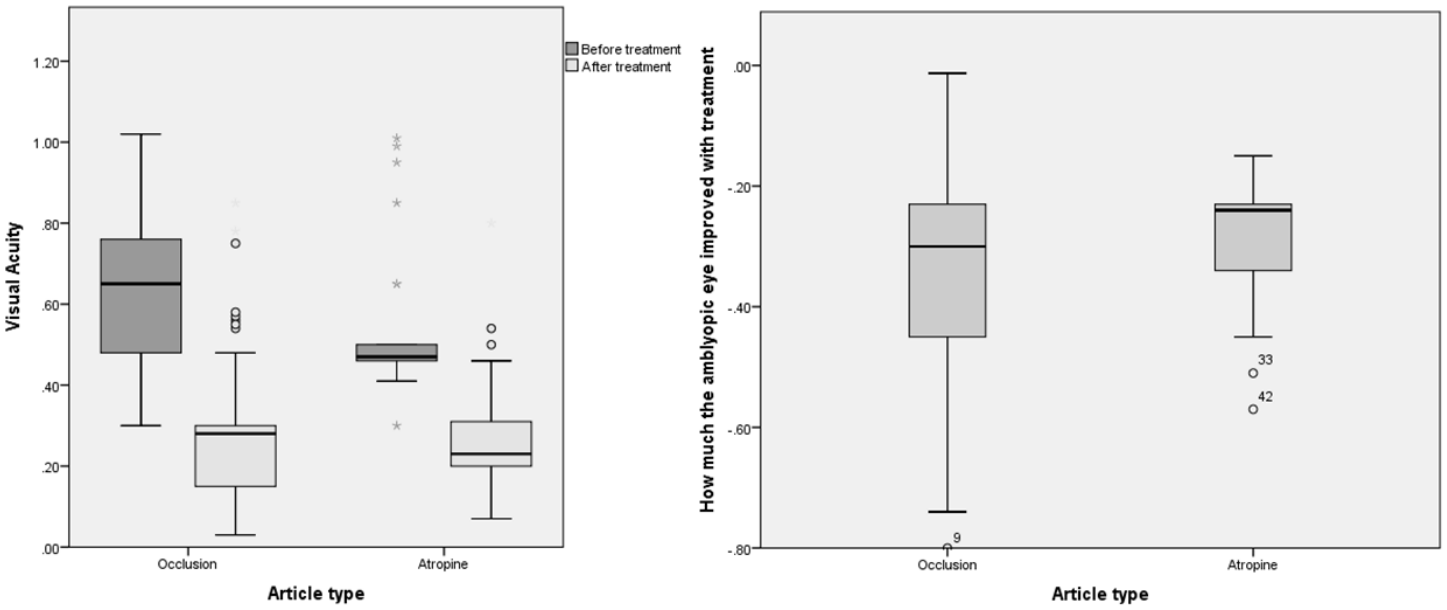

FIGURE 3. (left) Visual acuity measured before and after treatments, in LogMAR; (right) Visual acuity improvement for occlusion and atropine patients, in LogMAR.

The main outcome measure considered in this meta-analysis is the improvement of the visual acuity of participants in the amblyopic eye. It is represented by negative values as, when using the LogMAR chart, lower values mean better visual acuity. The VA measures in occlusion and atropine studies are displayed in **Figure 3** and **Table 1**.

Table 1. Mean, median, minimum and maximum of the visual acuity measures and improvement reported for patients in occlusion and atropine studies.

Treatment type \ Visual acuity		Mean	Median	Minimum	Maximum
Occlusion	before treatment	0.63	0.65	0.30	1.02
	after treatment	0.29	0.28	0.03	0.85
	improvement with treatment	-0.34	-0.30	-0.80	-0.01
Atropine	before treatment	0.54	0.47	0.30	1.01
	after treatment	0.26	0.23	0.07	0.80
	improvement with treatment	-0.28	-0.24	-0.57	-0.15

Both techniques ensured VA improvements. There is a statistically significant difference in improvements between atropine and occlusion treatments, assessed by a Mann-Whitney test ($Z = -10201$, $p < 0.001$).

