

The Observation for Ocular Surface Diseases in Respiratory Care Center in One Regional Teaching Hospital in Southern Taiwan

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Abstract: Purpose: To discover the incidence of ocular surface diseases in the RCC in one region hospital in southern Taiwan. **Methods:** A prospective study was performed from January 2014 to May 2014. We recorded the causes of admission, eyelid position, abnormal findings of the conjunctiva and cornea. Besides, we also collected data about age, sex, sedation score, the intubation or not, the ventilator setting, date of admission, endotracheal tube or tracheostomy used et al. **Results:** Total 30 patients were examined in RCC. The mean age of the patients was 60.5 years (range 32-82). 18 patients were male and 12 were female. 24 patients had been sedated or non-sedated with various ventilators. 6 patients were in T-piece trial. 22 patients had tube intubation and 8 patients had received tracheostomy. Mean stay time was 20.5 days. The percent of ocular surface diseases were 33.3% (10/30), and lagophthalmos was observed about 33.3% due to sedation. 23.3% (7/30) patients had conjunctival problems and 26.6% (8/30) had keratopathy. We found that 80% (8/10) patients with lagophthalmos had eye disorders. The endotracheal tube intubation group had a relatively higher incidence of ocular surface diseases (7/22 ; 32%). If the sedation score lower than 8, 26 % patients may have eye diseases. **Conclusion:** The incidence of ocular surface diseases is closely related to heavy sedation or muscle relaxants. The assessment of eyelid position in relation to the ocular surface disease is the most important observation required in RCC. How to set up the routine protocol for eye care for the staff in ICU becomes valuable and serious today. We must keep in mind that prevention is always better than cure.

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1. Introduction

Patients in the respirator care center (RCC) just transferred from intensive care unit (ICU) was sometimes unstable. They always needed further evaluation by medical doctors and are considered risk of developing ocular surface diseases [1]. However, many clinicians pay attention to the vital signs for electrolyte imbalance, cardiovascular disorders, infectious problems and respiratory stress et al. Therefore, the RCC staffs always omitted the ocular diseases because the comatose patients usually kept "silent" until it reached the advanced stage, especially the junior doctors with no previous experience in ophthalmology [2,3,11]. The incidence of eye disorders in ICU and RCC population is difficult to quantify because of poor documentation and that

compared to the nursing care required to stabilize vital body, eye care is often seen as a relatively minor problem [22]. However the patients in ICU and RCC, especially ventilated patients are at risk of developing several ocular surface diseases for conjunctivitis and keratitis. The key points of the patients suffering from ocular diseases are due to temporary sedation (propofol) and muscle relaxants. Then, muscle paralysis, impaired blink reflexes, loss of eyelid tone, fluid imbalance and positive pressure ventilation may lead to conjunctival chemosis. These factors often resulted in incomplete eyelid closure and a consequent exposure keratitis [4,5]. Due to the poor immune system in ventilated or non-ventilated patients in ICU and RCC, they are easily to developing to bacterial keratitis and even corneal ulcer, especially

with *Pseudomonas aeruginosa* from exposure keratopathy [6,7] . The release of proteolytic enzymes, toxins and associated reaction will rapidly progress to corneal ulcer. In one study about bacterial keratitis, the patients even suffered from perforation requiring penetrating keratoplasty [43] . The mean visual acuity of the surviving patients at discharge was only 6/60 [8] . Now many RCC doctors began to realize the importance of the routine eye care protocol, and they tried to make some new guideline for critically ill patients [9] . Eye care is therefore an important aspect of maintaining the integrity of the ocular surface. If not careful treatment, those patients who develop conjunctivitis and especially keratitis, which may consequently develop into visual loss [10] . In this study, we will discover the incidence of ocular surface diseases (ex. conjunctivitis, conjunctival chemosis, any type of keratitis, corneal erosion, ulcer and even perforation) in RCC.

