

Dry eye disease in adults and their treatment options: Are punctum plugs the best option in the Netherlands?

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ABSTRACT

This literature review aims to provide current estimates of DED prevalence among the adult population and their treatment options for optometrists in developed countries, specifically in the Netherlands. It examines which treatment options are currently mostly used, which ones have the highest patient compliance and comfort, and which ones yield the best results.

A systemic and thorough literature research has been conducted using Pubmed, Cochrane Library and Google Scholar. After applying specific criteria, a total of 43 articles were studied, of which 19 were included in this study. The aim was to focus on the latest treatment options and data. The main reason for exclusion was that many studies were published before 2015. Secondly, a survey is done in our practice on 41 patients (n=81 eyes) and we contacted 19 colleague optometrists.

This review confirmed that there is sufficient data supporting the efficacy of dry eye disease treatments. Although eyedrop therapy is an effective treatment, it shows lower patient compliance. Only 10.2% of a patient group of 2645 used the drops as prescribed. Punctum plug therapy requires no patient compliance, as it involves a one-time insertion with no need for revisits. It resulted in an 80% improvement in quality of life. In comparison, the IPL group showed a 100% improvement, but the higher costs and need for multiple revisits were noted as disadvantages.

As optometrists, we have more treatment options for DED than ever before, including new devices. The most commonly used options are mentioned in this review. Artificial tears, punctum plugs and IPL technology each have their pros and cons. In the Netherlands, some treatments are preferred over others.

Keywords: *dry eyes in adults, punctum plugs, IPL laser, treatment of dry eyes, punctal occlusion and developed countries.*

INTRODUCTION

If the eye is unable to produce an adequate amount of tear with good quality, there is an imbalance between tear production, absorption and drainage. Alternatively, if the eye produces an acceptable amount of tears but they fail to provide good lubrication, protection against infection, and support for wound healing of the ocular surface. This medical condition is known as dry eye disease (DED) or keratoconjunctivitis sicca (Craig et al., 2017; Messmer, 2015; Modis and Szalai, 2011; Perry, 2008; Pflugfelder and de Paiva, 2017).

DED is a very common ocular condition for which affected individuals regularly seek medical attention. The prevalence is high with a variable reported range. Worldwide estimates in adult populations range from 5% to 50% and the prevalence increases significantly with age (Modis and Szalai, 2011). Diagnostic criteria differences contribute to the uncertainty in decision making. Clinical signs of DED often poorly correlate with known characteristic signs and symptoms of the condition. Thus, manifestation of DED is often underestimated or misdiagnosed by practitioners, institutions and society in general and diagnoses may be delayed (Downie & Keller, 2015).

There are two major categories of DED, aqueous-deficient and evaporative, in which the first is due to a reduced lacrimal gland function and the latter is because of a meibomian gland dysfunction. The latter is far more common (Lemp et al., 2012).

DED has a multifactorial aetiology involving the entire ocular surface. The key elements of DED are abnormalities of tears (short

break-up time) and of ocular surface tissues (corneal and/or conjunctival epitheliopathy). The aetiological mechanisms involved in DED are very diverse, resulting in a self-sustained condition that eventually affect aspects of the lacrimal function unit. Corneal nerves, meibomian glands, lacrimal glands and even emotional centres associated with chronic pain perception are all included. This cycle of events on the ocular surface leads to symptoms of discomfort and visual impairment with a significant impact on visual tasks. Ocular symptoms vary widely ranging from minor transient irritation, to continuous itchiness, burning, dryness, pain, redness, visual disturbances and ocular fatigue (Lee et al., 2002). Daily activities including driving, reading and more generally the use of phones, TV and computers may be negatively affected. Also a decrease in performance and productivity in the workplace is reported (Nichols et al., 2016).

Additionally, DED is a cause of chronic pain, which explains the physical fatigue and the substantial effect on mental health like, sleep disorders, psychological stress, anxiety and depression that have been reported (Ayaki et al., 2016; Hackett et al., 2012; Stapleton et al., 2017). Overall, there is a significant impact of DED on the quality of life and functionality.

