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The effect of contact lens wear on corneal sensation

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The corneal nerves play an important role in the protection and maintenance of corneal health, and the corneal epithelium has the highest density of free nerve endings in the body. Contact lenses are increasingly used to correct refractive error or for cosmetic purposes. It is therefore important to study the relationship between these factors. Studies have revealed that contact lens wear can produce a reduction in corneal sensitivity, with the extent of sensation loss related to the type of contact lens, the material it is made from, and the frequency and duration of wear. In summary, as the time of wear increases, both in the short-term (days) and long-term (months), the greater the loss of sensation. Recovery to normal levels, with the cessation of lens wear, is also prolonged with extended durations of contact lens wear. Newer lens materials that have improved oxygen permeability have less of an effect. The two principle mechanisms by which the corneal nerves are affected are the mechanical action of the lens and interference with the metabolic function of the cornea, as a result of the reduced oxygen supply. The impaired metabolic function produces an increase in acidosis and a change in corneal pH as a result of hypercapnia. Both of these can alter nerve function, and so reduce corneal sensitivity.

Key words: **Contact lenses - Cornea, physiology - Cornea, metabolism.**

Contact lenses have become one of the principal methods for correcting refractive error over the last 30 years. The development of the soft contact lens by Wichterle *et al.*[1] created a safe and comfortable method for patients to change from spectacle wear. New developments in lens materials led to the introduction of rigid gas permeable (RGP) lenses and, more recently, to silicone-hydrogel lenses. Indeed, the silicone hydrogel lens holds the promise of the first successful continuous wear lens.[2]

The clinical care of contact lens wear has revealed a wide number of unwanted adverse reactions, *e.g.* corneal oedema, neovascularisation, papillary conjunctivitis, dry eye, marginal ulcers.[3] However, each reaction has encouraged the development of new lens designs and materials to avoid/overcome the problem.

One of the more unusual side effects of contact lens wear is a reduction in corneal sensation. For PMMA (poly-methylmethacrylate) and RGP lens wear, the practitioner is actively encouraging a reduction in sensitivity, but this improved comfort also brings the risk of undetected foreign bodies or pathology. It is this paradoxical situation that we will review in this paper.

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Corneal nerve supply

The cornea has the highest density of free nerve endings in the body, and these produce an exquisite level of sensitivity to noxious stimulation.[4] They play a vital role in the detection and prevention of damage to the cornea and anterior ocular surface. The cornea performs several important roles in the eye – transmission of light to the retina, refraction of the light as part of focussing the image, maintaining the intraocular pressure and protection of the internal eye. The tears, corneal nerves and eyelids all perform roles in the defence of these functions. The nerves also play a role in the maintenance and health of the corneal epithelium. Research on rabbits has shown that a total lack of corneal nerve supply will result in impaired wound healing, decreased corneal metabolism and reduced epithelial cell adhesion.[5] The manner in which this influence is exerted is unknown, but may be due to axonally transported substances, such as proteins.[6]

The corneal nerves are derived from the Nasociliary nerve, a branch of the Ophthalmic nerve, a division of the Vth Cranial Nerve (Trigeminal). The nerves supplying the cornea pass along the long ciliary nerve branch of the nasociliary nerve. They penetrate the posterior of the eye and pass between the sclera and choroid, coursing anteriorly to supply the cornea, iris and the sensory fibres of the ciliary body, trabecular meshwork and sclera.

Upon reaching the cornea, 70-80 nerve axons (in man) enter the corneal stroma in a radial fashion from various sites around the corneal limbal circumference. The nerves enter in the middle third of the stroma and run towards the centre of the cornea, giving rise to branches that innervate the anterior and mid stroma. As the axons pass towards the epithelium, they ramify and divide to form a poorly characterised nerve plexus beneath Bowman's Layer in the superficial stroma.[4, 7-9] The nerves then penetrate Bowman's Layer at an estimated 400 sites to enter the basal epithelial layer.[10] As they do so, the nerve bundles lose their remaining Schwann cell coverings. These nerves then combine with nerves that enter the basal epithelium from the limbus to form the basal epithelial plexus.[11]