Several factors may affect the outcome of a treatment for amblyopia, notably its frequency and duration and the age of the patients. In particular, we start by assessing whether the improvement of occlusion treatments is associated to the hours of occlusion and the duration of the treatment in weeks. For this analysis, it is important to recall that we exclude the article that performed a much longer treatment duration (325 weeks), which reports an improvement in visual acuity of -0.34. As for the other articles, one may expect the total number of hours of treatment to correspond to a bigger improvement in acuity. Indeed, a strong correlation[10] was found between the total hours of treatment and acuity improvement in the amblyopic eye (Spearman test, $\rho=-0.697$, $p<0.001$), see **Figure 4**.

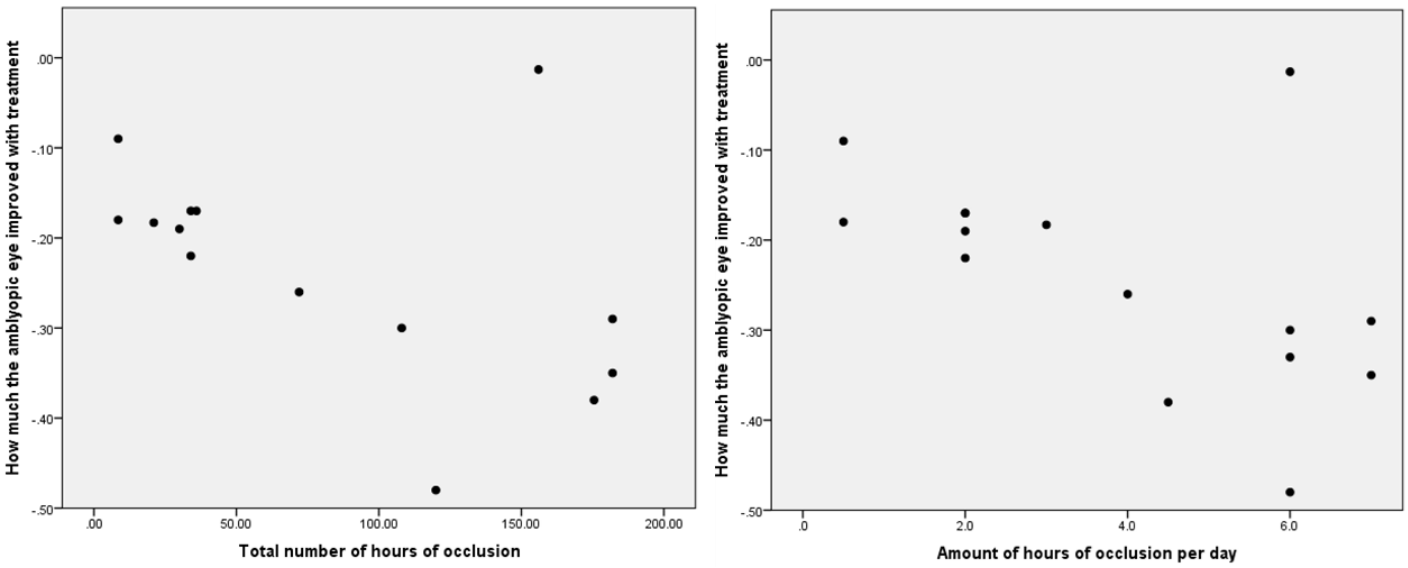

FIGURE 4. (left) Improvement of visual acuity in amblyopic eyes and total number of hours of occlusion, in LogMAR; (right) Improvement of visual acuity in amblyopic eyes and the amount of hours of occlusion per day, in LogMAR.

Similarly, the improvement in acuity increases as the number of hours of occlusion per day in subjects grows, also illustrated in **Figure 4**. The correlation between the improvement and the number of hours per day is strong (ρ=-0.652, $p<0.001$). One article performing six hours of occlusion a day displayed a visual acuity improvement that seems not to be aligned with the remaining results (-0,013).[11] Finally, the improvement in acuity also seems to increase as the number of weeks of treatment of occlusion grows, as a strong correlation was found (ρ=-0.607, $p<0.001$).

