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ORIGINAL ARTICLE

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A randomised controlled study of the efficacy of hypromellose and Lacri-Lube combination versus polyethylene/Cling wrap to prevent corneal epithelial breakdown in the semiconscious intensive care patient

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Abstract *Objective:* To compare the efficacy of two forms of eye care (hypromellose and Lacri-Lube combination vs polyethylene/Cling wrap covers) for intensive care patients. *Design:* Randomised-controlled trial. *Setting:* University affiliated, tertiary referral hospital. *Patients and participants:* One hundred ten patients with a reduced or absent blink reflex were followed through until they regained consciousness, were discharged from the facility during study enrolment, died or developed a positive corneal ulcer or eye infection. *Interventions:* All patients received standard eye cleansing every 2 h. In addition to this, group one (n=60) received a treatment combining hypromellose drops and Lacri-Lube (HL) to each eye every 2 h. Group two (n=50) had polyethylene covers only placed over the eye to create a moisture chamber. *Measurements and results:* Corneal ulceration was determined using corneal fluorescein stains and mobile slit lamp evaluation, performed daily. No patients had corneal ulceration in the polyethylene cover group, but 4 patients had corneal ulceration in the HL group. *Conclusions:* Polyethylene covers are as effective as HL in reducing the incidence of corneal damage in intensive care patients.

Keywords Clinical nursing research · Critical care · Eye · Epithelium · Corneal

Introduction

Patients in intensive care require a high standard of nursing practice to ensure patient comfort and safety. In patients with lowered levels of consciousness, providing basic eye care is an essential part of that practice. These patients, due to impairment of protective eye mechanisms, are susceptible to corneal dehydration, abrasions, corneal perforation and infection. The reported incidence for corneal abrasion ranges from 3 to 60% [1, 2, 3], with the peak incidence between 2 and 7 days from intensive care unit (ICU) admission. [2, 4].

Previous reports have outlined the frequency and considerable variability of eye care treatments performed among institutions [5]. In the majority of units, eye care is often carried out every 2 h. Normal saline irrigation, eye drops, taping, paraffin-based gauze, ointments, gels and polyethylene are among methods used to prevent eye trauma. There is limited research available to determine or compare the efficacy of treatment modalities, making the description of evidence-based practices limited. As a result, eye care treatment continues to be performed by nurses on the basis of individual beliefs and tradition.

In our ICU, two methods of eye care have been frequently employed to prevent drying of the eyes. The first, "open chamber" method is a combination of the lubricant Lacri-Lube (Allergan Australia Pty Ltd) and an artificial tear preparation containing hypromellose (Methopt-tears, Sigma Pharmaceuticals). A review of the literature found that there have been no studies examining the effectiveness of this hypromellose/Lacri-Lube combination (HL). The second, "closed moisture chamber"

method involves polyethylene covers (Cling wrap) secured over the eye. In our ICU, this treatment is generally only for patients with gross lagophthalmos (the inability to close, or poor closure, of the eyelids) or eyelids that are swollen shut, e.g. from burns or trauma. One study has been published that suggests polyethylene covers are effective in preventing corneal ulceration in critically ill patients [6].

To improve the evidence-based practices within the unit, a study was undertaken to evaluate the effectiveness in preventing corneal damage of two methods of eye care: the open chamber treatment using HL vs the closed moisture chamber method using polyethylene.

Materials and methods

A randomised controlled trial was conducted with institutional ethics committee approval. The Royal Brisbane Hospital is a 700-bed university-affiliated, tertiary referral hospital with specialties including burns and bone marrow transplantation. The ICU has 18 beds and over 1400 patients are admitted per annum with an average length of stay of just under 4 days.

Patients were recruited from the ICU over a 7-month period and included in the study if they were aged over 18 years, mechanically ventilated and unconscious, as assessed by the bedside nurse. The frequency of eye opening was limited to less than five blinks per hour, to allow for patients who were unconscious, but opened their eyes briefly in response to stimuli, such as during suctioning.

Exclusion criteria were patients with a pre-existing eye condition (history of eye trauma, disability or inflammation, chronic lagopthalmos) or patients with a previous admission to ICU within a month of enrolment. Patients excluded from the study received eye-care treatment determined by the bedside nurses' discretion.

The ICU patients meeting the inclusion criteria were simply randomised to either of the two treatment groups using a computer-generated random number. All patients received a standard eye cleansing regime of second hourly washes to the external eye using 0.9% saline and sterile gauze. Patients randomised to HL received two drops of hypromellose and a 1-cm strip of Lacri-Lube to each eye every 2 h. The other patients had pieces of polyethylene cut to cover the eye from the eyebrow to the cheekbone. To ensure the area was sealed, Micropore (3 M Healthcare) was used around the edges of the polyethylene. The polyethylene was changed each shift or as needed if they became unclean or torn.