The nerve fibres continue to divide and ramify anteriorly within the corneal epithelium to distribute free nerve endings across the whole of the cornea anterior surface. The nerve fibres innervating the cornea are of several different types, each responding to a different set of stimuli. These different nerve types are also arranged within the corneal epithelium according to their type – myelinated A∂ fibres that respond to mechanical stimuli run parallel to the corneal surface within the basal cell layer, unmyelinated C fibres that respond to thermal and mechanical stimuli turn upwards from the epithelial plexus towards the surface.[12] These two nerve types are the principal moderators of the corneal nerve response to the current corneal aesthesiometers used to assess corneal sensitivity.

Corneal sensation measurement

The two principal methods used to assess corneal nerve function in this review are the Cochet-Bonnet Aesthesiometer and the Non-Contact Corneal Aesthesiometer (NCCA). The Cochet-Bonnet instrument uses a thin nylon thread that is pressed against the corneal surface.[13] This produces a mechanical deformation in the anterior corneal surface that stimulates the A∂ fibres. A variation in the intensity of the stimulus is achieved by varying the length of the nylon thread, which in turn alters the force that must be applied to produce a bend in the thread. By this indirect method the stimulus intensity can be determined.[14] In contrast, the NCCA uses a controlled pulse of air, of a predetermined intensity and duration, to produce a localised cooling of the pre-corneal tear film.[15] This cooling stimulus is transferred to the corneal epithelium and detected by the C fibres.[16, 17] For both instruments, the patient is asked to respond verbally as to whether they felt the stimulus or not – for the Cochet-Bonnet Aesthesiometer the subject feels a touch on the eye, and for the NCCA the subject feels a gentle cooling of the eye.

Pattern of corneal sensitivity loss and recovery

The extent of corneal sensitivity loss and recovery with contact lens wear depends on the contact lens type, the oxygen permeability of the material, the number of hours of daily lens wear, the number of years of wear, and the length of any recovery period. For this review, we shall consider the pattern of sensitivity loss and recovery of hard and soft contact lenses, over both short-term and long-term wear.

Short term effects

Hard/PMMA contact lenses.—As mentioned earlier, Hard/PMMA lenses actually require a reduction in corneal sensitivity to improve their comfort and allow long-term wear. This is most clearly seen when a lens is inserted in the eye of a naïve wearer. An immediate lacrimal response occurs, which gradually reduces with neural adaptation. A further more significant reduction in corneal sensitivity occurs over a full days wear.

A large number of studies have investigated this effect.[13, 18-33] The most interesting series of studies were completed by Millodot. He found a reduction in corneal sensitivity of about 110% over a 12-hour wear period. His subjects had worn their lenses for at least 3 months and he assessed their corneal sensation prior to insertion, after 4 hours, 8 hours and 12 hours of continuous uninterrupted wear. He found that sensitivity diminishes progressively with the length of wear to a maximum after the 12-hour wear period. He also found a high correlation between central and peripheral corneal sensitivity, although the loss was less in the centre than in the periphery.[34] This effect presumably relates to the increased mechanical effect of the edge of the lens. It is reasonable to assume that if the lenses are worn for more hours without removal, the loss will continue to some unknown maximum level.

The recovery of sensitivity after short-term PMMA contact lens wear is rapid. When lenses are removed after 8 hours of wear, a statistically significant recovery occurs within 1 hour, although complete recovery takes longer and is related to the number of hours of contact lens wear.[29, 34]

Soft contact lenses.—Soft contact lenses do not require any reduction in corneal sensitivity to improve their ease of wear because of the flexibility of the material. At the same time, investigations have shown that soft contact lenses still produce a progressive decline of corneal sensitivity, but to a much lesser degree than hard contact lenses.

A number of studies have considered this effect,[27, 30, 37-39] although the most interesting studies were completed by Millodot and Velasco *et al.* Millodot measured the corneal sensitivity in 15 subjects before and after 4 hours, 8 hours and 12 hours of uninterrupted HEMA soft lens wear. He observed a small, but significant, decrease in corneal sensitivity after 8 hours of wear, and this loss increased with continuing wear.