Several studies have shown that DED is associated with an economic burden due to direct (consultations, medication, treatment and surgical costs) and indirect costs (absenteeism on work) as highlighted in the Tear Film and Ocular Surface Society Dry Eye Workshop (DEWS) II Epidemiology Report (Stapleton et al., 2017). Traditional treatment options for DED include over-the-counter artificial tears, warm compresses and

lid hygiene with baby shampoo (Thode et al., 2015).

A working group from the National Eye Institute and Industry in the United Kingdom, offered a definition for dry eye disorder in 1995: 'Dry eye is a disorder of the tear film due to tear deficiency or excessive tear evaporation, which causes damage to the interpalpebral ocular surface and is associated with symptoms of discomfort' (Lemp, 1995).

In 2017, the International Dry Eye Workshop, consisting of 150 experts from 23 countries, offered a new definition: 'Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities have aetiological roles' (Nelson et al., 2017).

The new features of this definition include the multifactorial nature, defining emphasis on increased osmolarity, the use of the term disease, loss of homeostasis and neurosensory abnormalities. Of the above, all are useful clinically in that it may help to determine approaches to management.

METHODS

A bilateral research approach is used to pursue this literature review. First, an extensive literature search took place of databases such as Google Scholar, Cochrane Library and PubMed. This search was conducted using different keywords and combinations of them, such as: 'dry eyes', 'IPL laser', 'punctum plugs', 'ocular surface', 'DED', 'treatment of dry eyes',

'dry eyes in adults', 'DED in the developed countries' The second process is a survey done with 41 patients (n=81 eyes) and 19 colleague optometrists in the Netherlands.

The initial search on dry eye disease gave so many results, which says a lot about the extent of the problems regarding this disease. There were over 1000 results obtained in the databases. These results were specified by using keywords as mentioned above and only English written studies were included. The aim of this review is to look at the recent insights about DED, so search results who were from before the year 2015 were excluded. Also, by looking at only the developed countries and search specific on adults, the results were less. The search was further made more specific by looking at the treatment options, optometrists in the Netherlands, have. Because of the difference in country/state laws, education levels and prescribing options, not all optometrists have the same qualifications. Prescribing medication is not allowed for optometrists in the Netherlands, so the articles found on prescribing certain medication are excluded also. Finally, there were 19 results included in this review.

RESULTS

When we talk about the prevalence of dry eyes, a study by Stapleton et al. (2017) showed that it ranges from 5% to 50%. The treatment of DED is often chronic and multifaceted and potentially involves both pharmacologic and non-pharmacologic interventions (Jones et al., 2017). Treatment commonly progresses in a stepwise fashion, beginning with appropriate conservative therapies and advancing to more intensive treatments as indicated based on the severity

of the disease as researched by Jones et al. (2017).

As optometrists in the Netherlands, we can't prescribe pharmacological agents, but a short list is going to be mentioned.

In the treatment of DED, many pharmacological agents are used like topical and systemic medications. Commonly used topical agents include lubricants, corticosteroids, lifitegrast and cyclosporine A. Systemic oral agents may include antibiotics (azithromycin and tetracyclines), poly-unsaturated omega-3 fatty acid- and antioxidant supplements (Jones et al., 2017). Over the counter products like some lubricants, omega 3 and antioxidant supplements can be sold by optometrists in the Netherlands.

Non-pharmalogical interventions used in the treatment of DED comprise procedural and device-based therapies as well as lifestyle modifications. According to Jones et al. (2017) and Stonecipher et al. (2020) common procedural therapies include punctal occlusion, meibomian gland thermal pulsation and expression, intense pulsed light therapy, low-level light therapy and microblepharo-exfoliation. Device-based therapies include eyelid hygiene devices, neurostimulation devices, heat or moisture goggles and warm compresses.

Lifestyle modifications like, indoor humidity-level increase, avoiding of air-conditioners, open car windows, blowing fans and extended airline flights, can be implemented to improve DED.

Additionally, taking breaks when doing a lot of computer work, maximizing general wellness by ensuring adequate sleep, hydration, nutrition and psychological

wellbeing may improve the DED state according to Jones et al. (2017).

