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Pain in the treatment of vitreoretinal diseases

Jefferson A. S. Ribeiro[1,2], José A. da Silva[3], Bianka Y. N. Y. Katayama[1], and Rodrigo Jorge[1]

1. University of São Paulo, Ribeirão Preto, SP, Brazil
2. University of the State of Amazonas, Manaus, AM, Brazil
3. University of São Paulo, São Paulo, SP, Brazil

Abstract

Treatment of vitreoretinal diseases comprises a range of options that has increased in the past several years, allowing more individuals to benefit from new therapeutic approaches. The use of lasers in the retina, new surgical techniques, and intravitreal drug administration constitute common treatment options. These retinal and vitreal procedures have both benefits and drawbacks. Among the drawbacks is discomfort associated with the procedure, constituting a relevant issue because it can compromise adherence to treatment. We reviewed aspects of pain associated with vitreoretinal procedures and the available options for its control. With regard to vitreoretinal procedures, laser photocoagulation is associated with a higher pain score compared with vitrectomy and intravitreal injection using traditional anesthesia methods, suggesting that laser photocoagulation still needs to be improved with regard to comfort during the procedure. In some cases, a combination of analgesic options may be the best choice for pain-sensitive individuals. Individual differences and the specific condition that is treated should be considered when deciding the best treatment option. **Keywords**: pain, vitrectomy, laser photocoagulation, intravitreal injection, treatment.

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Introduction

Treatment of vitreoretinal diseases comprises a range of options that has increased in the past several years, allowing more individuals to benefit from new therapeutic methods. The use of lasers in the retina, new surgical techniques, and intravitreal drug administration constitute common treatment options. The increase in the number of invasive procedures in the retina has both benefits and drawbacks. Among the drawbacks is discomfort associated with the procedure, constituting a relevant issue because it can compromise adherence to treatment. Therefore, pain associated with vitreoretinal procedures and their treatment options have been the focus of several ophthalmological studies.

Jefferson A. S. Ribeiro (M.D.), Bianka Y. N. Y. Katayama (M.D.), and Rodrigo Jorge (M.D., Ph.D.), Department of Ophthalmology, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, Brazil. Jefferson A. S. Ribeiro, Superior School of Health Sciences, University of the State of Amazonas, Manaus, AM, Brazil. José A. Da Silva (Ph.D.), Department of Psychology, School of Philosophy, Sciences, and Literature, University of São Paulo, Brazil. Correspondence regarding this article should be directed to: Dr. Rodrigo Jorge, Division of Ophthalmology, Ribeirão Preto Medical School, Avenida Bandeirantes, 3900, Ribeirão Preto, São Paulo, 14049-900, Brazil. Phone: +55-16-36022523. Fax: +55-16-36022860. E-mail: rjorge@fmrp.usp.br

Ophthalmological procedures

Among the procedures most commonly used in the treatment of vitreoretinal diseases are pars plana vitrectomy, laser photocoagulation, and intravitreal drug administration.

Laser

Photocoagulation of the retina using lasers can be used to treat various vascular diseases in the retina such as diabetic retinopathy (Diabetic Retinopathy Study Research Group, 1978; Early Treatment Diabetic Retinopathy Study Research Group, 1991), vascular occlusions (Central Vein Occlusion Study Group, 1993; Branch Vein Occlusion Study Group, 1986), retina ruptures, and peripheral degeneration (Pollak & Oliver, 1981), and macular diseases such as diabetic macular edema (Early Treatment Diabetic Retinopathy Study Research Group, 1985).

Two laser wavelengths are most commonly used, infrared and green. The type of wavelength can be associated with greater discomfort caused by pain that occurs during the procedure. The use of infrared lasers is associated with greater pain intensity compared with green lasers (Lira, Nascimento, Arieta, de Carvalho, & Silva, 2010).

Pain is an important complication associated with retinal panphotocoagulation (Hitchings, 1980). The pain associated with this procedure tends to be more salient in the superior temporal quadrant, particularly the regions at 3, 9, and 12 hours that correspond to the long ciliary nerves and anterior to the equator.

However, the treatment of conditions that affect the posterior pole such as diabetic macular edema has been associated with a lower incidence of pain (Weinberger, Ron, Lichter, Rosenblat, Axer-Siegel, & Yassur, 2000). Pain frequently irradiates in areas such as the ipsilateral upper eyelid and frontal, parietal, and temporal regions and is particularly intense in the superior orbital edge and temporal region immediately following the lateral canthus (Tamai & Mizuno, 1984). To reduce pain during retinal photocoagulation, the laser pulse has been modified with regard to the way the energy is delivered, in which the wave amplitude of the laser is changed (Friberg & Venkatesh, 1995). The exposure time can also be reduced with a proportional increase in potency such that a shorter laser exposure time is associated with a lower pain sensation. Importantly, this benefit can be obtained without compromising the efficacy of treatment (Al-Hussainy, Dodson, & Gibson, 2008).