Velasco *et al.* found a significantly greater decrease in corneal sensitivity with 38% water content hydrogel lenses than with 55% water content lenses. This reflects the influence of lens water content on the oxygen concentration at the corneal surface - more hydrated lenses produce a higher corneal surface oxygen tension. Similar investigations found that high water content soft lenses produce practically no change in corneal sensitivity over a 12-hour period, although different lenses and fits cause slightly different results.[35, 42, 43]

The recovery of sensitivity after soft contact lens wear is usually more rapid than that found with hard contact lenses and depends on the nature and duration of wear. Recovery usually occurs within one hour of lens removal.[40, 41]

Long term effects

Hard/PMMA contact lenses.—Most reports of sensitivity reduction have paid attention to short term wear of contact lenses. However, a number of investigations have considered the effects of longer periods of wear.[13, 19, 25-27, 30, 33, 44, 45]

The most interesting studies were completed by Millodot who assessed the effect of long-term PMMA lens wear. He found a marked decline in sensitivity after the first

few years of wear. In one study, the subjects were divided between an experimental group, who had worn hard contact lenses for 1-22 years, and a control group who had never worn lenses. Subjects who had worn lenses for only 1-2 years had no significant difference in corneal sensitivity when compared to those subjects in the control daily group. This indicates that the recovery which occurs after removal of the lens is sufficient to return sensitivity to normal levels. However, the effect of prolonged wear is easily seen after 5-7 years. Subjects in the experimental group have a significant decrease in corneal sensitivity in comparison with the control group. If we describe corneal sensitivity in terms of its inverse, the corneal touch threshold (CTT), then 5-7 years wear produces a 100% increase in CTT and after 17-22 years wear a 200% increase in CTT.

A similar study has been completed by Sanaty and Tenel who found the same pattern of sensitivity loss. They also found a greater loss of sensitivity in the periphery, which presumably again relates to the increased mechanical edge effect of the lens.

The recovery of corneal sensitivity after long-term wear can take many months and depends on the length of time the subject has worn PMMA lenses. For example, with a subject who has worn lenses for 10 years, recovery to normal levels can occur within 1 month, but for a subject who has worn lenses for 15 years, recovery takes 4 months. The main point is that the longer the initial wear, the longer it takes to recover.[29, 46]

Soft contact lenses.—A number of studies have considered the effect of long-term daily wear of soft contact lenses on corneal sensitivity. Two studies considered the effect of high water content extended wear lenses. Larke and Hirji followed patients who were wearing Sauflon 85 lenses and Millodot examined people who were wearing X-Ten lenses. In both studies, corneal sensitivity reduced progressively over the weeks of wear, with approximately a 50% increase in CTT by the end of 3 months with the X-Ten lenses. From these results it is evident that, even with lenses of high oxygen permeability, some loss of corneal sensitivity occurs.

A more recent study by Murphy *et al.* assessed the long-term effects of daily-wear soft contact lenses and rigid gas permeable (RGP) contact lenses on corneal sensitivity using the non-invasive air-pulse stimulus (-NCCA). Interestingly, while both lens reduced corneal sensitivity from normal levels, no significant difference was found between the results of each contact lens types: soft and RGP. A similar pattern of significance was found when the results for the peripheral test locations were compared, suggesting that there is no topographical variation in the effect of the two lens types. RGP lenses generally have a higher oxygen permeability than soft lenses and so should produce less of an effect on corneal sensitivity as a result of an impaired metabolic function. However, RGP lenses also produce a mechanical adaptation effect in the corneal nerves and this adds to the effect from the reduced metabolic function. In contrast, soft lenses do not have a mechanical action. When the metabolic and mechanical effects are combined for each lens type, they appear to produce a similar total effect on corneal sensitivity.

The second significant finding was that the duration of lens wear for both soft and RGP lenses doesn't affect the extent of sensitivity loss. It appears that with adaptation to the metabolic change and mechanical action of lens wear, a new balance between the metabolic requirements of the corneal nerves and their oxygen supply produces an altered corneal touch threshold.