Eye drop therapy

Eye drop therapy is the principal approach for treating DED according to Jones et al. (2017). This is also the case in the Netherlands. When using eye drop treatments, it is necessary to regularly use them as prescribed. On the contrary, DED has a lot of subjective symptoms, and the frequency of using eyedrops may change in order to alleviate these symptoms. If the frequency of eyedrop use is low, the effects of them will not persist and make it difficult to improve symptoms.

Since the assessment by Mengher et al. (1986) on the benefits of hyaluronic acid (HA) on the tear film stability, it has become a standard component in many artificial tears according to Hynnekleiv et al. (2022). The (pre)clinical studies showing acute and long-term therapeutic benefits. HA is a natural glycosaminoglycan which is present in the human body. The composition of disaccharide units of glucuronic acid and N-acetyl-D-glucosamine is what makes it. The molecular weight (MW) of it varies based on the number of disaccharide units forming the molecule.

The higher the MW (>1000 kilodaltons) according to Aragona et al. (2019), the greater the therapeutic potential, including better hydration, improved corneal muco-adhesion, and anti-inflammatory properties. On the contrary, lower MW (< 500 kilodaltons) studies, by Lee et al. (2021) tends to act as a strong pro-inflammatory molecule.

In the Netherlands, as a result of the taken survey, the colleague optometrists all advice

eyedrops containing HA due to the advantages above and the high patient satisfaction. This results in the fact that these eyedrops are the first choice option in our country. One downside for the patient is that these drops are not covered by the insurance.

Another general downside is the non-compliance of the patients. Uchino et al. (2022) researched the reasons for non-compliant behaviour in the eye drop treatment of 2645 patients. Their research shows the proportions of participants grouped by their reasons for not following eye drop instructions. It is shown that most participants with DED, did not instill their eye drops at the specified frequency. Only 10.2% of the investigated group, used the drops at the frequency as prescribed. The group of patients that used the drops only when having symptoms was 61.3%. According to the patients, there were a lot of disadvantages for the use of eyedrops. The most common reason for not using the eye drops was because they were used on an only when needed basis, only to alleviate subjective symptoms. Other reasons were: forgetting the drops when going out, eyedrops ruining make-up, the frequency prescribed being too high and eyedrop bottles being too bulky to carry around.

During our survey in our practice on the advantages and disadvantages of eyedrops, we asked a patient group of n= 41 (81 eyes) on their thoughts about the drops. All of the patients were satisfied when using the drops, despite the disadvantages they noticed. The main problem was that the satisfaction decreased as soon as the drop usage was less. We also called a few colleagues, n=19, to ask their experiences when prescribing eyedrops. They noted that the key problem with eyedrops is the compliance.

Compliance was the biggest reason for not noticing any alleviation of the complaints. Another disadvantage is the use of the drops. Not everyone is capable of using these drops for multiple reasons. Patients who for example have neurological problems and motor disorders, are having problems using the drops. Make-up use is also a reason for not using the drops.

Although eyedrops are a relatively cheap and effective treatment option, the impracticality is a reason for a lower compliance. For us as optometrists, it doesn't require a big investment to start with the drops in our practice. Therefore it is an affordable treatment option.

In order to obtain the appropriate effect of the eye drops, we as optometrists must consistently emphasise to patients the importance of regular instillation.

Punctal occlusion

Freeman et al. (1975) and Ervin et al. (2017) showed that when eye drop therapy alone can't improve DED sufficiently, punctal occlusion via the insertion of a punctal plug or by punctal occlusion surgery is an effective treatment for cases of severe dry eyes. In this review, only the punctal occlusion with punctal plugs is going to be discussed because the latter is not a treatment option for optometrist in the Netherlands. Punctum plugs have been around since the 1970s. The concept of blocking the lacrimal drainage system was first described in 1935. It was forty years later that the first punctal plug was developed, which was composed of silicone material. Punctal plugs make the retention time of tears and instilled eye drops longer and gives an increase in the aqueous fluid volume over the ocular surface. These changes improve the three essential

mechanisms of dry eye pathophysiology: tear film instability, increased friction and the associated inflammation. Thus, severe aqueous deficient dry eye is considered to be the best indication of punctal occlusion (Yokoi et al. 2004).