Likewise to the analysis above, we looked at how the number of days of treatment per week, the treatment duration in weeks and the total amount of days that the treatment was

administered affect the outcome of atropine studies. The correlation between the improvement of atropine patients and the latter was found to be significant but rather weak (ρ=-0.272, $p<0.001$), see **Figure 5**. However, note that there is no great variability in the total amount of days of treatment reported in the different studies.

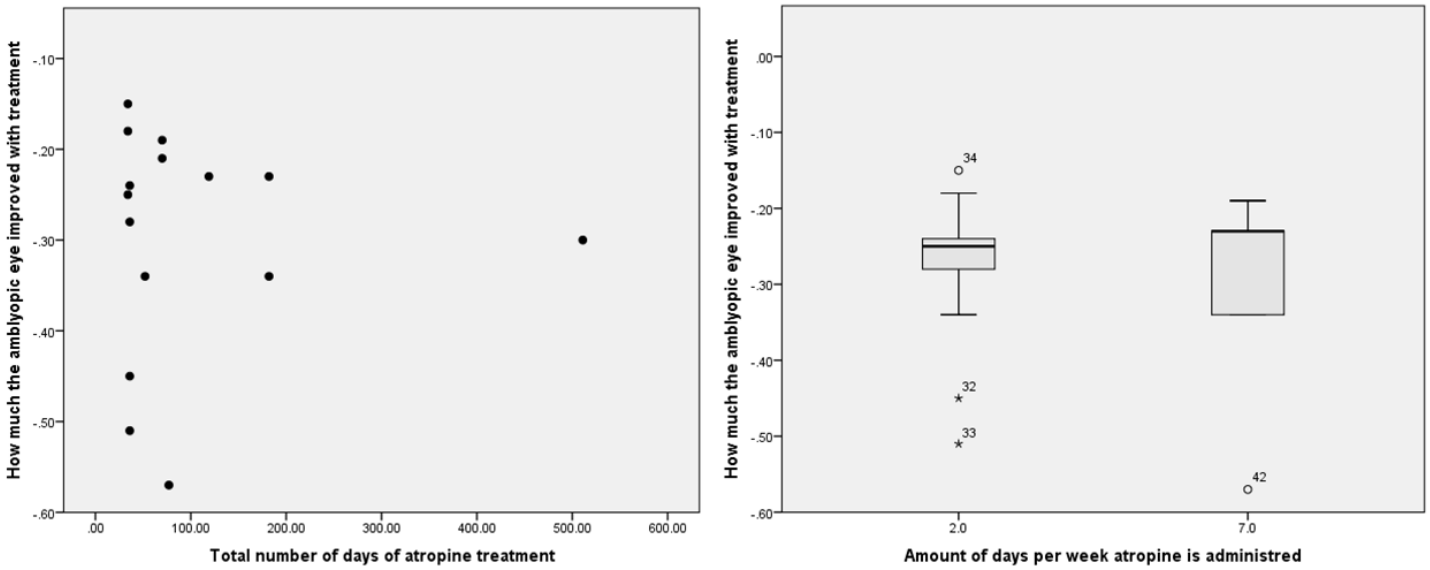

FIGURE 5. (left) Improvement of visual acuity in amblyopic eyes and total number of days that that atropine was administered, in LogMAR; (right) Improvement of visual acuity in amblyopic eyes and the number of days per week that the treatment was administered, in LogMAR.

When instead we look at the amount of days per week the treatment is administered, statistically significant differences were found (Mann-Whitney, Z = -2004, p = 0.045). However, the differences in improvements between subjects undergoing 7 days of atropine per week and those undergoing a 2 day per week treatment were not very pronounced, see again **Figure 5**. Indeed, those who made 2 days of atropine per week had an average improvement of visual

acuity of -0.27, a median of -0.25, minimum and maximum of -0.51 and -0.15 points, respectively, whilst in the case of those who made 7 days of treatment the average was -0.30, median -0.23, minimum -0.57 and maximum -0.19 points. Finally, it is hard to discern a pattern when the improvement in acuity is taken as a function of the number of weeks of atropine treatment. The correlation between the improvement and the number of weeks is statistically significant but very weak (ρ=-0.112, p=0.001).