2. Material and Methods

Material

A prospective study was performed in one RCC (total 25 beds) in Kaohsiung Armed Forces General Hospital (Southern Taiwan, Republic of China) from January 2014 to May 2014. The mean stay time less than 10 days which lead to the improper and incomplete follow-up should be excluded. The causes of the underlying diseases were recorded (reasons of admission). We got the approvals for the families of the patients which were granted by the institution review board of Kaohsiung Armed Forces General Hospital (No: 102-016). The ethics all meet the Declaration of Helsinki. A record was made of eyelid position, the severity of conjunctiva redness, chemosis, and discharge. The epithelial surface was assessed by fluorescein and a portable slit-lamp with cobalt blue filter. The presence of any corneal epithelial defect, erosion, ulcer and even perforation should be recorded carefully. We defined the ocular surface diseases and recorded in table 2. The diagnosis and grade of eyelid position, conjunctival lesions and keratopathy were according to the studies of Mercieca F et al. and Surech et al. (table 3, 4, 5) [1,11] . If any ocular surface disorders were highly suspected, the swab cultures were arranged at once. All the ocular examinations were performed by the same ophthalmologist (Dr. Horng) and checked the ocular condition twice one day (9AM and 5 PM every day). Most RCC patients were sedated to some degree. The depth of sedation was assessed according to the scale shown in table 6, and then we can calculate the sedation score (shown in table 7) according to the criteria of Dawson's study [9] .

In the same time, we gained data from documents about age, sex, sedation score, intubation or not, the ventilator setting, date of admission, endotracheal tube or tracheostomy, and any positive findings from the respiratory, blood or other wound cultures.

3. Results

Total 30 patients were examined in RCC. The mean age of the patients was 60.5 years (range 32-82). 18 patients were male and 12 were female. Twenty-four patients had been sedated or non-sedated with various ventilators. 6 patients were in T-piece trial. 22 patients had the endotracheal tube intubation and 8 patients had already received tracheostomy. The mean stay time was 20.5 days. The cause of the underlying diseases included pneumonia, CVA (Cerebral vascular accident), Stroke, Septic shock, heart failure and even ICH (intracranial hemorrhage) (shown in table 1)..

Table1. The underlying causes of the patients in the RCC

Pneumonia	10 cases
CVA	7 cases
Stroke	5 cases
Septic shock	3 cases
Heart failure	3 cases
ICH	2 cases

The surface ocular examinations include lagophthalmos, conjunctivitis, conjunctiva chemosis, superficial punctate keratitis (SPK), corneal erosion, and corneal opacity (shown in table 2). The percent of ocular surface diseases were found in the patients in RCC was about 33.3% (10/30). The lesions in the conjunctiva or cornea all persisted at the lower one third of the eye. There was no endophthalmitis in this survey.

The percent of abnormal eyelid position (lagophthalmos) is about 33.3% (10/30) (Grade 1: 2, Grade 2: 3, Grade 3: 5) (shown in table 3). The incidence of conjunctivitis and chemosis was 23.3% (7/30) (7 cases showed conjunctivitis, 5 cases owned conjunctival chemosis, 5 patients were the victims of conjunctivitis combined with severe chemosis) (shown in table 4). According to the observation of corneal condition, keratitis was noted in 3 cases (Grade 2). Besides, we also found out 3 patients with corneal erosion (Grade 3) and 2 patients with corneal opacity (Grade 3). The total corneal problems were 26.6% (8/30) in sedated patients (shown Table 5).

Lagophthalmos	10 cases
Conjunctivitis	7 cases
Conjunctiva chemosis	5 cases (Table 4: grade 1 and 2)
Superficial punctuate keratitis	3 cases
Corneal erosion	3 cases
Corneal opacity	2 cases

Grade 1	Eye lids apposed
Grade 2	Conjunctiva exposed
Grade 3	Limbus exposed

Grade 0	Absent
Grade 1	Conjunctival oedema (chemosis) with dellen
Grade 2	Conjunctival oedema (chemosis) without dellen

Grade 0	Absent
Grade 1	Superficial punctuate keratitis (SPK)
Grade 2	Corneal erosion
Grade 3	Corneal opacity (or ulcer)

In our study, the malposition of eyelids (lagophthalmos) was considered as the cause, not the ocular diseases. Thus, only the conjunctiva problems and keratopathy were identified as ocular surface diseases (table 2). The most cause of incomplete eyelid closure is due to heavy sedation by medication. The sedation score of patients varies through their stay in RCC. General the patients were deeply sedated initially and gradually weaned as the clinical status improved. We found that 80% (8/10) patients with lagophthalmos had various degrees of ocular surface diseases. Nevertheless, a fair proportion of patients (10%; 2/20) without lagophthalmos also had mild superficial punctuate keratitis caused by some sedative agents leading to the decreased tear production.