When punctal occlusion with plugs is selected, two types of plugs are the most used ones in the Netherlands. The first is a plug that's made from a collagen solution. When the plug is inserted, as a result of body temperature, it turns into a white-coloured gel. It will be absorbed within 1 to 16 weeks. The second one is the non-absorbable or permanent plug. These are silicone based and exist in a wide variety of designs. The plug is inserted using a preloaded dispenser.

In a study done by Kato et al. (2023), 16 eyes with severe aqueous deficient dry eyes were studied. Of these 16 eyes, 1 was performed with surgical punctal occlusion and punctal plugs were inserted in 15 eyes. The background diseases were as follows: Sjogren's syndrome (n= 7 eyes), ocular cicatricial pemphigoid (n= 3 eyes), graft-versus-host disease (n= 2 eyes) and non-Sjogren's syndrome (n= 4 eyes). All eyes were evaluated at before and at more than a month (62.3 ± 45.4 (28-168) days) after punctal occlusion. The result of this study was that there was an improvement in all of the subjective symptoms.

Another study done by Mohamed et al. (2016) on 90 eyes at a mean age of 48.2 ± 9.3 showed a statistically significant decrease in the subjective symptoms and also a decrease in the frequency of application of artificial tears. In this study, two different plugs were inserted. A silicone and a thermosensitive smart plug. The overall conclusion is that there is an improvement in symptoms between 37.5% and 95.5%, due to the

placement of punctal plugs. The difference is explainable due to the several advantages of a smart plug: no protruding head on the plug, no need to dilate the punctum during insertion and only one size plug to fit all patients. Especially the fact that there is no protruding head on the plug reduces the possible irritation of the ocular surface and the risk of spontaneous extrusion according to Chen and Lee (2007). The thermosensitive plug can change the physical state between solid and soft gel when exposed to body temperature.

There is not much compliance needed after the insertion of punctal plugs. With smart plugs, the chances of losing the plugs is minimized. But there are few cases in which it led to an increased incidence of canaliculitis (Fezza et al. 2011). The infection caused by the smart plugs typically occurred three years after insertion. For this reason, every patient with an ocular infection, even after a few years of plug insertion, should be suspected with canaliculitis. Hill et al. (2009) reported a rate of canaliculitis of 7.2%. The study done by Fezza et al. (2011), showed an almost similar rate of 6%, but with the remark that the rate must be higher, because of the long development time of the infection and the loss of the patients during the follow up time. With them, the average time for developing canaliculitis was 2.7 years. For this reason, Klein-Theyer et al. (2015) recommend that only long term follow up periods, such as more than 10 years, can identify the majority of complications associated with smart plugs. With the regular silicone plug it is important to notify the patient that rubbing in the eyes can cause loss of plugs. Burgess et al. (2008) found that the overall use of tear supplements was decreased by 55.6% with

silicone and by 61.1% with smart plug treated eyes.

After our survey, we noticed that all optometrists in the Netherlands were familiar with punctum plugs. None of the patients had ever heard of the plugs. All optometrists did inform their patients about the plugs. From the 19 colleagues, 16 of them treated their patients with plugs. The others referred the patients to the hospital for different reasons. The main reason was the unfamiliarity with the method and, consequently, the fear of placing the plugs. They didn't know how to insert the plugs and were afraid of complications. They also didn't want to risk their good relationship with the ophthalmologists nearby by doing a procedure that they were not so familiar with. The second reason is the cost aspect. In the Netherlands, we have a compulsory deductible system with the health insurance. This meaning that the first €385 of health costs are for the patient. When patients go to the ophthalmologist, the insurance covers the punctal plugs. The coverage is €820 for both eyes, but only if it's installed by the ophthalmologist. When you've already used your deductible, the rest of the costs are covered. The patient with health costs that exceed the deductible, go to the ophthalmologist for the plugs. The patients who don't exceed it, can choose for the optometrist. The 6 optometrist who placed the plugs asked prices varying from €249 to €399, but these costs are not covered by the insurance. The others who didn't insert them, don't want the hassle of explaining every financial aspect of the plugs and again wanting to keep a good relation with the ophthalmologist. They didn't want to start an uneven competition. If there would be a change in the coverage structure, more patients would choose for the plugs and more

optometrists would insert them. The investment needed to insert the plugs is not a big one. The procedure is not time consuming. It is important to inform the patient about the chances of loss of plugs and the possible irritation. When installed, the patient notices a decrease in DED complaints. Almost every patient (>95%) noticed an alleviation. The few who were not very enthusiastic, were the ones who had a higher expectation. When looked at the literature and also the survey done, punctal plugs are a practical, not time consuming and a relatively inexpensive treatment option.

