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Ocular surface bacterial colonisation in sedated intensive care unit patients

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SUMMARY

We investigated the time-dependent ocular surface bacterial colonisation of sedated patients hospitalised in an intensive care unit and aimed to evaluate whether proper topical antibiotic prophylaxis could prohibit corneal infection.

The study lasted 12 months and included 134 patients undergoing sedation and mechanical respiratory support for various medical reasons. Patients hospitalised for less than seven days and those with pre-existing ocular surface pathology were excluded. All patients were examined on admission by inspecting the cornea for erosions. Follow-up examinations were performed each subsequent day. Cultures were also obtained from the conjunctival sac of both eyes on admission and every seventh day until the end of sedation. Standard laboratory techniques were used for isolation, identification and antibiotic susceptibility testing of bacteria. Antibiotic treatment for prophylaxis was administered accordingly.

Analysis was carried out for 70 patients. Duration of sedation ranged from seven to 122 days. Fifty-four (77%) patients were colonised by at least one bacterial species other than normal flora within seven to 42 days. Multiple bacteria were isolated from 28 patients undergoing prolonged sedation. Prevalent isolates were Pseudomonas aeruginosa, Acinetobacter spp. and Staphylococcus epidermidis. Infectious keratitis was prohibited in all cases.

Ocular surface of long-term sedated patients was found to be colonised by various bacterial species and their isolation was closely associated with the time period of hospitalisation. The results of this study suggest that the early identification of ocular surface bacteria colonisation and the administration of topical antibiotics for prophylaxis can prohibit corneal infection in these patients.

Key Words: acinetobacter ocular infection, intensive care unit, keratitis, microbial colonisation, Pseudomonas ocular infection, sedated patient

Prolonged eye closure, such as occurs in intensive care unit (ICU) patients, causes a cascade of biochemical, cellular and microbial events culminating in inflammation, hypoxia and dry-eye states[1]. Eyelid closure during sleep is an active process involving contraction and relaxation of eyelid muscles. This active contraction and relaxation is lost with the heavy sedation and use of muscle relaxants in ICU patients. The blink reflex is also lost. Incomplete lid closure leads to drying of the mucosal surface and desiccation of the corneal epithelial tissues, resulting in ulceration. Lesions can range from punctate epithelial erosions involving the exposed inferior third of the cornea to more extensive erosion termed macroepithelial defect. Disruption of the epithelial surface increases the risk of bacterial infection.

The cornea is affected most often, with the most severe lesion being bacterial keratitis that may cause corneal opacity and blindness[2,3]. Protective measures such as instillation of ocular lubricants[4,5] or masking the closed eye with tape and creating of a moisture chamber[6-8] do not seem to efficiently prevent keratitis in all sedated patients.

We prospectively studied all patients who were under sedation in the adult general ICU of a large

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university hospital in Southern Greece, to investigate the time-dependent ocular surface bacterial colonisation and to evaluate whether early detection and proper topical antibiotic prophylaxis could prohibit corneal infection.

MATERIALS AND METHODS

The study lasted 12 months (1 June 2007 to 31 May 2008) and included all patients under sedation and mechanical respiratory support admitted at the adult general ICU of Patras University Hospital, Patras, Greece.

Exclusion criteria included duration of sedation of less than seven days, transfer from another hospital department, pre-existing ocular surface pathology or recent ocular trauma and conjunctival cultures demonstrating bacteria other than those of the normal conjunctival flora, on admission.

The standard eye care protocol for all sedated patients in the ICU included frequent instillation of eye lubricants, while special care was given by the nursing staff so that lids remained closed.

Upon admission, patients' corneas were inspected for erosions by inserting fluorescein strips on the lower conjunctival sac and by using a magnifying lens (×20) and a cobalt blue filter light. Inspection was repeated each subsequent day.

Cultures were also obtained from the conjunctival sac of both eyes using a sterile cotton swab on admission and every seventh day, until the end of sedation. The swab was directly inoculated onto blood, chocolate and brucella blood agar and was transferred to the microbiology laboratory. Standard laboratory techniques were used for isolation, identification and antibiotic susceptibility testing of bacteria. Cultures were considered positive even if a single colony forming unit, in either eye, of *Proteus, Klebsiella* spp., *Pseudomonas aeruginosa*, *Acinetobacter* spp. was observed or more than 100 colony forming units for *Staphylococcus epidermidis*.

In cases of positive cultures, but in the absence of clinical signs of keratitis, topical antibiotic solutions were administered for prophylaxis three times a day, according to susceptibility testing. In cases of positive cultures, but in the presence of signs of keratitis, topical antibiotics were administered more frequently. Detection of two or more species of bacteria required combined prophylactic therapy. Antibiotic drops were prepared by adding required amount of parenteral antibiotic formulation to a 15 ml dropper bottle of a tear substitute (Tears Natural®, Alcon Inc., Hüneberg, Switzerland).

This work was performed according to the guidelines of the declaration of Helsinki and it was approved by the Institutional Review Board.

RESULTS

A total of 134 patients were studied during a 12-month period. Sixty-four were excluded due to less than seven days sedation (59 patients) or for pre-existing ocular surface pathology (five patients). Analysis was carried out on the remaining 70 patients (48 male, 22 female). Patients' age ranged from 20 to 73 years (mean 51), while sedation lasted seven to 122 days (mean 27 days). Patient demographic data are shown in Table 1.

Of the 70 patients, 54 (77%) were colonised by at least one bacterial species other than normal flora within seven to 42 days, while remaining patients did not show any alteration to their normal conjunctival flora they had demonstrated upon admission. Of the 54 patients, 26 (48%) were colonised by a single bacterial species and 28 (51%) were colonised by two or more species. Forty-six patients (85%) were colonised by day seven, two by day 14, two by day 21, two by day 28 and the remaining two by day 42 from sedation and intubation.