Patients completed the study if they regained spontaneous eye opening, were discharged from the facility during study enrolment, died or developed a corneal ulcer or eye infection.

Eyes were examined for corneal ulceration using fluorescein drops and a portable slit lamp (Kowa, SL-14). This was conducted by one of two intensivists, who had both received training by the staff ophthalmologist. Inter-rater checks were performed prior to the study commencement and established reliability between these two operators. The corneal fluorescein stains were performed daily on all patients enrolled in the study.

A sample size estimate for the study used the findings of Cortese et al. [6], where 8 of the 30 patients (26.7%) receiving methylcellulose drops had positive fluorescein stains compared with only 1 of 30 patients (3.3%) with polyethylene covers. With a significance level of 0.05, power of 0.8 and a difference in the proportions between cases and controls of 0.24, a minimum of 42 subjects per group were required [7].

Data were collected on demographics including age, gender, diagnosis, APACHE II score, hours on the study and reason for completing the study. Additional data was collected on potentially confounding variables including the amount of time patients received sedation or muscle relaxants, gross resting position of the eyelids and number of times the pupil response was checked as this observation was considered essentially a manual blink.

Descriptive and potentially confounding variables were tabulated by groups. Differences in categorical variables were tested using chi-square. Continuous variables were assessed for normality of distribution using the Kolmogorov-Smirnov statistic. Normally distributed continuous variables were tested for difference using Student's t test. Non-parametric continuous variables were tested for difference using the Mann-Whitney U and Fisher's exact tests.

Results

One hundred ten subjects were recruited for the study. Of these patients, 106 (96.4%) completed the study with no eye damage: 77 (70%) regained spontaneous eye opening, 24 (21.8%) died and 5 (4.5%) discontinued treatment on discharge from the ICU. Four (3.6%) patients developed corneal damage.

After randomisation, 50 patients were assigned to treatment with polyethylene and 60 patients to treatment with HL. Demographic criteria were similar between the groups (Table 1). The confounding variables relating to eye care, mean study hours, number of patients with lagopathalmos, number of pupil checks and the mean hours of sedation and muscle relaxant used showed no statistically significant difference between the two groups. The populations were comprised of mainly medical and neurological admissions, but also included surgical, burn and trauma cases (Table 2).

No patients had corneal ulceration in the polyethylene group. Four patients had corneal ulceration in the HL group (three in burn patients). This represented 6887 h of follow-up in the polyethylene group and 8796 h of follow-up in the HL group. The incidence of corneal ulceration in the two groups was not significantly different (Fisher's exact, p=0.12).

Table 1 Success of randomisation: descriptive and potentially confounding variables. *HL* hypromellose drops and Lacri-Lube

	Polyethylene	HL	p
Percentage	45.5	54.5	–
Male (%)	66.0	51.7	0.13
Age (years)[a]	50.1 (18.6)	55.1 (18.5)	0.16
APACHE II[a]	22.2 (6.6)	21.1 (7.1)	0.41
Hospital length of stay (days)[b]	29.5 (43.3)	27.0 (30.3)	0.51
ICU length of stay (days)[b]	12.5 (12.3)	11.0 (12.8)	0.47
Time on Study (h)[b]	104.5 (97.3)	126.5 (136)	0.61
Lagopthalmos present	5	7	0.78
Pupil checks/day[b]	10.5 (17)	19.0 (17.8)	0.59
Sedation (h)[a]	117.3 (89.7)	89.7 (72.6)	0.08
Muscle relaxant >2 h (%)	44.0	26.7	0.06

[a] Mean (standard deviation)
[b] Median (interquartile range)

Table 2 Distribution of diagnostic categories

Diagnostic category	Polyethylene		HL		Total	
Burn	6	(5.5)	5	(4.5)	11	(10)
Medical	17	(15.5)	24	(21.8)	41	(37.3)
Elective surgery	1	(0.9)	0	(0)	1	(0.9)
Emergency surgery	6	(5.5)	2	(1.8)	8	(7.3)
Trauma	2	(1.8)	5	(4.5)	7	(6.4)
Neurosurgical	18	(16.4)	24	(21.8)	42	(38.2)
Total	50	(45.5)	60	(54.5)	110	(100)

Fisher's exact test=0.357

Table 3 Burn patient summary. *TBSA* total body surface area assessment

Descriptor	Polyethylene	HL	*p*
TBSA[a]	55 (47.5)	75 (61)	0.65
Facial burns present (%)	66.7	80.0	1.0
Mechanism=flame burn (%)	100	80.0	0.46