Intense pulsed light

Intense pulsed light treatment (IPL) is also a treatment which reduces both signs and symptoms of DED (Toyos et al., 2015; Dell et al., 2017). Being widely accepted as a treatment for skin rosacea (Papageorgiou et al., 2008). Toyos et al. (2005) noticed that facial skin rosacea patients treated with IPL reported a significant improvement in their dry eye symptoms.

The most common form of DED, as mentioned earlier, is the evaporative one, which is mainly due to meibomian gland dysfunction (MGD) (Lemp et al., 2008). The meibomian glands are responsible for the production of lipids which will integrate the tear film. Its secretions comprise a mixture of several lipids with free fatty acids, phospholipids, among others (Messmer, 2015). MGD can be divided in two groups, accordingly to secretion by the meibomian glands: low- and high-output.

Low-delivery MGD is characterized by closure of the terminal ducts secondary to epithelial keratinization and increased meibum viscosity. This leads to intraglandular dilation, gland atrophy and

low secretion. This process is influenced by several factors, such as hormonal changes, gender, age, but also by drugs (e.g. systemic retinoids). An association can be found with several skin conditions (e.g. acne rosacea) and cicatricial conjunctivitis (e.g. trachoma) (Craig et al., 2017).

High-delivery MGD is characterized by accumulation of meibomian oil within the glands. This promotes bacterial growth and the release of toxic mediators, which may trigger the inflammatory aspect with subsequent atrophy (Tomlinson et al., 2011). IPL systems are light sources of high-intensity that produce polychromatic and noncoherent light with wavelength ranging from 515 to 1200 nm, which corresponds to visible and infrared light (Raulin et al., 2003; Vora et al., 2015).

The ultimate principle of this technology is light induced thermolysis, in which light energy is selectively absorbed by a chromophore and converted to heat, targeting specific tissue without damaging its surrounding structures. The produced wavelength can interact with several chromophores within the human body, such as melanin (400–750 nm) and haemoglobin (578 nm), to generate heat. The absorption of yellow light by haemoglobin can convert it to heat, therefore coagulating and ablating blood vessels, such as eyelid margin telangiectasias.

The broad wavelength option is useful as it can be changed to each patient's skin type, to minimize melanin absorption and subsequent hypopigmentation, as melanin absorption

decreases with increasing wavelength (Tashbayev et al., 2020; Raulin et al., 2003; Vora et al., 2015). According to these last

researchers, IPL-induced photothermy melts abnormal meibum more efficiently than conventional therapy, since heat is transmitted both inside and out, therefore promoting tear film stability and reduced evaporation. Selective photothermolysis also coagulates abnormal telangiectasia at the eyelid margin (by energy absorption by haemoglobin), which may interrupt the release of inflammatory markers and subsequent bacterial invasion to the meibomian glands.

IPL technology may also induce a local heating effect, which may warm meibomian gland secretions, which can improve viscosity, stabilize the tear layer, and reduce the evaporative component of DED. Some studies suggest that IPL may also have a local antibacterial and anti-parasitic effect. There are reports of existence of coagulated *Demodex folliculorum* as well as reduced lymphocytic infiltration in patients submitted to this type of treatment (Vora et al., 2015).

The technique used for IPL consists of device parameters, namely wavelength filter, pulse duration, fluency, are selected depending on the pathology to be treated, so that the target is reached. Each manufacturer has specific recommendations regarding each device. After the diagnosis of MGD and DED has been made, and in the absence of contraindications for IPL treatment (namely periocular skin tattoos/piercings, skin malignancy anywhere or pigmented lesions on the surrounding skin, ocular trauma, previous eyelid or lacrimal surgery and inability to adhere to either the treatment or the follow-up regimen), the risks and benefits of the procedure are explained to every patient, and informed consent is obtained.