Finally, we look at how the age of patients influences the outcomes of the treatments. Significant correlations have been found, both for occlusion and atropine treatments, between the acuity improvements observed and the ages of participants (respectively, a moderate correlation with ρ=-0.425, p<0.001 and a strong correlation with ρ=-0.727, p<0.001), see **Figure 6**.

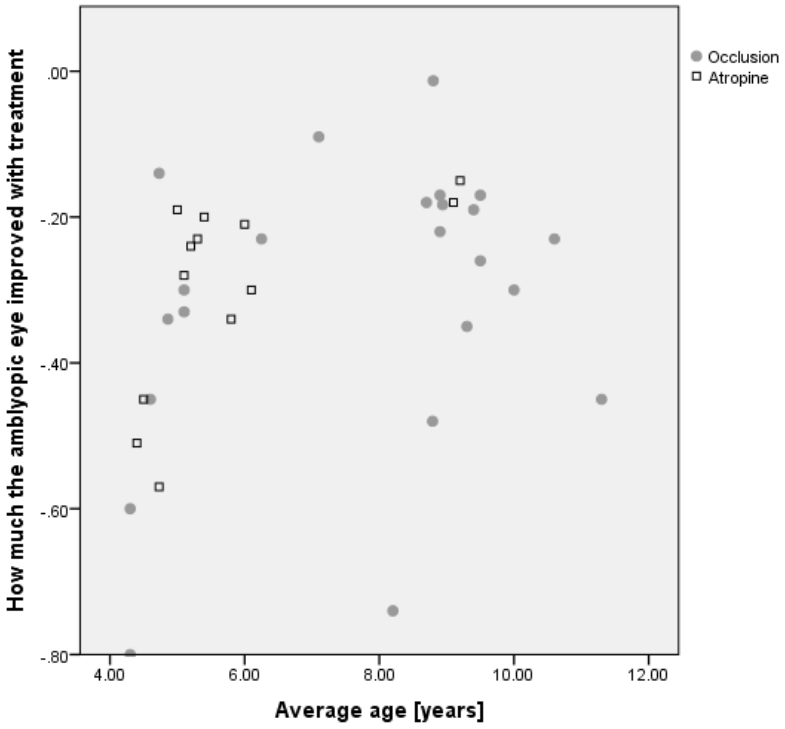

FIGURE 6. Improvement of visual acuity in the amblyopic eye and average age, in LogMAR. Occlusion studies are represented by grey dots and atropine studies by squares.

A global visualisation of the improvements reported in each study in terms of the treatment duration in weeks is displayed in **Figure 7**. In the figure, black dots correspond to occlusion studies where the average age of participants was reported to be below or equal to 6, grey squares to occlusion studies where the average age of participants was reported to be above 6, red dots to atropine studies where the average age of participants was reported to be below or equal to 6 and orange squares to atropine studies where the average age of participants was reported to be above 6.