Outpatient treatment with lasers is commonly performed with the use of local anesthesia by means of instilling eye drops. However, different drugs and administration routes have also been used to produce analgesia during laser photocoagulation, including the injection of drugs (e.g., lidocaine and ropivacaine) in peri- or retrobulbar areas (Wu et al., 2006; Kallio, Puska, Summanen, Paloheimo, & Maunuksela, 1999) and intramuscular, subtenonian, and subconjunctival injections (Wu et al., 2006; Stevens, Foss, & Hamilton, 1993; Schlote, & Derse, 2001; Patel, Jenkins, Benjamin, & Webber, 2006; Tesha et al., 2010). Moreover, the local and oral administration of nonsteroidal antiinflammatory drugs (NSAIDs), anxiolytics (alone or in combination), and inhalant analgesics have been used (Wu et al., 2006; Weinberger et al., 2000; Vaideanu, Taylor, McAndrew, Hildreth, Deady, & Steel, 2006; Cook, Newsom, Mensah, Saeed, James, & Ffytche, 2002).

The administration of NSAIDs before the procedure is one option for alleviating pain. The use of diclofenac sodium (0.1%) eye drops prior to laser photocoagulation reduces pain associated with panphotocoagulation in the treatment of proliferative diabetic retinopathy (Weinberger et al., 2000). In another study, oral diclofenac potassium (50 mg) administered 45 min prior to retinal panphotocoagulation in individuals with diabetic retinopathy was superior to placebo in reducing procedural pain (de Faria Rodrigues, Messias, Da Silva, Ribeiro, Jorge, & Scott, 2010).

Intravitreal injection of drugs

The administration of drugs via intravitreal injection has become a common procedure in the age of pharmacomodulation (Anijeet, Hanson, Bhagey, & Bates, 2007; Fung, Rosenfeld, & Reichel, 2006, Aiello et al., 2004; Jager, Aiello, Patel, & Cunningham, 2004). It is a minimally invasive and efficacious intervention in the treatment of several vitreoretinal diseases (Jaissle, Szurman, & Bartz-Schmidt, 2005). The intravitreal injection represents a direct route of drug administration in the posterior segment of the eye. The use of this technique results in immediate levels of high vitreal concentrations of various drugs including antibiotics, antiviral agents (Taskintuna et al., 1997), antifungal agents (Scott, Cruz-Villegas, Flynn, & Miller, 2004), steroids (Bonini-Filho, Jorge, Barbosa, Calucci, Cardillo, & Costa, 2005), and agents that act against vascular endothelial growth factor (VEGF; Gragoudas, Adamis, Cunningham, Feinsod, & Guyer, 2004; Rosenfeld, Moshfeghi, & Puliafito, 2005; Bonini-Filho, Costa, Calucci, Jorge, Melo, & Scott 2009).

The type of anesthetic used for intravitreal injections varies according to the experience of the surgeon. The methods employed for anesthesia during intravitreal injection include topical administration of eye drops and gels (Friedman & Margo, 2006; Kozak, Cheng, & Freeman, 2005), peribulbar and subconjunctival injections (Kishore, Conway, & Peyman, 2001; Kaderli & Avci, 2006), and the use of cotton-tipped applicators soaked with anesthetic and applied to the injection site for a short period of time prior to the injection (Kaderli & Avci, 2006). Due to the fact that multiple intravitreal injections may be necessary to maintain the desired effect in some conditions such as age-related macular degeneration (Gragoudas et al., 2004; Rosenfeld et al., 2006), the patient's comfort becomes a relevant issue.

To determine the best treatment options, studies have compared three types of anesthesia (Cintra, Lucena, Da Silva, Costa, Scott, & Jorge, 2009): local anesthesia using proximetacaine chloridrate (0.5%) drops applied using a cotton-tipped applicator soaked for 30 s, subconjunctival injection of 0.4 ml xylocaine (2%), and peribulbar injection of 4 ml xylocaine (2%). The pain that was exclusively associated with the intravitreal injection was lower in the group that received peribulbar anesthesia, whereas subconjunctival and local anesthesia had similar effects. However, the pain associated with the entire procedure (anesthesia + intravitreal injection) was higher in the peribulbar group, demonstrating that the local route with eye drops applied using an anesthetic-soaked cotton-tipped applicator may cause less pain during the entire procedure and reduce the frequency of subconjunctival hemorrhage compared with subconjunctival injection of the anesthetic.