The patients phototype is evaluated by the Fitzpatrick score (types 1–6). This is a scale in which the different skin types are classified, which helps determine the safest energy parameters since fair skin patients (i.e. lower Fitzpatrick score) require more energy than darker skin patients. This happens because melanin absorbs energy, which can result in temperature elevation and thermal burns, and damage of the surrounding skin. Therefore, classically, for safety reasons, IPL treatment was not offered to patients with Fitzpatrick skin type higher than 4 (Vora et al., 2015).

However, new technology devices have emerged: an IRPL technology (by ESW vision, France) is approved for use in Fitzpatrick skin type 5, with reduction of the flash intensity. In addition, Thermaeye Plus (by MDS Medical Technologies, Spain) and Lumenis M22® (by Lumenis Be Ltd, Israel) allow treatment in all skin types, including skin type 6.

Every treatment starts with the patient removing glasses if worn and the facial skin is cleaned. Protective eye shields are placed to avoid damage to intraocular structures. Hyperpigmented skin lesions are covered with a protective adhesive. Afterwards, ultrasound gel is then placed on the infraorbital and temporal skin (the area to be treated) to cool down the area and avoid thermal burns. It may also improve light transmission, allowing more efficacy in every treatment session. However, this is not always strictly required – the Optimal Power Energy® IPL (by Espansione Group, Italy), due to its technology, enables treatment without using any type of protective gel, with additional comfort for every patient. The patient and the operator have to wear protection goggles during the emission of

pulses. The pulse settings are selected given every patient's skin type and tolerance. The number of pulses (most frequently 4–6) and treatment protocol vary according to each device manufacture's indications and the experience of the health professional. The pulses are applied on the inferior and temporal periocular zones. The gel is removed, and the skin cleaned and washed with water and a sunscreen and sun protection are advised on the following days. At the end of the procedure, manual expression of the Meibomian glands with the slit-lamp can be performed.

Each induction treatment cycle comprises more frequently 3–4 sessions, which can be, if necessary, followed by a maintenance session after 4–12 months (Vora et al., 2015).

In the earlier mentioned survey, we have found that 13 optometrists had an IPL device. The optometrists who placed plugs, also had an IPL device. The results with the IPL devices are variable. About half of the optometrists had good results, and the other half did not. These patients did not notice any difference in their signs and symptoms. This is a significant difference compared to the literature found. The main reason for this difference could be found in the economic reasons. There is no standardisation available in the Netherlands for the use of an IPL. The investment done by an optometric practice is high, and for commercial reasons, the colleagues keep the machine running. A more precise diagnoses could result in a higher patient satisfaction due to the real need of using the IPL.

An IPL device, depending on the model and brand is around €25000. For the optometry practice, this is a big investment and not every optometrist is capable of purchasing

one. Every Dutch optometrist, questioned during the survey, works in the same way. There are 3 sessions, once per month, at first and then an annual session. Each session varies between €200 and €275 per session. This is an investment for the patient also. Especially when kept in mind, that the insurance doesn't cover this.

In the studies done by Toyos et al. (2015) and Dell et al. (2017), IPL therapy comprised several sessions given several weeks apart. Each session consisted of IPL pulses applied from tragus to tragus, just below the lower eyelids and including the nose.

Eyelid temperature significantly influences the physical properties of meibomian gland secretions, also known as meibum (Nagymihalyi et al., 2004).

At higher temperatures, meibum becomes less viscous, which more easily allows its normal distribution over the cornea. At room temperature, the temperature at the eyelids is ~33°C (Butovich et al., 2008). In patients with MGD, lipid composition may be altered, reflecting changes in the configuration of hydrocarbon chain and lipid-lipid interaction strength. As a result, the phase-transition temperature (the temperature at which the meibomian lipids switch from an ordered and gel-like phase to a disordered and fluid-like phase) may increase, compared to healthy subjects. A study by Borchman et al. (2011) analysed the physical properties of meibum, the phase-transition temperature was ~28°C for meibum from healthy donors (below eyelid temperature), and just above 32°C for meibum from donors afflicted with MGD (above eyelid temperature). Because the phase-transition temperature of human meibum is near physiological body temperature, a small increase of 4°C is

sufficient to change the meibum from gel like to fluid. Craig et al. (2015) noted that IPL application could increase in skin temperature. However, these authors argued that any increase is modest and temporary: immediately after IPL application, the skin temperature increased by < 1°C. However, it should be noted that, in their study, skin temperature was measured with infrared thermography a few seconds after treatment and only after removal of the conducting gel. During these few seconds, the skin could cool down considerably and lose heat. It is therefore difficult to infer from this measurement what the temperature of the eyelids would be during IPL treatment itself.