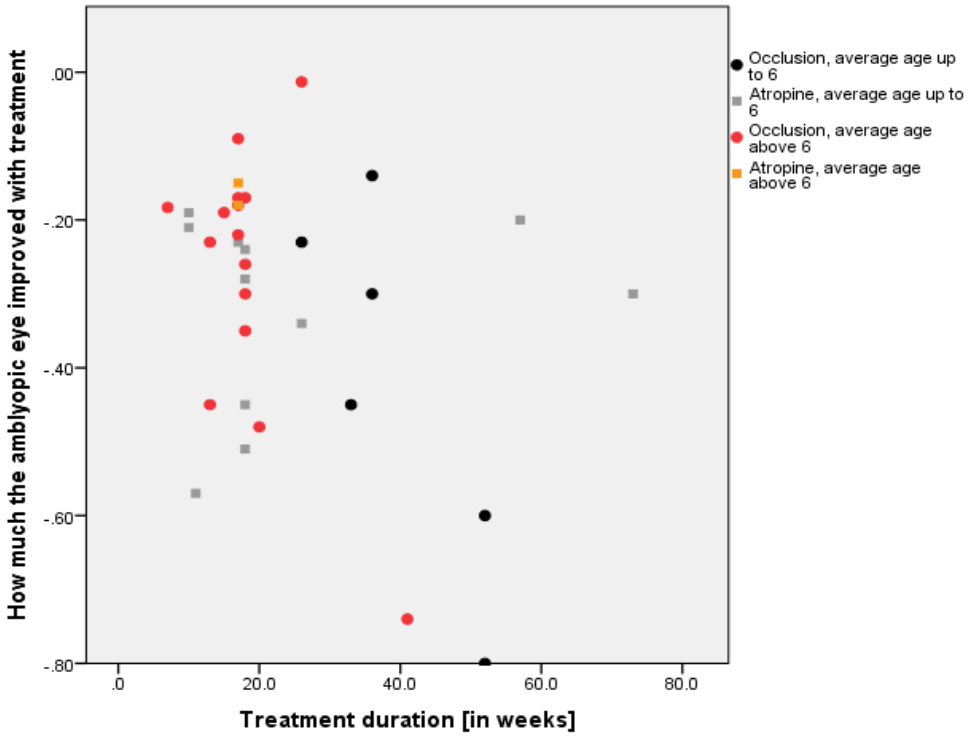

FIGURE 7. Improvement of visual acuity in the amblyopic eye and treatment duration in weeks, in LogMAR.

Older children often appear to do less time of treatment. This is a sort of bias that future studies should address. It is noted that the 3 cases of major improvements are related to children who undergone occlusion treatment for 40 or more weeks. Two out of these three studies reporting the best results included younger children (with average age up to 6 years). The 3 worst results were also obtained by occlusion studies. All of them reported performing treatment for less than 40 weeks and two of them included older children (average age above 6).

DISCUSSION AND CONCLUSIONS

The present review combines data across studies in order to compare the performances of atropine and occlusion treatments for amblyopia. Though both treatments have long been available for ophthalmologists and consequently their patients, to the best of our knowledge no systematic review addressing what technique guarantees better results had previously been reported.

Studies which assessed visual acuity before and after treatment were included in the review. The main outcome measure considered was the visual acuity improvement. A significant statistical difference was found between occlusion and atropine, the absolute mean value of improvement of visual acuity being 0.34 and 0.28, respectively and in LogMAR. However, it is not possible to assert the superiority of occlusion as a form of treatment. Though indeed the best results were achieved by patients prescribed the former, the same holds true for the studies presenting the worst results, as displayed both in the right-hand side of **Figure 3** and on **Figure 7**. In that sense, atropine studies results are more consistent, though the improvement is in average not as great. Some factors may be taken into account when comparing occlusion and

atropine studies. In particular, the range of ages of children participating in the former is wider. Occlusion patients presented worse baseline VA measures before treatment. The frequency and duration of treatments varied greatly between studies. The adherence to either treatment, which may depend on family support, is hard to measure and is seldom addressed in articles. Particularly for occlusion, the social stigma of having an eye covered may interfere with the compliance of patients. Currently some articles focus solely on measuring compliance. [12, 13, 14]

Occlusion patients had higher benefits when the duration of the therapy lasted more weeks. Additionally, the improvements were shown to increase with the total number of hours of treatment as well as the number of daily hours of treatment, with strong correlations being found. One article stands out on the top right of both plots of **Figure 4** as its performance is not in line with other articles with the same number of daily hours of treatment.[11] The author mentions that in this study, which includes 17 patients, signals generated by the non-amblyopic eye of patients were a possible negative influence on those of the amblyopic eye, hindering success.

Whereas the improvements in occlusion were strongly correlated with the total amount of weeks of treatment, the correlation is very weak for atropine patients. Additionally, the correlation with the total number of days of treatment is weak. Finally, a statistical difference between administering atropine twice weekly or everyday exists, favouring the latter, but it is clinically not pronounced. As such, it is not clear whether administering atropine for a greater number of days always improves effectiveness of treatment.