Awake	17-19
Asleep	15-17
Light sedation	12-14
Moderate sedation	8-11
Deep sedation	5-7
Anaesthetized	4

1.	Eyes open (lid movement) Spontaneously To speech To pain None	4 3 2 1
2.	Response to nursing procedures Obeys commands Purposeful movement Non-purposeful movement None	4 3 2 1
3.	Cough Spontaneous Spontaneous On suction only None	4 3 2 1
4.	Respiration Extubated Spontaneous intubated SIMV triggered Against ventilator No respiratory effect	5 4 3 2 1
5.	Loading for spontaneous communication	+ 2
SIMV, spontaneous intermittent mandatory ventilation.		

In this study, 80% (24/30) cases of patients had ocular surface diseases. The regular treatment in our hospital is to use the tape vertically to attach to the forehead if incomplete eyelid closure. There was no bandage directly on the eye. Beside, we used the artificial tear (tear-Nature) four times one day and gentamycin ointment two times one day on the lagophthalmos. Fortunately, most of the signs usually improved within 7 days after the treatment (except corneal opacity). In addition, no positive findings in swab culture of lesion eyes were noted.

We also found that there are no obvious relationship between ocular surface diseases and age, sex, and diagnosis. However, the group of patients with endotracheal tube intubation had a relatively higher incidence of ocular surface diseases (32%, 7/22) than the tracheostomy group (25%, 2/8). The sedation score greater than 15, no superficial punctuate keratitis or corneal erosion was noted. Nevertheless, the sedation score lower than 8, 26 % patients (8/30) will be bothered by ocular problems. Besides, no positive findings from the respiratory, blood or urine cultures were found.

4. Discussion

Patients admitted to RCC often required mechanical ventilation setting. In common hospital wards, patients are usually able and eager to convey

their significant ocular symptoms. However, medical attention is strongly toward to respiratory, cardiovascular, and neurological stabilization in RCC. Preventive eye care measures and effective evaluation are often easily neglected due to the sedated, obtunded or pharmacological paralyzed patients [3,12,13] . Thus, the real incidences and mobility of the ocular surface diseases were always underestimate [3] . Furthermore, too more RCC doctors forgot to the uncommon but complicated ophthalmological disorders which may be lethal [15] including metastatic endogenous endophthalmitis, acute angle closure glaucoma, pupil abnormalities due to some drugs of neuromuscular blocks (NMBs), dopamine, cocaine, amphetamine and significantly CNS pathology and trauma [16] , ischemic optic neuropathy, retinal vascular occlusions, and even rhino-orbital cerebral mucormycosis. The higher prevalence of corneal epithelial defects were to be emphasis recently because of the next step of corneal exposure and even the following microbial keratitis are serious complication in unconscious patients in ICU and RCC [1,5] .

The patients in RCC often required mechanical ventilation and were sedated to ensure comfort and facilitate treatment. They were always paralyzed with muscle relaxants or sedatives to decrease the fight the ventilator and improve the compliance (Muscle relaxants now is rare used in Taiwan because of the difficulty in help the sedated patients to wean off the ventilators). To the knowledge, normal eyelid closure is maintained during sleep [21,22] , however, the effects of sedative agents may reduce the tonic of the orbicularis oculi muscle and result in the eye closure only with massive force [12] . Lagophthalmos would increase the tear film evaporation and impair corneal and conjunctival surface defense. Some drugs used in ICU and RCC including hypnotics, sedatives, anxiolytics, atropine, antihistamine and tricyclic antidepressants (TCA) may also affect the formation of lacrimal film [27] . The decreased tear volume may induce dry eye and the damage of the ocular surface. Neuromuscular blockers could abolish the blink reflex, reduce the protective function of the eyelid and result in impaired tear film function and stability [5,29] . In addition, these agents should cause loss of the corneal reflex mechanisms, as a result of corneal anesthesia, leading to exposure keratopathy [4,36] . Baum had reported that ICU patients are at increased risk of bacterial corneal ulcer, especially pseudomonas keratitis, which attributing to

decrease the blinking reflex or lagophthalmos [41] .

