DETERGENT PENETRATION INTO YOUNG AND ADULT EYES

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Summary

Using animal models, we have examined the effects in the eye of one of the detergents, sodium lauryl sulfate (SLS), that is included in soaps and shampoos. We also have determined how SLS is taken up by the eye. Four findings have ensued: first, SLS is rapidly taken up and accumulated by eye tissues. SLS is retained for up to five days in most eye tissues. Second, SLS uptake is greater in younger rabbits with decreasing amounts with increasing age. Third, SLS causes changes in the amounts of some proteins of eye tissues whether they are treated in the living animal or tissues are bathed in SLS while in tissue culture. Fourth, SLS treatment extends the healing time of the corneal epithelium (the cellular surface layer of the cornea) to 10 days, far beyond the normal two days.

Our findings lead us to call for more judicious use of detergents such as SLS by both manufacturers and users of soaps and shampoos. This is particularly true when possible accidental exposure to SLS could occur in infants, where growth is occurring, and in any instance where a healing process occurs.

Significance

Because SLS and related substances are widely used in many populations on a daily basis in soaps and shampoos, there is an immediate concern relating to the penetration of these chemicals into the eye and other tissues. This is especially important in infants where considerable growth is occurring, because a much greater uptake occurs by tissues of younger eyes, and SLS changes the amounts of some proteins in cells from eye tissues. Tissues of young eyes may be more susceptible to alteration by SLS.

We offer a cautionary note, therefore, on the use of SLS as an ingredient of soaps and shampoos, not only because of the possibility of accidental exposure to the eye particularly in infants, but also in any eye that is healing, such as after surgery, after injury or during contact lens wear. Thus, the use of SLS should be more judicious until safety is totally proven. The accidental (as with infants or adults using shampoos), or deliberate (as with using shampoos as eye scrubs before surgery), exposure to SLS results in accumulation in eye tissues, a process that could retard healing as well as potentially have long-term effects.

Background

Three types of detergents occur: cationic, anionic and non-ionic. Cationic detergents are the most irritant to the rabbit eye, followed by anionic and non-ionic detergents (Draize and Kelly, 1952). In man, non-ionic detergents made the cornea more permeable, as was found in a study of the penetration of a dye called fluorescein into the eye (Marsh and Maurice, 1971). A cationic detergent, benzalkonium chloride, has been included in topical ophthalmic solutions, such as those used to treat glaucoma, for many years. As an illustration of detergent effects one drug (carbachol) that does not normally enter the eye, but which causes pupillary constriction when given into the eye, could be made to induce is pharmacological effect after the inclusion of benzalkonium chloride in an eye drop. This detergent has bacteriocidal **activity** and sustains the sterility of eye-drop solutions while assisting the penetration of drugs. The concentration of benzalkonium chloride in eye drops is sufficiently low not to cause any toxic effects on eye tissues.

Because of our long-standing interest in the effects of benzalkonium chloride on corneal permeability, we undertook studies on the penetration of radioactive benzalkonium chloride into eye tissues. This detergent only penetrated into the cornea (the transparent "window" of the eye), and the conjunctiva (the tissue lining the eyelids and ocular surface [except the cornea]) (Green and Chapman, 1986). Tissues of young animals accumulated greater quantities of material than those of adult animals (Green et al., 1987a).

We then examined an anionic detergent, sodium lauryl sulfate which is commonly found in soaps and shampoos, that showed penetration into the eye, as well as systemic tissues (brain, heart, liver, etc.). SLS also showed long-term retention in tissues (up to five days after a single drop, and was absorbed much more readily in young animals than in adult rabbi (Clayton et al., 1985). The retina and lens of the neonatal eye contained twice as much SLS as animals of other ages (Green et al., 1987b,c).

We took tow approaches to study the effect of SLS on amounts of different proteins in cells. We treated animals with eye drops containing SLS, and also grew cells in tissue culture which were exposed to the same SLS concentrations in the test tube as were found in the living eye. Some proteins increased and others decreased. We are unsure of the significance of these findings, but changes of any kind raise questions regarding long-term effects. Protein changes can occur either through direct effects on the production and breakdown by the cell, or longer-term effects at the level of regulation, of protein metabolism.

There has not been sufficient time to determine whether the protein changes are deleterious to the eye, are reversible, or whether they are associated with an acceleration of some natural process (such as cataract formation, a clouding of the lens). No evidence exists that there is an observable response, but many changes in the eye are reflected in protein alterations. Due to the widespread use of such detergents where exposure to the eye may occur, any immediately dangerous situations should have been readily

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observable. Certainly by all acceptable criteria materials such as SLS product no undue effects. What we have found, however, is that there may be far more subtle changes occurring that are not revealed in classical toxicity testing which is required before over-the-counter products are put on the market.