This review assessed whether the average age of the children influenced the outcomes of the treatments. Early detection and introduction to therapy are thought to be critical to the success of the recovery of the amblyopic eye.[2] Indeed, correlations between improvement of VA and the

mean age of patients were found both for occlusion and atropine studies. The former was moderate and the latter strong. Treating patients as early as possible seems to be more effective, and indeed some authors propose the existence of a period of neuronal plasticity including younger children.[15, 16] However, improvements – though differing in magnitude - were reported on all articles reviewed despite of patient's average age. Moreover, articles are available in the literature focusing on treating amblyopia on older patients.[16, 17]

Finally, on the basis of these findings, there are potential directions for future research that could help to fill knowledge gaps. As a starting point, more research is needed to provide a better understanding of the causal pathways through which interventions for amblyopia work. Also, the effect of the treatments in adults has yet to be assessed systematically, though the literature on this subject is still scarce.

DECLARATION OF INTEREST

The authors declare no conflicts of interest.

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APPENDIX

I. Visual Acuity Conversion Table, by Pediatric Eyes Portal. Available from: http://pedseyes.org/Peds_Eyes/Home.html

20 ft	6 m	Decimal	4 m	Log MAR
20 / 630	6 / 190	0.032	4 / 125	+1.5
20 / 500	6 / 150	0.04	4 / 100	+1.4
20 / 400	6 / 120	0.05	4 / 80	+1.3
20 / 320	6 / 95	0.06	4 / 63	+1.2
20 / 250	6 / 75	0.08	4 / 50	+1.1
20 / 200	6 / 60	0.1	4 / 40	+1.0
20 / 160	6 / 48	0.125	4 / 32	+0.9
20 / 125	6 / 38	0.16	4 / 25	+0.8
20 / 100	6 / 30	0.2	4 / 20	+0.7
20 / 80	6 / 24	0.25	4 / 16	+0.6
20 / 63	6 / 19	0.32	4 / 12.5	+0.5
20 / 50	6 / 15	0.4	4 / 10	+0.4
20 / 40	6 / 12	0.5	4 / 8	+0.3
20 / 32	6 / 9.5	0.63	4 / 6.3	+0.2
20 / 25	6 / 7.5	0.8	4 / 5	+0.1
20 / 20	6 / 6	1.0	4 / 4	0
20 / 16	6 / 4.8	1.25	4 / 3.2	-0.1
20 / 12.5	6 / 3.8	1.6	4 / 2.5	-0.2
20 / 10	6 / 3	2.0	4 / 2	-0.3

II. Data collection sheet

Table II.1 - Data collected from articles.