Now muscle relaxants were instead of other non-analgesic sedatives such as propofol [22] or haloperidol [32] because of difficult weaning off in muscle relaxants. New approaches to mechanical ventilation often involving permissive hypercarpna (allowing the partial pressure of arterial carbon dioxide to reach 50 mmHg or higher) can cause patients substantial discomfort, necessitating high level of sedation [38,39] . Now propofol is very popular in many countries for the ventilated patients because of increasing their comfort. However, the impeding factor of ocular surface diseases due to lagophthalmos may also be found [35] . In our hospital, the propofol is routine given and 33.3% patients showed incomplete eyelid closure. In one report from Korean, the incidence for eye disorders in the sedatives users (odd ratio: 4.2) and muscle relaxants users (odd ratio: 2.3) is very apparent [39] .

For example, some literature indicate as possible risk factor for corneal injury included intubation, mechanical ventilation, sedation, eye blink per minute, and presence of edema [3,18,49] . Werli-Alvarenga et al. had demonstrated that intubation, MV or TQT would increase the chance of the patient developing into corneal injury by 117.11 times when compared to those are not using these devices [23] . Thus, coma and sedation may compromise the random eye movement, cause loss of the blinking reflex and compromise the lacrimal glands. To our surprise, the patients with another ventilatory support device, such as macronebulization, venture mask and the nasal cannula also have a 1.96 times higher change of developing punctate type injury when compared with those who are not using. It could be explain by the corneal exposure to oxygen at concentration greater than 21% [26] .

Therefore, lagophthalmos induced by sedation and the following dry eye may induce the incidence of exposure keratopathy and conjunctivitis. The prevalence of corneal epithelial defects including SPK and corneal erosion [3,17,25,26] . Grixti et al. had that the major ocular disorders identified in ICU patients were exposure keratopathy (3.6 to 60%) and conjunctival chemosis (9 to 80 %) [20] . A study of 33 ventilated patients of Hernandez revealed that 55% patients showed superficial punctate keratitis and corneal erosion [17] . Among 50 patients examined in other study, 40 % had corneal abnormality and 90% of them with bilateral abnormalities. Punctate epithelial keratopathy (SPK ; micro-epithelial defects) was the common

disorders (20 patients, 38 eyes). Microepithelial defects (5 eyes) and filamentary keratitis (4 eyes) was also noted [22] . Werli-Alvarenga et al. had ever reported that 59.4% developed into corneal injury (55.1% was punctuate, 11.8% belonged to corneal ulcer) and the mean time to onset was 8.9 days [19] . Imanska found that the peak incidence was between 2 and 7 days because of impaired protective eye mechanism [20] . Another prospective study by Merceica demonstrated that the rate of keratitis in 26 patients and the signs were highly associated with incomplete lid closure [11] . The keratopathy will easily develop into corneal ulcer and even penetrate into the stroma by pseudomonas aeruginosa which may induce corneal perforation and even blindness [19,20,21] .

The patients in ICU and RCC also had physiologic changes including the decreased the blinking mechanism because of sedatives use [23] . If the eye blink rate less than 5/min, it may increased the corneal problems by 45.46 times compared to blink rate more than 5/min. Patients treated with neuromuscular blockers are 14.085 times more likely to develop the corneal injury, when compared to those in which not administrated.

Exposure keratopathy which is the most common ocular symptoms plays a key factor in the development of corneal erosion, bacterial keratitis and even corneal perforation. The exposure of ocular globe could increase the change of a patient developing a corneal ulcer by 2.7 times when compared to those who have no exposure. Cortese et al. believed that all the ocular surface diseases may induce ocular exposure, ineffective palpebral closure and inadequate lacrimal fluid quality [28] . Thus, the importance of ocular care in ICU and RCC is to prevent from lagophthalmos. Ezra et al. also suggested that exposure of the ocular globe and the Glasgow scale was related to the corneal ulcer in ICU patients [29] . The patients in the RCC and ICU, sedation score greater 15, no superficial punctuate keratitis or corneal erosion was noted. Nevertheless, the sedation score lower than 8, 26% patients will develop into corneal disorder [11] . The possible reason may be patients with lower sedative scale needing the longer time to wean off the ventilators and prolong the hospital stay. In our study, the corneal problems including SPK, corneal erosion and even opacity were near to 40% which were near to other studies. However, no apparent infection was found. They may be related to different eye care methods. (We used the artificial tears, prophylactic antibiotics ointment and micropore eyelid vertical taping if lagophthalmol persisted).

