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Research article

Interpreting the corneal response to oxygen: Is there a basis for re-evaluating data from gas-goggle studies?

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ABSTRACT

When anoxia (0% oxygen) is created within a gas-tight goggle, ocular physiological responses, including corneal swelling, limbal hyperaemia and pH change, are known to vary, depending on the presence or absence of a low, oxygen transmissibility contact lens. A new theory is proposed to account for this discrepancy based on the concept of lid derived oxygen, whereby oxygen originating from the vascular plexus of the palpebral conjunctiva supplements that available to the ocular surface in an open, normally blinking eye, even when the surrounding gaseous atmosphere is anoxic. The effect of a lid derived contribution to corneal oxygenation was assessed by using existing experimental data to model open-eye, corneal swelling behavior as a function of atmospheric oxygen content, both with and without the presence of a contact lens. These models predict that under atmospheric anoxia, contact lens wear results in 13.2% corneal swelling compared with only 5.4% when the lens was absent. Lid derived oxygen acts to provide the ocular surface in the non-contact lens wearing, normally blinking, open-eye with up to 4.7% equivalent oxygen concentration, even within the anoxic environment of a nitrogen filled goggle. Correcting for lid derived oxygen eliminates previously observed discrepancies in corneal swelling behavior and harmonizes the models for the contact lens wearing and gas-goggle cases. On this basis it is proposed that true anoxia at the ocular surface cannot be achieved by atmospheric manipulation (i.e. a gas-goggle) alone but requires an additional presence, e.g. a low, oxygen transmissibility contact lens, to prevent access to oxygen from the eyelids. Data from previously conducted experiments in which the gas-goggle paradigm was used, may have been founded on underestimates of the real oxygen concentration acting on the ocular surface at the time and if so, will require re-interpretation. Future work in this area should consider if a correction for lid derived oxygen is necessary.

1. Introduction

Some years ago, it was observed that during open-eye, anoxic conditions produced in a gas goggle, greater corneal thickening occurred when a thick, low oxygen transmissibility, hydrogel contact lens was on the eye than when it was absent (Sweeney, 1991). At this time, the availability of atmospheric oxygen had long been understood as the key driver of corneal oedema (Smelser and Ozanics, 1952) and a clear, inverse relationship between the amount of swelling and the oxygen transmissibility of the contact lens was already established (Holden and Mertz, 1984). Against that background, these observations were something of a surprise. The nitrogen filled goggles used for the experiment eliminated any possibility that atmospheric oxygen could reach the ocular surface, so the presence or absence of the contact lens should have made no difference to the resulting corneal swelling. The fact that swelling was greater with a lens in place confirmed that the lens and no-lens responses to hypoxia are not comparable, a situation that had been suggested by an earlier experiment in which contact lenses were used to produce equivalent oxygen percentages at the cornea which matched those created in gas-goggles (Brennan et al., 1988).

Awareness of this discrepancy prompted speculation as to its cause (Brennan et al., 1988) and some factors, such as lens induced

Abbreviation are used: LDO, lid derived oxygen; TFOT, tear film oxygen tension; Dk/t, oxygen transmissibility.

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humidity changes and temperature increases, were investigated without a successful solution being found (Sweeney, 1991; Bonanno and Polse, 1987).

Work conducted a few years earlier, had observed a difference between the levels of acidosis during gas-goggle anoxia and contact lens wear and demonstrated that this could be explained if there was significant carbon dioxide accumulation beneath the lens (Bonanno and Polse, 1987). Although this study did not directly measure the corresponding lens induced corneal thickness changes, it did seem to offer an explanation for the lens vs no-lens problem by raising the possibility that hypercapnia related acidosis could contribute additional amounts of swelling when a lens was present.

The issue resurfaced a few years later however, when a similar anomaly occurred while observing the limbal hyperaemia response. On this occasion, roughly twice the level of vascular activity accompanied open-eye, contact lens wear (peripheral Dk/t ~ 6×10^{-9} [(cm/s) (mlO_2/ml x mm Hg)]) as under conditions of total anoxia (Papas, 2001). Like corneal swelling, limbal hyperaemia is understood to be influenced by the availability of oxygen (Papas, 2003), albeit through a different physiological mechanism. Evidently, the two responses are also alike in that the presence of a contact lens accentuates behavior beyond what would be expected in the absence of oxygen alone. In this case however, it was not possible to explain the behavior on the basis of hypercapnia, since the vascular response appeared to be independent of the level of central corneal oedema (Papas, 2003) and was not influenced by the presence of carbon dioxide in the local atmosphere (Papas, 2001).

Consideration of the similarities and differences between these situations, together with a careful analysis of the relevant physical and anatomical factors has suggested the need for an alternative hypothesis to explain the observed effects. The purpose of the present communication is to propose such a hypothesis and demonstrate its consistency with available data. Not only do the results offer a potential means of unifying the lens and no-lens responses of the cornea and ocular surface to hypoxia but they raise the possibility that outcomes of experiments where gas goggles have been used to adjust oxygen exposure to the ocular surface may need reinterpretation.