The spectrum of indications of intravitreal injections has increased in recent years, making it an option or adjuvant for treatments that use laser photocoagulation for diabetic retinopathy and venous occlusions of the retina (Tonello, Costa, Almeida, Barbosa, Scott, & Jorge, 2008; Costa, Jorge, Calucci, Melo, Cardillo, & Scott, 2007). Thus, comparing the discomfort associated with these two treatment options would be interesting, which may guide the choice of the method used. A recent study investigated patients with proliferative diabetic retinopathy and persistent retinal neovascularization who could receive retreatment with laser or intravitreal anti-VEGF injection (Lucena et al., 2013). The study reported that retreatment with the injection was more comfortable than with the laser, in

addition to having beneficial effects on the regression of neovascularization and an improvement in visual acuity.

Pars plana vitrectomy

When vitrectomy surgery was initially introduced, the principal indications were severe and persistent vitreous hemorrhage and tractional retinal detachment that involved the center of the macula (Aaberg, 1977). With the advance of surgical techniques and reduction of severe complications, new indications have emerged (Ramsay, Knobloch, & Cantrill, 1986; Bustros, Thompson, Michels, & Rice, 1987). One of these technical improvements is the use of smaller incisions (i.e., 23 and 25 gauge) as opposed to 20 gauge, allowing faster surgeries and less manipulation of the ocular surface (Chen, 1996; Kwok et al., 1999a; Jackson, 2000; Theelen, Verbeek, Tilanus, & van den Biesen, 2003; Schmidt, Nietgen, & Brieden, 1999). A shift has occurred from the initial trend of performing vitreoretinal procedures under general anesthesia to the use of local anesthesia (e.g., peribulbar, retrobulbar, and subtenonian); (Rao, Wong, Groenewald, McGalliard, Jones, & Ridges, 1998; Kirkby, Benson, Callear, & Loo, 1999; Javitt, Addiego, Friedberg, Libonati, & Leahy, 1987; Duker et al., 1991; Demediuk, Dhaliwal, Papworth, Devenyi, & Wong, 1995; Davis & Mandel, 1986; Benedetti & Agostini, 1994; Batterbury, Wong, Williams, Kelly, & Mostafa, 1992; Stevens, Franks, Orr, Leaver, & Cooling, 1992; Kwok et al., 1999b). Some studies have reported the use of local anesthesia that produces adequate analgesia while maintaining ocular movement during the procedure (Theocharis, Alexandridou, & Tomic, 2007; Tang, Lai, Lai, Zou, Li, & Li, 2007).

Peribulbar, subtenonian, and retrobulbar anesthesia appears to be equally effective in pain control during surgical procedures (Roman, Chong Sit, Boureau, Auclin, & Ullern, 1997; Newson, Wainwright, & Canning, 2001; Lai et al., 2005). Another point that should be considered with regard to anesthesia during surgical procedures is preemptive analgesia for vitrectomy. Peribulbar injections of anesthetics prior to general anesthesia surgery appear to be a good option for decreasing postoperative discomfort in patients who undergo vitreoretinal surgery compared with general anesthesia alone (Schönfeld, Hierneis, & Kampik, 2012; Kristin et al., 2001).

Final considerations

With regard to vitreoretinal procedures, laser photocoagulation is associated with the highest pain score (Tesha et al., 2010; Hillier, Aboud, Thind, & Clark, 2009; de Faria Rodrigues et al., 2010; Lucena et al., 2013), whereas vitrectomy and intravitreal injections are less painful (Yau, Jackman, Hooper, & Sheidow, 2011; Blaha, Tilton, Barouch, & Marx, 2011; Lucena et al., 2013; Lai et al., 2005). Notably, such a comparison is made by measuring pain after completion of a procedure that used traditional methods of anesthesia, suggesting that laser photocoagulation still needs to be improved with regard to procedural comfort.

The complexity of options for the treatment of retina and vitreous diseases requires knowledge of the various aspects of available therapeutics and methods that may be useful for facilitating patient adherence to treatment by reducing discomfort and pain. In some cases, a combination of analgesic options may be the best choice in individuals who are more susceptible to pain, and each case should be considered individually. Therapeutic options that cause less patient discomfort, regardless of the analgesic technique, may also be used, provided they are proven to be as effective as traditional treatments.

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