The last important finding was the lack of topographical variation across the cornea in corneal sensitivity change. For negative power lenses, we might expect to find greater sensitivity loss in the periphery due to the increased lens thickness. However, the periphery should also receive more oxygen dissolved in the tears, via tear exchange under the lens, and so these effects may cancel each other out. In contrast, RGP lenses do not cover the corneal periphery, but have an increased mechanical action from the edges of the lens during blinking that may cause the corneal sensitivity loss in the periphery.

There have been no published studies that have considered the recovery of sensitivity af-

ter long-term soft lens wear. Nevertheless, we can expect a similar pattern of recovery to occur as with long-term PMMA lens wear. The only main speculation might be the length of time required to recover to normal levels. However, since soft lenses generally produce less of an effect on corneal sensitivity, a more rapid recovery should occur.

Possible mechanisms of corneal sensitivity loss

There are two main answers to the question of what causes the sensitivity loss with contact lens wear - metabolic impairment of the cornea or mechanical pressure on the cornea.

Polse passed 100% nitrogen gas over a subject's eye via a modified swimming goggle. After 2 hours wear, corneal sensitivity was unaltered, although corneal swelling was present. In a second experiment, he fitted subjects with PMMA lenses and this produced a loss of sensitivity, but no swelling. Polse concluded that it was not the oedema which induced the changes in corneal sensitivity, but rather the effect from mechanical stimulation.

Although there is some anectodal evidence that lenses which produce less mechanical stimulation give rise to a smaller decrease in corneal sensitivity, the mechanical action of a lens on the corneal nerves cannot be the only mechanism for corneal sensitivity loss. This is evident in a number of ways. Firstly, soft lenses still produce a reduction in corneal sensitivity. Secondly, when the eyes are closed overnight, corneal sensitivity declines as a result of a lower oxygen pressure at the corneal surface and not as a result of mechanical stimulation.[48] Thirdly, when the cornea is exposed to a reduced partial pressure of atmospheric oxygen, a reduction in sensitivity occurs.[49] In an experiment by Millodot and O'Leary (1980), the cornea was exposed to two different gas mixtures containing 2.1% oxygen and 3.15% oxygen, (normal atmospheric oxygen contains 10% oxygen). They found a strong relationship between the time of exposure to a reduced pressure of atmospheric oxygen and a reduced corneal sensitivity. They also found a time delay between the start of the experiment and the reduction in corneal sensitivity. With the 2.1 and 3.15% oxygen pressures, it took 3 and 4 hours respectively to produce a measurable change sensitivity. In the study by Polse described earlier, no change in corneal sensitivity occurred with a 100% nitrogen atmosphere, but the measurement was taken after only 2 hours and a longer period may be needed before any change can be detected.

The comparative impact between the mechanical action and the corneal oxygen supply can be demonstrated by considering the differing effects of PMMA and RGP lens wear on corneal sensitivity. In one experiment, subjects were fitted with a PMMA lens in one eye and a RGP (CAB) lens in the other. After 3 months of wear, a reduction in sensitivity was measured in the PMMA wearing eye, while practically no change occured in the RGP wearing eye.[36] Another experiment compared the effect of three RGP lenses, each with a different oxygen permeability, and found a relationship between the epithelial oxygen availability and changes in corneal sensitivity.[50] Bergenske and Polse also found that patients who are refitted with RGP lenses after having worn PMMA lenses often regain lens awareness.

From this series of experiments we can conclude that corneal sensitivity reduction is mediated by a change in the oxygen supply to the cornea and not simply by any mechanical stimulation. However, the mechanism by which the corneal nerves are affected by a reduced oxygen pressure is not clear. There is some evidence that acetylcholine is involved in corneal sensitivity. The corneal epithelium has the highest concentration of acetylcholine in the body. Tanelian *et al.* showed that acetylcholine instilled into the eye increases the action potential in the long ciliary nerves of the rabbit cornea. Pesin and Candia proposed that acetylcholine in the corneal epithelium plays a role in the regulation of sodium positive and chloride negative transport, both of which are necessary in the production of nerve impulses. The synthesis of choline acetyltransferase, the enzyme that

synthesises acetylcholine, is interfered with when the oxygen supply is reduced.[54, 55] Since such a situation occurs in contact lens wear, this may be one pathway for a reduced corneal nerve function.