article_type	id	n	age_average	age_sd	age_minimum	age_maximum	daily_occlusion_hours	number_days_per_week_atropine	treatment_duration	pre_treatment_acuity_amblyopic	post_treatment_acuity_amblyopic	amlyopic_eye_improvement	whether_results_were_in_Snellen_scale	whether_results_were_in_Logmar_scale	whether_results_were_in_another_scale
1	O1	17	8.8	1.2	6	10	6		26	0.3	0.287	-0.013	0	1	0
1	O2	98	8.9	1.5	7	12	2		17	0.5	0.28	-0.22	0	1	1
1	O3	25	8.9	1.7	7	12	2		18	0.65	0.48	-0.17	0	1	0
1	O3	25	9.5	2.1	7	12	4		18	0.8	0.54	-0.26	0	1	0
1	O3	25	10	1.8	7	12	6		18	0.68	0.38	-0.3	0	1	0
1	O3	25	9.3	2.1	7	12	23.5		18	0.76	0.41	-0.35	0	1	0
1	O4	58	4.86	1.62			6		325	0.54	0.2	-0.34	0	1	0
1	O6	18	4.3		4.1	5.2			52	0.7	0.1	-0.6	0	1	0
1	O6	20	4.3		4.1	4.6			52	0.9	0.1	-0.8	0	1	0
1	O7	18	9.5	1.5			2		17	0.95	0.78	-0.17	1	1	0
1	O8	69	5.1	1.5			6			0.48	0.15	-0.33	0	1	0
1	O9	29	8.79	0.98	8	12	6		20	0.51	0.03	-0.48	0	1	0
1	O10	64			4	13			39	0.76	0.28	-0.48	0	1	0
1	O10	29			4	13	4.5		39	0.7	0.32	-0.38	0	1	0
1	O10	7			4	13			39	0.74	0.29	-0.45	0	1	0
1	O11	35	6.25	2.11	2	9			26	0.44	0.21	-0.23	1	1	0
1	O13	61	5.1		3.5	8			36	0.4	0.1	-0.3	0	0	1
1	O14	52			3	6	7		26	0.65	0.3	-0.35	0	1	0
1	O14	39			3	6			26	0.66	0.27	-0.39	0	1	0
1	O14	104			3	6	7		26	0.43	0.14	-0.29	0	1	0
1	O14	20			3	6			26	0.45	0.2	-0.25	0	1	0
1	O16	21	10.6	2.5	6	18	24		13	0.79	0.56	-0.23	0	1	0
1	O16	19	11.3	3,9	6	18	24		13	1.02	0.57	-0.45	0	1	0
1	O17	42	4.73	1.12	2.75	6.5	24		36	0.99	0.85	-0.14	0	1	0
1	O18	98	4.6		3.5	9	24		33	0.75	0.3	-0.45	0	0	1
1	O20	36	8.2		7	10.3	24		41	-0.83	-0.09	0.74	0	1	0
1	O21	13	8.94	1.81	7	12	3		7	0.763	0.58	-0.183	0	1	0
1	O23	45	9.4	1.9	7	12	2		15	0.49	0.3	-0.19	1	1	0
1	O24	7	8.7	3.5	5	15	0.5		17	0.73	0.55	-0.18	0	1	0
1	O24	8	7.1	1.9	4	10	0.5		17	0.84	0.75	-0.09	0	1	0
2	A1	95	9.1	1.6	7	12		2	17	0.5	0.32	-0.18	0	1	1
2	A2	26	4.5	0.9	3	6		2	18	0.99	0.54	-0.45	1	1	0
2	A2	34	4.4	0.1	3	6		2	18	1.01	0.5	-0.51	1	1	0
2	A2	22	9.2	1.8	7	12		2	17	0.95	0.8	-0.15	1	1	0
2	A3	90	5.2	1.1	3	6		2	18	0.47	0.23	-0.24	1	1	0
2	A3	90	5.1	1	3	6		2	18	0.5	0.22	-0.28	1	1	0
2	A4	35	5.8	2.12	2	9		2	26	0.41	0.07	-0.34	1	1	0
2	A5	83	5.3	1.1		6		7	17	0.46	0.23	-0.23	1	1	0
2	A5	85		1.1		6		2	17	0.46	0.21	-0.25	1	1	0
2	A6	101			3	6		7	26	0.65	0.31	-0.34	0	1	0
2	A6	103			3	6		7	26	0.41	0.18	-0.23	0	1	0
2	A7	42	4.73	1.12	2	6		7	11	0.85	0.28	-0.57	0	1	0
2	A9	38	6.1		2	11		7	73	0.5	0.2	-0.3	1	1	0
2	A9	73	5.4		1	12			57	0.3	0.1	-0.2	1	1	0
2	A10	8	6		3	8		7	10	0.41	0.2	-0.21	0	1	0
2	A10	8	5		3	8		7	10	0.65	0.46	-0.19	0	1	0

Table II.2 - Codes for the variables extracted from articles.

Variables	Description
article_type	1=occlusion, 2=atropine
id	Article identification code
n	number of subjects in the study
age_average	Average of ages of subjects
age_sd	Standard deviation of ages of subjects
age minimum	Minimum age of subjects
age maximum	Maximum age of subjects
daily_occlusion_hours	Amount of hours of occlusion per day
number_days_per_week_atropine	Amount of days per week atropine is administred
treatment_duration	Treatment duration in weeks
pre_treatment_acuity_amblyopic	Visual acuity of the amblyopic eye, before treatment - LogMAR scale
post_treatment_acuity_amblyopic	Visual acuity of the amblyopic eye, after treatment - LogMAR scale
nonambyopic_eye_improvement	How much the nonamblyopic eye improved with treatment - LogMAR scale
ambyopic_eye_improvement	How much the amblyopic eye improved with treatment
whether_results_were_in_Snellen_scale	Whether the article reported visual acuity using the Snellen scale. 1=yes, 0=no
whether_results_were_in_Logmar_scale	Whether the article reported visual acuity using the Logmar scale. 1=yes, 0=no
whether_results_were_in_another_scale	Whether the article reported visual acuity using another scale. 1=yes, 0=no

Table II.3 – Study identification.