The contributing factors leading to lagophthalmos in ventilator machine may be due to the higher jugular venous pressure which leads to fluid leakage in the periocular region [24] . The raised venous pressure was closely associated with positive pressure ventilation, thigh endotracheal tube tape, and mal-nutrition (hypo-protemia). Most of the researchers strongly believed that punctuate type injury of cornea was associated with age, gender, ventilatory method, duration of hospitalization, APACHE II, duration of postoperative period, Glasgow Coma Scales(GCS), intubation, tracheostomy, duration of mechanical ventilation, inspired oxygen fraction(FiO₂), positive end-expiratory pressure (PEEP), eyes blinks per minutes, medication (ex. vaso-active drugs, antihypertensive agents, diuretics, some antibiotics, vitamin, bronchodilators, sedatives, antifungal agents and neuromuscular blockers), temperature of the ward, nutritional status, and the degree of headboard elevation [3] . In our study, we also can easily identify the association of many impacting factors about the ocular surface disease. The results are consistent with other literatures [25,26] .

In ICU and RCC, ventilatory support may lead to body fluid retention and increase venous pressure which may result in oedema sequestration [30] . Mercieca et al. found that all patients who had lagophthalmos exhibited some degree of chemosis [11] . Intubation can generate an acute in the intraocular pressure and may predispose to or exacerbate the corneal and conjunctival disorders [31] . Besides, the excessively tight endotracheal tube may also compromise venous return from the head thus leading to venous congestion, higher jugular venous pressure, fluid leakage in the periocular tissues which resulted in conjunctival chemosis (so called “ Ventilator eye”) [24] . Therefore, how to adjust the proper position of endotracheal tube is very important. In some literatures, the patients with endotracheal tube showed more signs of exposure keratitis than patients with tracheostomy. The one reason is related to the effects of pressure. The others may be due to the patients with endotracheal tube group need to be weaned off sedation and the relatively long stay in the ward. According to the study, the increasing duration of hospitalization may develop the injury by 0.03 times [3] . In our study, the incidence of chemosis is about 23% which is strongly associated with lagophthalmos. Hernandez et al. suggested that the patients intubated, lower score in Glasgow Coma Scale evaluation and who are expected to be hospitalized in ICU for extended periods required

further and even prophylactic eye care [17] . This is a good guideline for us.

Various ocular surface protective measurements are in use ranging from simple cleansing to suturing the lids to achieve adequate eye closure. Katz et al. suggested that the most simple and satisfactory method for exposure eye was to tape the eye shunt. The medical staff could use a piece of tape, firstly applying to pull up the cheek and lower and thereby closing the eye (vertical taping). The tape was then attached to the forehead. Some researchers suggested that the Bland ointment (antibiotics) may be applied to the eye conjunction with taping the lids [37] . In Taiwan, we usually used the horizontal taping to prevent from the complications of lagophthalmos. The benefits or disadvantage between vertical and horizontal taping were still discussed. The advantage of micropore taping to incomplete eyelid closure is controversial. For example, Suresh et al. commented that placing securing tape in a horizontal position may be the most effective to close the eyelid [1] . Dua addressed that taping is able to maintain good eyelid closure and allow visualization of the lid margins due to its transparency [38] . However, Farrell et al. did not support the eyelid taping because of potential risk of damage to the eyelid. Repeated removal of the tape may also lead to some degree of facial skin or eyelid injury [2] . Some patients also may develop allergic reaction (ex. dermatitis) to the tape materials [1] . Thus, the method of eyelid taping needed more evaluation in the future.