Whether or not IPL energy is sufficient to warm the skin is less important than its thermal effect on blood vessels under the surface. The eyelids are extensively fed by capillaries and arterioles branching off the facial artery. A mathematical model demonstrates that in medium and large blood vessels (>150 µm), a single IPL pulse of 30 ms duration raises the temperature at the centre of the vessel to 80°C–90°C, above the temperature required to cause coagulation and thrombosis as discussed above. In contrast, in small (60 µm) blood vessels, the temperature may reach only 45°C–70°C, depending on fluence (Baumler et al. 2007). This temperature elevation is insufficient to cause the destruction of blood vessels, but it is probably enough to raise the temperature of eyelid skin (and meibomian glands) by a few degrees, possibly above the phase-transition temperature. This thermal response could be enough to unclog the meibomian glands and restore the excretion of meibum during blinking.

Yan Shi et al. (2021) conducted a randomized controlled trial composed of 123

patients for the efficacy of IPL. Their results show that IPL significantly improves eye symptoms, meibomian gland quality scores and 30-day tear secretion Schirmer test.

A systemic review by Leng et al. (2021) showed that IPL improved the TBUT and Ocular Surface Disease Index (OSDI) of patients.

A randomized trial enrolling 90 eyes of 45 patients by Arita et al. (2019) assigned patients with dry eye to IPL. Each patient was submitted to eight sessions with intervals of 3-weeks. At 32 weeks of follow-up, the IPL group had significantly improved lipid layer thickness, non-invasive breakup time (NIBUT), fluorescein breakup time (BUT), and conjunctival fluorescein score (CFS). The Standard Patient Evaluation of Eye Dryness (SPEED) score showed a significant reduction.

According to the results by Toyos et al. (2022) after four sessions of IPL separated by 2-week intervals, patients showed statistically significant improvement in TBUT and meibomian gland secretion (MGS). When regarding the safety of IPL, Toyos et al. (2022) reported no harmful adverse events, except light pain ($n=1$) and moderate bacterial conjunctivitis ($n=1$).

Arita et al. (2019) found no significant differences regarding intraocular pressure, visual acuity, lens opacity, and funduscopy examination before and 32 weeks following treatment with IPL. Similarly, no adverse events were reported by Yan Shi et al. (2021). A randomized controlled trial by Piyacomn et al. (2020) showed significantly higher reported pain scores in the IPL group, but this difference was reduced after a few IPL sessions. Regarding skin type, Li et al. (2019) showed that IPL is an effective and

safe treatment modality in patients with Fitzpatrick types 3/4, particularly with low-energy settings (590 nm, 14 mJ/cm²). Despite this, purpura, edema, erythema, blistering, and purpura were encountered in some patients, particularly in the higher-energy settings (560 nm, 16 mJ/cm²). Therefore, caution is advised, especially in older patients which are more prone to hyperpigmentation.

IPL is positively correlated with the number of sessions and declines with increased observation time according to current evidence.

Arita et al. (2019) showed that after 8 treatment sessions (every 3 weeks) patients achieved a significant reduction in SPEED score and improvement in NIBUT, BUT, meibum grade, lipid layer thickness, and eyelid abnormalities. These effects persisted at the 32-week follow-up (which corresponds to 11 weeks after the last session).

In line with this evidence, Piyacomn et al. (2020) described that the IPL group (3 sessions on days 1, 15, and 45) showed an increase in TBUT after the first treatment session, peaked at day 45 and persisted for at least 6 months after the initial treatment session.

Similarly, Chen et al. (2021) and Yan et al. (2021) both submitted patients to 3 treatment sessions at 3-week intervals and reported the positive effects of IPL following 3-weeks and 3-months after the last treatment session.