Code	Article Title	First Author	Publication year
O1	Visual Functions and Interocular Interactions in Anisometropic Children with and without Amblyopia	Xin Jie Lai	2011
O2	Patching vs Atropine to Treat Amblyopia in Children Aged 7 to 12 Years: A Randomized Trial	Scheiman MM	2008
O3	Part-time occlusion therapy for amblyopia in older children	Inderpreet Singh, MD	2008
O4	Outcomes of 6 Hour Part-time Occlusion Treatment Combined with Near Activities for Unilateral Amblyopia	Kyoung Soo Park, MD	2008
O6	Randomized Evaluation of Spectacles Plus Alternate-Day Occlusion to Treat Amblyopia	Pia Agervi, MD	2009
O7	Treatment of severe amblyopia with weekend atropine: results from 2 randomized clinical trials	Michael X. Repka, MD	2009
O8	The effect of amblyopia treatment on stereoacuity	Catherine E. Stewart	2013
O9	Part-Time Occlusion Therapy for Anisometropic Amblyopia Detected in Children Eight Years of Age and Older	Young Rok Lee	2006
O10	The results of treatment of anisomyopic and anisohypermetropic amblyopia	Chekitaan B.	2009
O11	Comparative Efficacy of Penalization Methods in Moderate to Mild Amblyopia	JAIME TEJEDOR	2008
O13	The Relationship between Stereopsis and Visual Acuity after Occlusion Therapy for Amblyopia	Se Youp Lee	2003
O14	A Comparison of Atropine and Patching Treatments for Moderate Amblyopia by Patient Age, Cause of Amblyopia, Depth of Amblyopia, and Other Factors	Michael X. Repka	2003
O16	Levodopa-Carbidopa With Occlusion in Older Children With Amblyopia	Prashant Bhartiya	2002
O17	Combined Optical and Atropine Penalization for the Treatment of Strabismic and Anisometropic Amblyopia	Stephen B. Kaye	2002
O18	Against-The-Rule (ATR) Astigmatism as a Predicting Factor for the Outcome of Amblyopia Treatment	DENIZ SOMER	2002
O20	Successful Amblyopia Therapy Initiated After Age 7 Years	Helen A. Mintz-Hittner	2000
O21	Occlusion and Levodopa-Carbidopa Treatment for Childhood Amblyopia	Lawrence E. Leguire	1998
O23	Randomized Controlled Trial of Patching vs Acupuncture for Anisometropic Amblyopia in Children Aged 7 to 12 Years	Jianhao Zhao	2010
O24	Effectiveness of Telescopic Magnification in the Treatment of Amblyopia	Johnny Wu	2010
A1	Patching vs Atropine to Treat Amblyopia in Children Aged 7 to 12 Years: A Randomized Trial	Scheiman MM	2008
A2	Treatment of severe amblyopia with weekend atropine: results from 2 randomized clinical trials	Michael X. Repka, MD	2009
A3	Pharmacologic Plus Optical Penalization Treatment for Amblyopia: Results of a Randomized Trial	Susan A. Cotter OD	2009
A4	Comparative Efficacy of Penalization Methods in Moderate to Mild Amblyopia	JAIME TEJEDOR	2008
A5	A Randomized Trial of Atropine Regimens for Treatment of Moderate Amblyopia in Children	Michael X. Repka	2004
A6	A Comparison of Atropine and Patching Treatments for Moderate Amblyopia by Patient Age, Cause of Amblyopia, Depth of Amblyopia, and Other Factors	Michael X. Repka	2003
A6			
A7	Combined Optical and Atropine Penalization for the Treatment of Strabismic and Anisometropic Amblyopia	Stephen B. Kaye	2002
A9	Full-time Atropine, Intermittent Atropine, and Optical Penalization and Binocular Outcome in Treatment of Strabismic Amblyopia	Kurt Simons	1997
A10	Atropine Treatment of Amblyopia: Is a Swap in Fixation Necessary?	Josephine Leone	2010

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