Lastly, the reduction in corneal sensation may be due to corneal acidosis during contact lens wear. The pH of the body is carefully regulated to 7.4 and even a change of 0.05 can produce severe complications. Metabolic acidosis, and specifically lactic acidosis, can lead to depression of neural activity ranging from weakness and lethargy through to coma, depression of vital functions and ultimately death. Respiratory acidosis, due to hypercapnia (the accumulation of carbon dioxide), can lead to depression of neural function as well. The stromal pH is usually maintained at 7.54,[56] which is higher than that of the body, but closed eye wear of a PMMA lens can lead to a decrease of pH to 7.1.[57] Such a change would cause severe depression of neural function elsewhere in the body. Since both lactate accumulation and carbon dioxide are evident during contact lens wear, their increased concentration may be responsible for corneal hypoesthesia.

Conclusions

This review of the different studies has revealed the gradual effect of improved lens design on corneal sensitivity changes with contact lens wear. Early contact lenses, particularly PMMA but also soft lenses, had a greater impact on corneal physiology than more recent designs. These improvements have largely resulted from an improved oxygen supply to the anterior cornea. However, this continuing improvement in contact lens design may produce an interesting complication for silicone-hydrogel contact lens wearers. The high oxygen permeability of these lenses has encouraged their use in extended wear. However, the improved oxygen supply may also ensure that a higher level of corneal sensitivity is maintained, thereby reducing corneal comfort with the lens. Such a situation has not been reported anecdotally and there have been no published studies reporting on corneal sensation with silicone-hydrogel lenses, but this area still merits attention. Other areas of contact lens wear that require investigation are the influence of new generation, high oxygen permeable RGP lenses, and the recovery of corneal sensitivity after ceasing long-term daily soft lens wear.

This review has demonstrated the usefulness of assessing corneal sensitivity as a measure of corneal health with contact lens wear. Unfortunately, using the corneal sensitivity measurement as a predictor for contact lens wear success is not as useful. There are too many other variables, such as patient motivation and ambient environmental conditions, which can also have a significant impact.

Riassunto

Lenti a contatto e sensibilità corneale

Le fibre nervose corneali svolgono un ruolo importante nei meccanismi di protezione e di omeostasi della cornea e nell'epitelio corneale si osserva il maggior numero di fibre nervose libere dell'intero organismo. Le lenti a contatto vengono utilizzate sempre più spesso per correggere difetti di rifrazione o ai fini cosmetici. Di conseguenza, è importante studiare i rapporti fra uso delle lenti a contatto e innervazione corneale. Le indagini finora condotte hanno rilevato che l'impiego di lenti a contatto è in grado di causare una riduzione della sensibilità corneale di entità correlata al tipo e al materiale di costruzione delle lenti nonché alla frequenza e durata del loro impiego. Nel complesso, aumentando il periodo di tempo in cui le lenti vengono usate, sia in termini di giorni che di mesi, aumenta la perdita della sensibilità. Protraendo l'uso delle lenti, inoltre, si eleva il tempo necessario per riacquistare la sensibilità corneale originaria una volta sospeso l'uso delle lenti stesse. I materiali di costruzione di recente introduzione, caratterizzati da una maggiore permeabilità all'ossigeno, esercitano minori effetti sulla cornea. I sue meccanismi patogenetici principali alla base dell'alterazione della sensibilità corneale sono costituiti dall'irritazione meccanica da parte delle lenti e dell'interferenza con le funzioni metaboliche della cornea, secondarie al ridotto apporto di ossigeno. La ridotta funzione metabolica porta a un aumento dell'acidosi e a un'alterazione del pH corneale in conseguenza dell'ipercapnia. Entrambi questi fattori possono alterare la funzione delle fibre nervose e quindi ridurre la sensibilità corneale.

Parole chiave: Lenti a contatto - Cornea, fisiologia - Cornea, metabolismo.

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