[a] Median (interquartile range)

Previous literature suggested that burn patients may have different results to the other patients [8, 9]. Three (75%) of the corneal damage events occurred in the burn population; therefore, further analysis of this subgroup was conducted. Between the two groups in this study, there was no significant difference in burn total body surface area assessment (TBSA), involvement of the face or mechanism of injury (flame, scald, electrical, other; Table 3). The median hours to the development of corneal ulceration among the 3 patients with burns was 177. The one other patient developed corneal ulceration after 253 h. Although of small sample size, this demonstrated a trend towards earlier time to onset of corneal ulceration in the burn population (Kruskal-Wallis test, p=0.18).

Discussion

This is the first randomised study to assess the efficacy of eye care with polyethylene or HL in ICU. The cornea is an avascular layer of stratified, non-keratinised, non-secretory epithelium. It relies on a tear film to maintain adequate corneal wetting and carry oxygen particles for aerobic metabolism of nutrients [10, 11, 12]. Eyelid closure and blinking contribute to replenishing and spreading the tear film across the cornea and preventing tear film evaporation [10, 11, 13].

Improper "wetting" of the corneal surface through inadequate eyelid closure or production of tears can lead to tear film rupture, corneal drying and superficial corneal abrasions. Furthermore, once the tear film is ruptured, microbes are able to adhere to the damaged corneal epithelium [14, 15] and may further erode the ocular surface causing ulceration or perforation [16]. As a highly sensitised and extensive network of nerves is located between the epithelial cells of the corneal surface layer, corneal damage can result in considerable pain.

Corneal ulceration can be treated with eye lubricants and antibiotic eye drops. Although they often heal without incident, long-term problems can include scarring and visual acuity deficits including blindness [10, 12]; therefore, it is vital to prevent the deterioration of the ocular surface in ICU patients, in order to prevent the development of ocular disease.

In unconscious or semiconscious patients, several factors may contribute to inadequate tear film. Lagophthalmos may be present if the action of the obicularis occuli muscle is suppressed, resulting in the lower eyelid sagging away from the eyeball. This can occur in normal sleep, but also the depth of sedation and paralysis is reported to closely relate to the degree of lagophthalmos and the presence of ocular surface disease [4]. Corneal oedema can be a side effect of the raised venous pressure and reduced venous blood return experienced during positive pressure ventilation again limiting natural eyelid closure [17]. Sedatives and anaesthesia suppress the blink reflex, hindering adequate tear spread.

Prior studies conducted in patients undergoing anaesthesia have reported a high incidence of corneal abrasion when no treatment is given to the eye, particularly if the patient's eyes are lagophthalmic during surgery [19, 20, 21, 22, 23]. An array of approaches have been used to ensure the eyelids remain closed including the use of passive closure, hypoallergenic tape (e.g. Micropore), eye pads/patches, Geliperm, saline soaked pads, Jelonet and suturing. The application of Geliperm is a common method of maintaining eyelid closure [5]; however, there are no randomised controlled trials establishing its effectiveness and corneal abrasions may occur if the gel is allowed to dry [18]. Batra and Bali [19] examined the effect of taping, vaseline gauze or no treatment in 200 patients during general anaesthesia. They reported no corneal abrasions in the patients whose eyes were either taped closed or received vaseline gauze. Other studies support the efficacy of taping in the prevention of corneal erosions during anaesthesia [2, 19, 20, 21, 22, 23]; however, it can irritate the skin and it may be difficult to assess for or obtain adequate eyelid closure particularly if there is any lubricating ointment on the skin or conjunctival oedema. No other studies have been identified that effectively evaluate the use of eye pads/patches, gauzes or suturing during anaesthesia or intensive care for the purpose of maintaining eye closure.

Products that have been reported to prevent corneal drying and maintain tear film include polyethylene, hypromellose drops (e.g. Methopt tears), Geliperm (Geistlich Sons Ltd), paraffin-based lubricants (e.g. Lacri-Lube, Duratears [Alcon Laboratories (Australia) Pty Ltd)] or gauzes (e.g. Jelonet, Smith and Nephew) and lubricating antibiotics. There is limited research evaluating these methods of eye care; however, the use of certain

eye drops appears to be more effective than no treatment at all [3] and polyethylene may provide greater protection than hypromellose against corneal ulceration [6]. Lenart and Garrity [3] undertook a randomised controlled trial with 50 intensive care patients receiving neuromuscular blocking agents or propofol during mechanical ventilation. In each patient, Duratears was applied to one eye every 4 h and passive eyelid closure was performed by a nurse as necessary to the other eye (control). Two treated eyes compared with nine control eyes developed corneal abra-sions (p=0.004). Cortese et al. [6] evaluated the effectiveness of placing polyethylene over the eyes compared with instillation of hypromellose lubricating drops to the eyes every 2 h in 60 intensive care patients. Eight of the 30 patients who had received the hypromellose drops had positive fluoroscein staining, compared with only one in the polyethylene group (p<0.05).