2. The lid derived oxygen (LDO) hypothesis

Under normal circumstances, the open eye at sea level is bathed with atmospheric oxygen at a partial pressure (pO_2) of 155 mmHg. This direct source of oxygen becomes unavailable during eye closure, as the lids effectively block gas flow in either direction. Fortunately, even while trans-palbebral gas flow is prevented, the blood vessels of the palpebral conjunctiva provide an important alternative oxygen source capable of maintaining a partial pressure (pO_2) of about 55 mmHg (Sweeney, 1991; Fatt and Bieber, 1968; Efron and Carney, 1979) in the closed eye. This is shown schematically in Fig. 1 where the theoretical oxygen tension in the tear film of a closed eye under anoxic atmospheric conditions ($^{N}TFOT_2$) is ~55 mmHg.

Consider now a situation where an open, non-contact lens wearing eye, is placed in an environment intended to create anoxia, such as would exist within a nitrogen filled goggle. As no atmospheric oxygen is available, anoxic conditions are anticipated over all exposed ocular surfaces. Evidently however, large portions of the globe remain covered by the lids and so are in contact with the palpebral vascular system from where they can potentially receive oxygen. It is proposed that oxygen beneath the eyelids i.e. “lid derived oxygen” acts as a secondary source that is utilisable by the cornea and other exposed tissues so that they gain physiologically significant amounts of oxygen even when atmospheric conditions are arranged to be anoxic.

Usually the regions covered by the lids are the inferior and superior bulbar conjunctivae, though in many individuals, portions of the limbus and peripheral cornea are also hidden. These areas, where the interaction with the oxygen supply of the palpebral conjunctiva is more or less continuous, are thus relatively privileged when anoxic atmospheric conditions exist. While interpalpebral oxygen tension, i.e. at the corneal apex, might approach zero, it will be higher beneath the covering eyelids, up to a potential maximum of 55 mmHg. It also seems likely that significantly nonzero levels of oxygen tension will always exist across the ocular surface, even at the corneal apex. This is because the action of blinking brings essentially all parts of the cornea into intermittent contact with the palpebral vessels, and other processes, such as diffusion and blink assisted tear mixing, will act to distribute oxygen derived from the lids throughout the tear film. Tear film oxygen tension in the open eye will therefore always be greater than 0, though less than 55 mmHg ($^{N}TFOT_1$ in Fig. 1). From this analysis it follows that, provided normal blinking and respiration continue, preventing all atmospheric oxygen interacting with the open eye (as in a goggle) does not produce truly anoxic conditions at the ocular surface.

If a soft contact lens[1] is now placed on this cornea, the situation becomes that shown by $^{N}TFOT_3$ in Fig. 1. The lens acts to insulate the ocular surface from lid derived oxygen, so that, apart from the potential for the minor exchange of post-lens tears on blinking (believed to be less than 2% of the tear volume per blink (Polse, 1979; McNamara et al., 1999)), those parts of the eye lying beneath the lens can now only receive oxygen by transmission through its bulk. Thus, while the oxygen tension at the lens front surface will be essentially the same as at the ocular surface in the absence of the lens, the amount that percolates into the post-lens space depends almost entirely on the lens oxygen transmissibility and its level will lie between 0 and whatever is the value of $^{N}TFOT_1$.

Except in the case of infinite Dk/t, it can be said with some generality that in an imposed anoxic atmosphere, the open-eye, ocular surface oxygen tension will always be lower beneath a soft contact lens than when no lens is present ($^{N}TFOT_3$ in Fig. 1) and the size of this difference will increases as Dk/t diminishes.

In summary, the presence of lid derived oxygen prevents true anoxia from being achieved during nitrogen goggle experiments unless a lens of quite low oxygen transmissibility is on the eye at the same time. The discrepant findings for corneal swelling and limbal hyperaemia mentioned earlier can thus be understood as being the results of underestimating the true depth of anoxia created during the respective experiments. It should be further noted that lid derived oxygen will be available to the ocular surface in any circumstance where atmospheric manipulation is attempted, with the result that the true level of hypoxia achieved will be somewhat less than expected based on the oxygen content of the applied atmosphere. This will affect most gas-goggle type experiments involving reduced oxygen tension.

3. Consequences of LDO

To see how LDO affects the interpretation of previous findings, data derived from the series of corneal swelling studies conducted by Sweeney (Sweeney, 1991) were re-evaluated. For the present purpose, the key pieces of information emerging from those investigations were:

[1] This treatment primarily refers to soft lenses, however any lens that covered the entire cornea and extended beyond the limbus would be expected to produce similar effects.