Vision Research 114 (2015) 31–40

Contents lists available at ScienceDirect

Vision Research

journal homepage: www.elsevier.com/locate/visres

Compliance and patching and atropine amblyopia treatments ☆

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ARTICLE INFO

Article history:
Received 1 September 2014
Received in revised form 5 February 2015
Available online 2 March 2015

Keywords:
Amblyopia
Compliance
Occlusion
Patching
Atropine penalization
Children

ABSTRACT

In the past 20 years, there has been a great advancement in knowledge pertaining to compliance with amblyopia treatments. The occlusion dose monitor introduced quantitative monitoring methods in patching, which sparked our initial understanding of the dose–response relationship for patching amblyopia treatment. This review focuses on current compliance knowledge and the impact it has on patching and atropine amblyopia treatment.

1. Introduction

Unilateral amblyopia is a visual impairment that is secondary to an abnormal binocular visual experience (e.g., strabismus, anisometropia, form deprivation) during early childhood. Unfortunately, amblyopia cannot be corrected immediately with optical correction alone. Although providing accurate optical correction can treat about 25% of children with amblyopia (Cotter et al., 2012), the dominant approach to amblyopia treatment includes strategies to enhance visual input from the amblyopic eye (relative to the fellow eye). This can only be achieved by interventions that degrade visual input to the fellow eye. Currently, mainstream treatments for unilateral amblyopia are occlusion via patching or atropine penalization of the stronger fellow eye. Both treatments effectively generate significant visual acuity improvement in children if the patient follows the treatment regimens as described below:

(a) Patching treatment regimen: depending on the child's age and the severity of amblyopia, 2–6 h of daily patching is usually prescribed for a few months up to several years. The benefits of these patching regimens have been established for both moderate and severe amblyopia (Holmes, Beck et al., 2003; Holmes, Kraker et al., 2003; Repka et al., 2008; Wallace et al., 2006).

(b) Atropine penalization treatment regimen: Atropine penalization blurs the near vision of the fellow eye with an eye drop. Atropine is often prescribed with a dosage of 2 drops per week to daily (7 drops per week) treatment. Compared to patching, atropine is more manageable for parents and requires less effort from patients (Holmes, Beck et al., 2003). However, in order to achieve the same level of vision improvement associated with 3 months of patching, 6 months of atropine treatment is required (Pediatric-Eye-Disease-Investigator-Group, 2003). Such a result indicates that atropine treatment requires compliance for a longer period.

Both patching and atropine treatments require combined efforts from both children and their parents. Stewart (2005) reported that the occlusion dose is the leading factor for predicting a successful outcome in amblyopic children in agreement with other studies (Awan, Proudlock, & Gottlob, 2005; Loudon et al., 2006; Stewart et al., 2005, 2007b, 2013). Thus, both patching and atropine penalization depend on compliance, i.e., the ratio of actual patching/atropine dosage to the prescribed patching/atropine dosage in a certain treatment duration. The following article will review the current compliance knowledge relating to these two major amblyopia treatments: patching and atropine penalization.

2. Compliance with amblyopia treatments is generally low

Compliance can be classified into subjective compliance and objective compliance. Usually with a calendar log, self-report, or occasionally an interview, subjective compliance has been widely

☆ *Commercial relationship:* The author has no commercial relationship.

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http://dx.doi.org/10.1016/j.visres.2015.02.012
0042-6989/

estimated in both previous patching and atropine treatment studies (Holmes, Kraker et al., 2003; Pediatric-Eye-Disease-Investigator-Group, 2002; Repka et al., 2008). In contrast, objective compliance is usually estimated with a monitoring device. Objective compliance with patching treatments has been estimated in Europe while no such study has been reported for atropine treatment compliance.

2.1. Subjective compliance with patching

Using self-report calendar logs and clinical interviews, the Pediatric Eye Disease Investigator Group (PEDIG) often classifies subjective compliance with the prescribed treatment into four categories: "excellent" (76%–100%), "good" (51%–75%), "fair" (26%–50%) and "poor" (0–25%) (Pediatric-Eye-Disease-Investigator-Group, 2002). Overall, in PEDIG clinical trials, 50–70% of subjective compliance with patching has been reported. (Table 1) In addition, there have been many other studies investigating subjective compliance (Al-Yahya et al., 2012; Al-Zuhaibi et al., 2009; Pang et al., 2012). For instance, Al-Zuhaibi et al. estimated compliance with patching treatments using questionnaires and parent subjective reports; they reported that only 45% of patients had good compliance (Al-Zuhaibi et al., 2009). In a study on myopic anisometropic amblyopia, 41% of patients had excellent compliance and 47% of patients had good compliance (Pang et al., 2012). Note that patients in clinical trials and research studies may comply with the prescribed treatment better than the general population.