Prevalent isolates were multi-resistant bacteria commonly isolated from ICU patients, such as *Pseudomonas aeruginosa* (26 patients), *Acinetobacter* spp. (24), *Staphylococcus epidermidis* (24), *Enterococcus faecium* (4), *Enterobacter aerogenes* (4), *Proteus mirabilis* (2) and *Klebsiella pneumoniae* (2).

TABLE 1
Patients' demographic data

No. of patients	70
Age	20-73 (mean 51)
Male/female	48/22
Duration of ICU stay, days	7-122 (mean 27.37)
Mortality, no. (%)	24 (34.28)
Primary disease	
Trauma	33
Sepsis	13
Cerebrovascular stroke	7
Respiratory failure	5
Brain surgery	5
Abdominal surgery	3
Cardiovascular stroke	3
Miscellaneous	1

In the majority of cases, *Acinetobacter* spp. were susceptible only to colistimethate sodium whereas *S. epidermidis* only to netilmycin and vancomycin.

In most cases, ocular colonisation and systemic infection by the same bacteria co-existed in the same patient. However, in two cases ocular colonisation with specific bacteria was observed one to two days prior to their appearance in sputum or blood cultures.

Mean duration of ICU stay under sedation and mechanical respiratory support was 13 days (range 12 to 18 days) for patients who showed no alteration to normal conjunctival flora, 26 days (range seven to 64 days) for those who were colonised by one bacterial species and 40 days (range 10 to 122 days) for those who were colonised by more than one species.

Non-ulcerative sterile keratitis due to corneal exposure was observed in seven patients with ocular colonisation. In these cases, frequent topical antibiotics and tear substitutes instillation resulted in prompt healing of the lesions. Infectious keratitis was prevented in all cases.

DISCUSSION

The ocular surface, tear film, lacrimal glands and eyelids act as a functional unit to preserve the quality of the refractive surface of the eye and resist injury, as well as to protect the eye against changing bodily and environmental conditions. Events that disturb homeostasis of this functional unit can result in a vicious cycle of ocular surface disease[9]. Prolonged eye closure results in a loss of cleansing, mixing and pumping action of the blink, severely limiting the capacity to remove micro-organisms by means of fluid turnover. Defence mechanisms of the ocular surfaces are confronted with an entirely new set of challenges. These include potential proliferation of entrapped micro-organisms, repletion of ocular and microbial waste and toxic products that build up, as well as dealing with a cornea that is subjected to hypoxic stress[10]. Previous studies showed that prolonged eye closure results in corneal hypoxic stress[11,12]. Conditions associated with prolonged eye closure include an acidosis in corneal epithelium, a shift to a more anaerobic mode of glucose metabolism, production of lactic acid and CO_2 and corneal oedema.

Patients in the ICU lack blinking and have decreased tear production. In addition, administration of muscle relaxants in sedated patients causes lid relaxation, resulting to incomplete lid closure that predisposes to corneal epithelial drying and exposure keratopathy. The majority of such phenomena undergo spontaneous resolution. Occasionally, a rupture in the integrity of epithelial surface occurs and is by far the most serious risk factor. It is well known that bacteria in the preocular tear film may colonise an area of corneal epithelial defect. Other factors, such as impaired host resistance and constant exposure of the ocular surface to environmental pathogens, render the cornea vulnerable to infection.

Microbial keratitis as a complication of corneal exposure in ICU patients has been consistently reported despite preventative measures[13-15]. Common bacteria associated with eye infections include *P. aeruginosa*[13,15-17], *Staphylococci* spp.[17,18] and *Acinetobacter* spp.[18,19].

In this study, three major groups accounted for 92% of the single isolates and 100% of mixed isolates: *P. aeruginosa, Acinetobacter* spp. and *S. epidermidis*. Unfortunately these multi-resistant bacteria are frequently isolated from our ICU patients, despite strict antibiotic policy and usage only by infectious disease specialists.

Many sources have reported that corneal abnormalities in sedated patients are time-dependent[2,3,20,21]. Lesions observed in patients who stayed in ICU longer than seven days ranged from 20 to 70%, while the incidence increases upon continuous sedation. Other studies have shown that predictive factors for keratitis also include incomplete eyelid closure[13,20], Glasgow Coma Scale score[2,3], intubation[2,3], use of muscle relaxants[6,20], continuous sedation[20] and severity of illness[2,20].

We observed that microbial surface colonisation is also time-dependent: the longer the period of ICU hospitalisation under sedation and mechanical respiratory support, the higher the prevalence of positive conjunctival cultures for bacteria. Yet most patients (85%) showed ocular surface bacterial colonisation within the first seven days of sedation and intubation, whereas all patients were colonised by day 42.

Various measures have been proposed for prevention of keratitis in sedated ICU patients: the use of swim goggles and regular moistening of the eyelid with gauze soaked in sterile water every 12 hours[6], treatment combining artificial tears and eye lubricant[8], use of polyethylene covers to create a moisture chamber[7,8], application of artificial tear ointment[4] and lid taping and lubricants[5]. Unfortunately, none of these measures efficiently prevents all patients from developing corneal infection.

The setting in ICUs is quite different from the outpatient setting, as sedated patient cannot convey ophthalmic complaints and they should be closely monitored by the ICU staff for lid position and ocular surface disease. The results of this study suggest that the early identification of ocular surface bacteria colonisation and the subsequent administration of topical antibiotics for prophylaxis can prevent corneal infection in high risk ICU patients.

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