Xue et al. (2020) designed a randomized, double-blinding, randomized-controlled trial to evaluate the long-term effects of IPL therapy in patients with MGD. Patients were randomized to four or five light flashes or placebo treatment. Patients received 4

treatment sessions (on days 0, 15, 45, and 75). Patients were evaluated immediately before each treatment and at 4 weeks after completion of the last one. As expected, results showed the efficacy of both IPL arms. Sustained improvement in manifestations of DED was observed earlier in the five-pulse arm. Indeed, on day 45, only patients randomized to receive five flashes showed improvement of lipid layer thickness, meibomian gland capping, and OSDI symptoms score. Despite this, a consistent improvement in both IPL arms was not observed until 4 weeks following the final treatment session. This highlights the importance of four initial IPL sessions to achieve maximum beneficial effects.

In a study by Elbakary et al. (2024), the improvement of life quality of patients with dry eyes is evaluated. In this study, a comparison is been made between punctal plugs and IPL. The result of this study was that with both therapies, a significant improvement in the quality of life of the patients was noticed. In 100% of the patients treated with IPL, there was an improvement. With the punctum plug patients, there was a quality of life improvement found in 80% and 20% reported no symptomatic improvement. The quality of life was assessed using the OSDI questionnaire. A score of 33 or more indicated severe affection, 23-33 moderate, 12-22 mild and 12 or less represented the normal range. The reduction of the mean OSDI score, in patients treated with IPL, went from 56.9 ± 11.1 to 22.9 ± 16.4 . For the patients who received punctum plugs, the score was reduced from 53.8 ± 18.3 to 31.7 ± 19 . In 13.3% of the patients receiving punctum plugs, complications like punctal granuloma and proximal canalicular obstruction

occurred. In the IPL group, no complications occurred.

DISCUSSION

Current literature shows that IPL, punctum plugs and eyedrops are effective treatments for dry eye. Available evidence shows improvement of subjective symptoms and objective indicators, such as thickness of lipid layer, non-invasive breakup time and Schirmer test. Most studies show that both objective and subjective improvement appears after the initial session. Current evidence demonstrates that IPL significantly increases TBUT, OSDI score, and symptoms and signs of dry eye. However, its efficacy decreases over time. In addition, Ribeiro et al. (2022) concluded that the positive effects of IPL may lose some efficacy at 6-months after the initial session, and further sessions may be required. Thus, IPL treatment should not be considered as first-line therapy for MGD, but as an addition to the standard care.

IPL should be performed in cases of DED when conventional treatment options like palpebral hygiene, lid massage and ocular lubricants are not effective. It is a very useful treatment option in patients with DED due to MGD, since it is an effective, quick, and safe procedure, without relevant positive effects, as long as it is performed according to each device's manufacturer protocol. The number of required treatments and the costs could be a disadvantage for the patient. The investment needed to purchase an IPL is a possible drawback for the optometrist.

Punctum plugs are designed to block the lacrimal drainage. It is also helpful in the preservation of lubricant drops improving the tear film in a both quantitative as qualitative manner. The investments for the

patient as for the optometrist are lower than with IPL. This is a positive, in favour of the punctum plugs. Especially when kept in mind that the costs are not covered by the health insurance. There are no required revisitations necessary, which makes this procedure less influenced by patient compliance.

The low cost advantages are also there for the eyedrops. It is a simple and effective treatment option for dry eyes. The biggest problem with eyedrops is the patient compliance. Most patients use the drops on an 'only when needed' basis. This makes it difficult to treat the subjective but mostly the objective signs. The optometrist has a key role in educating the patient in the importance of consequent use of drops

CONCLUSION

IPL therapy is a safe and effective non-pharmacological treatment option for dry eyes. Compared to punctal plugs and eyedrops, IPL therapy offers better quality of life without any lasting complications. However, the high cost in purchasing an IPL for the optometric practice, the financial burden for the patient and revisits are disadvantages. Eyedrops are less effective because of the poor compliance of the patients. Punctal plugs are an effective treatment option for dry eyes at low costs and less revisits. Changes are needed in the Dutch health system to make IPL more affordable for the patients. As for now, with the health system of the Netherlands kept in mind, and their non-covering policy for the treatments done by an optometrist, punctal plugs may be the best treatment option.

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