There are also many protective methods and treatment for lagophthalmos and its complications. Some ICU or RCC staffs used various regimens for eye hygiene. For example, sterile packs containing a gallipot and cotton wool with a solution water, normal saline eye toilet, gauze soaked in normal saline (0.9%) or sterile water was performed at several intervals (2 to 6 hours) [2] . O'Gallaghan et al. strongly suggested the importance of maintaining lubrication of the cornea and cleansing the debris and bacteria from the eye [42] . Prevention from dry eye induced by lagophthalmos and sedatives is also necessary. A large number of different methods utilized to maintain the tear film and facilitate adequate corneal wetting to prevent drying of the ocular surface. The common use of agents in UK is Geliperma which is a polyacrylamide gels to ensure eyelid closure. Geliperma is transparent, soft, and non-allergenic. It also owns the therapeutic properties of optimizing cellular growth and inhibiting the development of secondary infection [2,11] . Besides, the polyacrylamide gel patches with high water content have been recommended to provide

adequate cover, moisture and protection for the patients with apposed eyelid, loss of tissue or rigidity (facial burns) or conjunctival prolapse in ICU and RCC [38] . Polyethylene moisture chambers [32] , Methylcellulose drops or ointment, lubricants (Duratears) [29] , vaseline gauze [45] , paraffin gauze, hypromellose drops (artificial tears, Methopt tears) [46,47] and even lubricating prophylactic antibiotics were used to maintain adequate corneal wetting and decrease the incidence of keratitis and corneal ulcer [1,5,44] . To prevent iatrogenic eye injuries in patients, Wincek et al. proposed that methylcellulose drops should be used every 1-2 hours [5] . Suresh et al. considered that lubricants should be used in the patients with mild lagophthalmos thus avoiding the unnecessary lid taping procedure inducing the distress of skin problem to the patients [1] . Parkin et al. suggested that if the microbial keratitis was suspected, prophylactic gentamicin and regular application of lubricants were given together [8] . Kirwan et al. proposed that prophylactic use of antibiotic ointment may prevent from secondary infection. Sometime lubricant ointment may be combined with antibiotics in patients with lagophthalmos [4] . In our hospital, the eye care protocol is to prescribe the artificial tears and gentamycin ointment together. No apparent infectious signs were found. If adequate corneal protection can not be achieved by taping and lubricant, temporary suturing of the lids may be considered. For example, temporary tarsorrhaphy (lateral or medial of Fuch's sutures) and frost suture are the commonly used [1] .

In ICU or RCC, the ophthalmologists may detect a higher rate of corneal erosion (37.5%) than the ICU doctors (31.3%). Although examination for erosion by ICU doctors had a sensitivity 77.8%, and specificity 96.7%, some ocular surface diseases may still be missed. Besides, some key points should be kept in mind. The first, we must avoid to touch ocular surface with tip ointment tube or drop application. The second, we did not cover the eye if yellow discharge was found. The third, suction of copious tracheal secretions causes much bacterial spread. Suction done over the patient's head (across the eyes) maybe induce contamination of the conjunctival sac from respiratory tract pathogens [38] . Today the newly closed suction technique is appreciated to reduce the incidence of ocular infection from copious sputum production apparently [10,12] . Finally, the routine eye swabs for culture in comatose patients and checking the contact lens if retained are necessary. The ICU or RCC doctors and nurses always neglect the eye care. The incidence of ocular

surface diseases and protocols of eye care in the ventilated patients became serious until now. Thus, Dawson suggested that developing a new eye care guideline for ventilated patients without the emergent help from ophthalmologists is very important for the ICU nurse and young doctors [9]. A great number of researcher appeal to design the protocolized eye care to reduce the risk of ocular surface in ventilated patients [39,40,49]. For example, the presence of discharge, red eye, and white corneal lesions (which may indicate corneal infection) should alert the nursing staff to seek the ophthalmologist's opinion.

5. Conclusion

The prevalence of ocular surface abnormalities happened at least 10% of patients in ICU or RCC [39]. Some impaired ocular protective mechanisms as a result of metabolic derangement, multiple organ dysfunction, mechanical ventilation and decreased level of consciousness. Such patients are at increased risk of ocular surface disorders, which, if not resolved, can result in serious visual impairment. In fact, many ocular diseases in ventilated patients in RCC are wrongly assessed by the nurses and untrained doctors. Therefore, it is essential to set up the evidence-base care protocol for the RCC staff which may provide the routine care to prevent from eye complications. Once the ocular complications suspected, the prompt ophthalmological consultation is warranted as soon as possible..

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