Hypromellose drops are designed as an artificial tear-film substitute. Based on a cellulose compound they are water soluble and reportedly maintain visual clarity post application. Hypromellose solutions decrease the viscosity of the tear film, which enhances the tear-film thickness and prolongs corneal contact time, thereby extending tear break-up time [24, 25].

Lacri-Lube consists of white paraffin, mineral oil, non-ionic lanolin derivatives and chlorbutol (0.5%). It is an eye lubricant recommended for dry eye complaints. It also assists in the stabilisation of the tear film. Dissolving at ocular surface temperature, it is applied as a 1-cm ribbon strip inside the lower eyelid margin where it is then spread with the tear film. Lacri-Lube has been noted to remain longer in the tear fluid than other eye solutions and is thought to be due to the paraffin and mineral oil composition, which is not removed easily by the lacrimal drainage system. Blurred vision is a documented side effect of its use, and significant reductions in visual acuity have been demonstrated for several hours after its use in patients undergoing general anaesthesia [20, 25].

Polyethylene is a recognised eye care treatment for unconscious or semiconscious patients. More commonly, it is known as Glad wrap or Cling wrap. The polyethylene covering creates a moisture chamber providing a barrier against tear-film evaporation and exposure to air currents. It may also keep the eye clean and closed by providing a physical barrier to organisms and preventing possible translocation of infections from sources such as the respiratory tract [26]. Cortese et al [6] reported a trend for more patients to have a closed resting eye position when treated with polyethylene. While further research is needed to determine a significant physical reduction in eye closure with polyethylene, its closed moisture chamber mechanism may provide an artificial means of attaining eyelid closure that is sufficient to prevent corneal drying. This may be advantageous over other methods of eyelid closure, which rely on a proper assessment and attainment of eyelid closure.

Assessing for eyelid closure can be difficult as the eyes in a muscle relaxed patient may appear closed, yet be open 1–2 mm in the medial inferior portion of the cornea [16]. Suresh et al. [27] found that despite education and awareness of the problem, corneal exposure continued to be missed during eye care assessments. Cunningham and Gould [28] also demonstrated that the quality of clinical assessment and eye care practice performed by nursing staff was not related to the extent of clinical experience and/or knowledge of eye care principles. The ease of application and removal of polyethylene may negate some of these concerns. Its transparency may facilitate assessment by allowing more frequent observation and monitoring of the cornea.

Prior research has demonstrated that the use of hypromellose drops appears to be more effective than no treatment at all [3], but polyethylene may provide even greater protection than hypromellose against corneal ulceration [6]. This study found no significant difference between polyethylene covers and a HL combination in their ability to prevent corneal ulceration.

Additional considerations for clinical practice include the ease of application and expense associated with the two techniques. In a busy ICU environment, two-hourly eye care is not always achieved due to factors such as additional procedures or operations being performed. During these times, failure to perform eye care may increase the risk of ulceration. Literature searches failed to provide any information on the duration a single application of eye drops (and/or Lacri-Lube) or polyethylene coverage remains efficacious. We presume that, when eye care is delayed, and a polyethylene cover remains intact, the moisture chamber effect would be maintained. Alternately, if the instilled HL agents have not retained efficacy after 2 h (e.g. due to evaporation or dilution), the risk of corneal ulceration may be increased. Unfortunately, this study did not record compliance to the protocol's regime of two-hourly saline cleaning of the external eye or the duration that techniques remained efficacious.

Polyethylene covers are cheap. The use of polyethylene over commercial eye care solutions was estimated to save our unit $10,000 per year. If larger studies are able to confirm the trends found in our data and support the superiority of polyethylene covers over HL, future cost savings would also be achieved though decreased incidences of corneal damage requiring specialist treatment.

Burn patients have increased susceptibility to exposure keratitis, infective keratitis and the progressive sequelae [8, 9]. The trend in this study for burns patients to have an even higher risk towards developing corneal damage if treated with HL than with polyethylene needs confirmation in a larger study.

This randomised controlled trial involving 110 patients found no statistical significance between the eye care treatments of HL and polyethylene. Polyethylene film is easy to apply and inexpensive. The results of this study

have been incorporated into our clinical practice with polyethylene now the standard preventative treatment for all unconscious patients.

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