There may be the induction of disadvantageous effect with a long latency period, i.e., the results of any changes may not be revealed for many years. This is particularly true in cells that are growing, differentiating (becoming specialized) and dividing, as in neonatal tissues. To illustrate effects on young cells we performed studies on embryonic chick retinal cells grown in tissue culture. These cells normally put out axons (projections) that ultimately would interconnect to form the retina. During incubation in SLS, however, no axonal outgrowth occurred (Clayton et al., 1985). It may be that other changes caused by SLS in the eye are subtle, but SLS may be another environmental material that could result in changes only after a considerable time period. The changes in cell proteins could result in tissue disturbance only after several years of function.

In the laboratory setting designed to study wound healing, SLS delayed the healing process of the corneal epithelium. We created lesions of a specific size and recorded healing using photography; such lesions normally heal in 48 hours. When treated with SLS, the lesion initially decreased but then expanded to a size larger than that created. At four days, the area was about 50% to 60% of the original size, and complete healing took about 9 or IO days. The model used for this study uses lesions that are larger than those that normally occur in the corneal epithelium. This may be explained by the high levels of SLS that are accumulated in the epithelium.'

Techniques

We used a radioactive form of SLS to more easily measure the small quantities found in the tissues since chemical methods are too intensive. The SLS concentration was 10% of that normally used in shampoos, etc. to allow for normal dilution that occurs before coming into contact with the eye. In the healing studies, lesions were created by scraping off cells. The area was measured from photographs using a computer graphics pad.

Statistics

During the tissue distribution and healing studies, a sufficient number of animals of all ages were used. The studies were initiated in 1982/83 during my sabbatical year at the University of Edinburgh, Scotland, and continued upon my return to the Medical College of Georgia in Augusta.

Human Interest

The observation that ultimately led to these studies began in the early 1970's when we noted that some ophthalmic drugs increased corneal penetration of a dye, and that the detergent benzalkonium chloride, which is included in these drug solutions, was the causative agent. Such results had been obtained in the 1940's but our work opened up further examinations using newer techniques, The availability of custom synthesized radioactive materials allowed measurements of the penetration of these detergents into eye tissues. Our interests also arose from studies of others (Miller and Patton, 1981, 1982) showing that drug distribution in the eye is modified by age.

REFERENCES

Clayton, R. M., Green, K., Watson, M., Zehir, A., Jack, J. and Searle, L. (1985). The penetration of detergents into adult and infant eyes: Possible hazards of additives to ophthalmic preparations. Fd. Chem. Tax. 23, 239. Draize, J.H. and Kelley, E.A. (1952). Toxicity to eye mucosa of certain cosmetic preparations containing surface-active agents. Proc. Scient. Sect. Toilet Goods Assn. 17,l. Green, K and Chapman, J.M. (1986). Benzalkonium chloride kinetics in young and adult albino and pigmented rabbit eyes. J. Toxicol, Cut *and Ocular* Toxicol, 5,133. Green, K., Chapman, J.M., Cheeks, L., Clayton, R.M., Wilson, M. and Zehir, A. (1987a). Detergent penetration into young and adult rabbit eyes: Comparative pharmacokinetics. J. *Toxicol, Cut and Ocular Toxicol, 6,89,* Green, K, Chapman, J., Cheeks, L. and Clayton, R.M. (1987b). Surfactant penetration into the eye. *Concepts Toxicol,* 4, 126. Green, K., Cheeks, L., and Chapman, J.M. (1987c). Surfactant pharmacokinetics in *the eye.* In, *"Ophthalmic Drug Delivery, Biopharmaceutical, Technological and Clinical Aspects."* (Ed., M.F., Saettone, G. Bucci and P. Speiser). Liviana Press, p. 171. Marsh, R.J. and Maurice, D.M. (1971). Influence of non-ionic detergents and other surfactants on human corneal permeability. Exp. Eye Res. 11, 43, Miller, S.C. and Patton, T.F. (1981). Age-related influences in ophthalmic drug disposition. I. Effect of size on the intraocular distribution of pilocarpine in albino rabbi. Biophannacol. *Dug Dispos. 2,215,* Miller, S.C. and Patton, T.F. (1982). Age-related influences in ophthalmic drug disposition. II. Drug-protein interactions of pilocarpine and chloramphenicol. Biophamacol. *Drug Dispos. 3, 115.*