Contact Lens Update
CLINICAL INSIGHTS BASED IN CURRENT RESEARCH

Ocular pain and discomfort: An overview

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Introduction

In general, pain refers to an unpleasant sensory and emotional experience associated with actual or potential tissue damage.[1] With respect to the eye, ocular pain typically relates to symptoms associated with a variety of ocular pathological conditions, particularly those affecting the anterior segment and ocular surface.[2]

Given that the pain experience involves complex underlying peripheral and central neural processes, this article will provide a brief overview of the causes of pain, the sensory signal processing of the eye, and how these particularly relate to dry eye symptoms and contact lens discomfort.

Nociceptive and neuropathic pain

Pain is usually generated by injuries that activate specific nociceptive receptors.[3] A nociceptor is a type of sensory receptor at the end of a sensory neuron's peripheral axon that responds to damaging or potentially damaging stimuli by sending signals of pain to the spinal cord and brain.[1] External physical or chemical stimuli that cause any form of tissue damage to the ocular tissues may activate these nociceptors.[3] The sensory information is processed at various levels of the neural pathways and finally projects to different areas of the brain, where pain sensations and unpleasant feelings associated with the eye are elicited.[2, 4] These sensory signals persist for a variable period of time until an appropriate level of healing takes place that the nociceptors are no longer stimulated. This so-called ''normal, physiological or nociceptive pain'' is a protective mechanism to prevent tissue damage and promote the healing process.[5] Acute eye pain may additionally trigger reflex responses such as blinking and tearing.[5-7]

While nociceptive pain is fairly common, another form of pain response ("neuropathic pain") can occur due to direct damage to the neurons of the body, resulting in messages of pain being sent to the central nervous system and brain regardless of the presence of noxious stimuli.[1] Peripheral neuropathic pain is evoked by damage to peripheral elements (such as nerve terminals and axons of the nociceptive neurons), while central neuropathic pain involves the higher-order neurons of the spinal cord, brain stem, thalamus, and various other subcortical and cortical structures that modulate the processing of peripheral nociceptive input.[1] Causes may include ocular surgery,[4] metabolic disease such as diabetes, ischemia, hemorrhage, mechanical compression of the nerves, infections, or degenerative processes occurring within the central nervous system that damage the neuronal structures composing the pain pathway.[8-11]

Sensory signal processing of the eye

The ocular surface, particularly the cornea, is densely innervated by sensory nerves that predominately derive

from the ophthalmic branch of the trigeminal (5th cranial) nerve.[12-13] The peripheral axons of the sensory neurons terminate at the ocular surface as naked free nerve endings and act as the nociceptors described above.[14]

Most of the sensory nerve fibers innervating the cornea and conjunctiva are so-called "polymodal nociceptors", as they are activated by mechanical, thermal and chemical stimuli, while a fraction of them are called "mechano-nociceptors" as they respond only to noxious mechanical forces.[2]

A further class of sensory nerve fibers on the ocular surface (about 10-15% of the total population) are termed "cold-sensitive receptors", which are activated by the reduction of ocular surface temperature and hyperosmolarity.[2,15]

Sensory information is detected and encoded by these differing types of receptors and transmitted to the higher levels of the processing pathway. The ability of these receptors to detect and convey information is dependent on the presence of a variety of complex and specialized transduction ion channels (protein molecules) embedded in the terminal membranes of nociceptors.[5]

The cell bodies of sensory neurons innervating the ocular surface are located in the trigeminal ganglion, from which the central axons of the neurons project and terminate in two regions of the trigeminal brainstem sensory complex (TBSC), the trigeminal subnucleus interpolaris/caudalis transition region (Vi/Vc) and the caudalis/upper cervical cord junction (Vc/C1).[16] Emerging evidence has suggested that ocular surface-responsive neurons at the Vi/Vc transition and caudal Vc/C1 region serve different functions in ocular homeostasis and sensation.[17-18] For example, the caudal Vc/C1 junction region mediates irritation and pain sensations, while the Vi/Vc transition region is more likely involved in other ocular sensations such as dryness, coolness, and itch, as well as homeostatic reflexes (tearing and eye blinking).[17-18] The second-order ocular neurons in the TBSC preferentially project to different areas in the brain to convey information associated with the sensory-discriminative and emotional aspects of pain.[19-20]

Dry eye symptoms and pain

The activity of corneal sensory fibers can be modified by inflammation caused by osmotic stress and tissue damage, as well as nerve injuries of the ocular surface.[5, 21] For example, noxious stimuli not only activate nociceptors causing pain but also can potentially damage ocular surface tissues, resulting in local inflammation. This can then increase the expression and lower the activation thresholds of transduction ion channels of the nociceptors.[22] In addition, sustained nociceptor activity itself could result in the release of sensitizing proinflammatory cytokines (neurogenic inflammation).[2] All these result in increased sensitivity and responsiveness to noxious stimuli of the nociceptors, a process called "peripheral sensitization" and lead to pain/irritation sensation being initiated with lower levels of stimulation.[22] During corneal axon regeneration due to injury or disease, the process of incoming signals from the ocular surface could be altered, producing central sensitization and enhanced pain.[15]

Recent studies have shown altered sensory responses in dry eye,[23-25] post-LASIK26 and contact lens discomfort,[5, 27] suggesting that dry eye may be viewed as a disease involved in a dysfunctional corneal and/or ocular surface pain system, including peripheral and central sensitization, and altered descending modulation of the nociceptive pathway.[28-29]

An understanding of the basic processes involved in ocular sensation is critical to development of methods to modify and overcome the pain and discomfort associated with conditions commonly encountered in everyday clinical practice. These include patients who have undergone LASIK, contact lens wearers who report discomfort and those who exhibit symptomatic dry eye.

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