2.2. Objective compliance with patching

Objective compliance with patching can be measured with an electronic device, an occlusion dose monitor (ODM), which measures skin conductance with a wire (Fielder et al., 1994, 1995) or temperature with thermistors (Fronius et al., 2006; Simonsz et al., 1999) at the border of the patch. ODM debuted in the early 1990s (Fielder et al., 1994, 1995) and has continued to be improved, refined and miniaturized (Chopovska et al., 2005; Fronius et al., 2006). ODM records and reports occluding activities up to the precise minute, and therefore provides the factual daily occlusion dose (dose rate) and cumulative dose.

With ODM use, objective compliance is often defined as the percentage of hours of actual patching compared to the hours of prescribed patching (Stewart et al., 2007b; Tjiam et al., 2012, 2013). To understand compliance comprehensively, Wallace, Stewart et al. (2013) drew a distinction between the days in which no patching is undertaken (no-patch days) and the days in which at least some patching is undertaken (patch days). Three operational measures of compliance were considered: (1) Compliance: the percentage of actual patching hours to the total prescribed patching hours; (2) Patch day compliance: ignoring no-patch days (days on which no patching was undertaken), the percentage of actual patching hours to the total prescribed dosage in the patching days; (3) Patch day proportion: the percentage of actual patching days to the total prescribed patching days.

According to ODM studies, objective compliance with patching is as low as 44% (Awan, Proudlock, & Gottlob, 2005; Pradeep et al., 2014; Tjiam et al., 2013; Wallace, Stewart et al., 2013) to 57% (Loudon et al., 2006). (Table 2) In addition, objective compliance variation among children was considerable, varying from 0 to 100% (Stewart et al., 2004).

2.2.1. Compliance is dynamic

Compliance variation within a child over time can be considerable (Loudon et al., 2006; Stewart et al., 2004). In addition to generally low compliance with patching, compliance follows a dynamic pattern, as it usually decreases over time. Not surprisingly, in 3- to 8-year-old children, compliance is lower when longer treatments are required (Loudon et al., 2006; Wallace, Stewart et al., 2013). In Fig. 1, the mean compliance decreased from 60% at the beginning to 40% by the 50th day, and to 30% by the 100th day (Wallace, Stewart et al., 2013). Similar significant decreasing patterns of compliance over time were found in older children (7–16 years old) too (Fronius, Bachert, & Luchtenberg, 2009). Interestingly, Loudon et al. reported that the dynamics of compliance might differ with intervention; compliance in their educational cartoon story intervention group decreased less than the reference group after 1 week of the study (Loudon et al., 2006). Compliance also varies by days of the week. For instance, weekends were not good compliance days, compared with weekdays (Wallace, Stewart et al., 2013).

In order to improve compliance, we must not only increase the average compliance, but we must also maintain a higher compliance level and/or reverse the decreasing trend of compliance over time.

2.3. Comparison of subjective and objective compliance with patching

Studies with ODM offer us a chance to compare objective compliance with subjective compliance. For example, diaries detailing patch time were inaccurate, and parents patched more to compensate after missing one or two days ("treatment days") (Simonsz et al., 1999). Subjective compliance is often better matched to the prescribed regimen than to the objective data, with instances of both under and over occlusion (Fielder et al., 1995). These findings emphasize the shortcomings of subjective compliance reporting.

2.4. Subjective compliance with atropine penalization

Generally, atropine penalization was assumed to have a higher rate of compliance for the following reasons: (1) It is easy to manage for parents and less disruptive to the child's daily life than traditional patching. (2) It is associated with lower psychosocial or cosmetic issues. (3) Since the cycloplegic effect of topical atropine

Table 1
Summary of subjective compliance with patching in PEDIG clinical trials (%).

Studies	Groups in paper	Excellent 76–100%	Good 51–75%	Fair 26–50%	Poor 0–25%
PEDIG 2002 (Pediatric-Eye-Disease-Investigator-Group, 2002)	At 6 months	49	34	13	5
PEDIG, 2003 (Pediatric-Eye-Disease-Investigator-Group, 2003)	At 5 weeks	87		13	
	At 16 weeks	82		18	
PEDIG, 2008 (Pediatric-Eye-Disease-Investigator-Group, 2008)	At 17 weeks: distance	72	17	6	6
	At 17 weeks: near	64	20	9	7
PEDIG, 2006 (Wallace et al., 2006)	At 5 weeks: 2-h patching group	68	22	7	2
PEDIG, 2010 (Rutstein et al., 2010)	At 24 weeks: 2-h patching group	82	14	3	1