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Review Article

The challenges of amblyopia treatment

*Gail D.E. Maconachie, Irene Gottlob**

Ulverscroft Eye Unit, Department of Neuroscience, Psychology and Behaviour, University of Leicester, RKSCB, Leicester Royal Infirmary, Leicester LE2 7LX, UK

Dr. Irene Gottlob

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ABSTRACT

The treatment of amblyopia, particularly anisometropic (difference in refractive correction) and/or strabismic (turn of one eye) amblyopia has long been a challenge for many clinicians. Achieving optimum outcomes, where the amblyopic eye reaches a visual acuity similar to the fellow eye, is often impossible in many patients. Part of this challenge has resulted from a previous lack of scientific evidence for amblyopia treatment that was highlight by a systematic review by Snowdon et al. in 1998. Since this review, a number of publications have revealed new findings in the treatment of amblyopia. This includes the finding that less intensive occlusion treatments can be successful in treating amblyopia. A relationship between adherence to treatment and visual acuity has also been established and has been shown to be influenced by the use of intervention material. In addition, there is growing evidence of that a period of glasses wearing only can significantly improve visual acuity alone without any other modes of treatment. This review article reports findings since the Snowdon's report.

Unilateral amblyopia is a loss in visual function in one eye in comparison to the other and is often caused by other associated factors that force the visual system to prefer one eye over another [1]. The most common of these factors is a difference in refractive error between the two eyes, usually in spherical correction (anisometropic amblyopia) and/or a strabismus (strabismic amblyopia). Many other forms of unilateral amblyopia occur as a result of pathological changes in the structure in or around the eye such as unilateral cataracts or ptosis (stimulus deprivation amblyopia). A challenge in the treatment of amblyopia is that there is often no apparent structural reason why there is a limitation of vision and yet many amblyopes, after several years of amblyopia treatment, fail to reach successful outcomes.

Since as early as the 1st century AD [2] covering of the dominant eye to increase visual acuity in the amblyopic eye, now referred to as occlusion therapy, has been suggested as the standard form of treatment in anisometropic and strabismus amblyopia. However, it was not until the Snowdon's report [3] in 1998 that it became apparent that evidence-based

* *Corresponding author*. Ophthalmology Group, University of Leicester, RKSCB, Leicester Royal Infirmary, Leicester LE2 7LX, UK. Tel.: +44 (0) 116 258 6291; fax: +44 (0) 116 255 8810.
E-mail address: Ig15@le.ac.uk (I. Gottlob).

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research about treatment modalities in amblyopia was lacking. As a result of these findings, there has been a significant increase in publications of randomized controlled studies in amblyopia. This review will explore the new findings since this report and discuss future areas of interest for amblyopia treatment.

Refractive therapy

In children with amblyopia, in particular when a strabismus is present, it is recommended that full refractive correction should be prescribed [4]. However, there is some confliction within literature with regards prescribing full prescription due to its possible effects on emmetropization. In a study by Atkinson et al. [5] they found that those who were prescribed a partial correction in comparison to those who were prescribed no refractive correction the process of emmetropization was the same. In contrast, a randomized control trial (RCT) study by Ingram et al. ($n = 287$) [6], showed that those who were prescribed full correction from the age of 6 months and had good adherence to glasses wear, the effect on emmetropization was significantly delayed in comparison to those who were poor compliers or were not prescribed any refractive correction. Further investigation regarding the amount of hyperopia that affects emmetropization is still required.

In 2002, Moseley et al. [7] reported the results of 13 anisometropic and strabsimic amblyopes who were prescribed refractive correction only, they showed for the first time that amblyopic subjects can gain significant improvements in visual outcome with refractive correction alone. In a later study [8], 14 of 65 amblyopic subjects (interocular difference in visual acuity of >0.1) had a resolution of their amblyopia with glasses alone, and no further treatment was required. The mean improvement in visual acuity for the 65 patients was 0.18 LogMAR with the majority of cases achieving maximum improvement within the first 18 weeks of wearing refractive correction. There was no significant difference in the level of improvement between different types of amblyopia, (anisometropic, strabismic or strabismus with anisometropia) $p = 0.29$. However, a recent survey of orthoptists reported 94% prescribe a period of refractive correction before implementing further treatment, although this is lower for strabismic (75%) or strabismic and anisometropic amblyopia (79%) [9]. This period of refractive correction is also commonly referred to as refractive adaptation or refractive treatment [8]. Limitations of this study include no randomized control group and the inclusion of patients with an intraocular difference of 0.1 which is not often described as amblyopia.

Since this study, a number of additional studies have confirmed that this period of refractive treatment does occur in anisometropic and/or strabismic amblyopes [10–12]. It has been also reported to have a greater effect in those with better baseline stereopsis, milder forms of anisometropic amblyopia and those with a worse baseline visual acuity in strabismus with anisometropia and strabismic patients. The least likely type of amblyopia to respond to refractive adaption has been reported to occur in strabismus with anisometropia amblyopia. There is also a wide variance in the length of time required to achieve the maximum outcome of refractive adaptation [12]. One of the possible factors is the influence of adherence to glasses wear. An unpublished pilot study including 26 patients [13], has revealed variable adherence to glasses wear. It has also shown a strong dose–response relationship between adherence and visual outcome ($r = 0.76$, $p = 0.0001$). Further work in this area with a larger cohort is needed to explore the relationships between glasses wearing, refractive adaption and visual outcome.

When refractive adaptation is translated into a clinical setting, it has been reported that the recommended 18–22 weeks may, for some patients, delay treatment. Norris et al. [10], recommend that patients should be reassessed at 6 and 14 weeks and if there is no significant improvement they suggest prescribing other forms of treatment. This highlights the need for further research into refractive treatment for example a RCT comparing refractive adaptation and other treatment modalities for amblyopia.

Occlusion

How much?

The use of occlusion therapy is the most well-known and commonly practiced way of treating amblyopia. Until occlusion therapy was prescribed based on clinical experience rather than scientific based evidence. This generated a wide variance between departments on how amblyopic patients were treated clinically [14]. In 1998, the PEDIG [15] sought to review the number of hours prescribed by recruiting, moderate and severe strabismic and anisometropic amblyopes into two groups with the moderate amblyopes receiving either 6 h or 2 h of occlusion, whereas the severe amblyopes received either full time (all or all but 1 h 4/day) or 6 h of occlusion [16,17]. Their results revealed that visual outcomes with more intensive occlusion, 6 h for moderate amblyopes and full time for severe amblyopes, were similar to the lower amount of prescription 2 h and 6 h respectively. In addition, their findings revealed no significant difference between cause of amblyopia and improvement in visual acuity ($p = 0.85$). Guidelines from the American Academy of Ophthalmologist [18] and the Royal College of Ophthalmologist [19] have changed as a result of these findings so that now both advise the use of 6 h for severe amblyopia and 2 h for moderates. Although at present there is still a wide variance in the number of hours of occlusion prescribed by those treating amblyopia.

Adherence to occlusion

There is some concern with basing guidelines on the PEDIG studies because adherence to occlusion therapy is less than optimal. Therefore, the results shown by the PEDIG group have been challenged by the work objectively exploring compliance in amblyopia treatment with the use of occlusion dose monitors (ODMs) [20,21]. In one study, it was shown that patients who were prescribed 6 h or 3 h a day only adhered to half of their prescribed amount, average 2 h 33 min and 1 h 45 min respectively, leading to there being no significant difference in the total amount of occlusion therapy undertaken