Methods for Detection of Dry Eye in Critically Ill Patients: an Integrative Review

REVIEW

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Abstract

Objective: To identify the best evidence for the methods used for the detection of dry eye in patients hospitalized in intensive care unit.

Method: This is an integrative review carried out from April to June 2015 in the following databases: Science Direct, SCOPUS, CINAHL, PUBMED, MEDLINE, LILACS, Cochrane and Web of Science. The final sample consisted of 17 articles.

Results: The main methods used for the detection of dry eye were: Test of Schirmer, Bengal Rose, fluorescein staining and tear film breakup time.

Conclusion: The results showed a variety of methods used of high value to managers, health professionals, and patients. It is essential to emphasize for further studies with high levels of evidence, thus, the consensus on the tests used and their measurements can be reached.

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Introduction

Dry eye can be defined as a multifactorial disorder of the tear film and ocular surface due to the reduced production or excessive tear evaporation, resulting in discomfort, visual disturbance, and tear film

instability with potential damage to the ocular surface. It may be accompanied by increased osmolarity of the tear film and consequent ocular surface inflammation [1].

Patients in intensive care unit (ICU) are at increased risk of developing ocular disorders because they are critical or potentially critical patients and need expert assistance to maintain vital parameters. Thus, complex care becomes the focus of professional assistance, and the basic care is neglected as in the case of eye care. It is noteworthy that these individuals are predisposed to lose the natural mechanisms of eye protection and, consequently, there is an ocular exposure and low quantity/quality tear mainly due to ineffective eyelid closure [2, 3, 4]. Moreover, research reports that patients admitted to the ICU are more likely to develop not only the dry eye, keratopathy and eye infections. Thus, they need an early diagnosis of various ocular surface disorders [5]. In this context, a study conducted in South Korea points out that the incidence of dry eye was 72.2% [6].

A study demonstrates that the indices of ocular lesions increase 117.11 times in patients with the use of the mechanical ventilator as well as sedation and other drug therapies, by favoring the dry eyes [2]. Another study asserts that 60% of ICU patients who receive sedation for more than 48 hours develop corneal abrasion, detected in 42% of cases in the first week of hospitalization. In turn, abrasion leads to high risk of infection and ulceration [7].

It is noteworthy that, despite not being prioritized, professionals knowledge about the risk factors for the development of the dry eye in ICU patients may prevent further damage, such as keratitis, corneal injuries, and blindness. Thus, proper care will provide lower costs invested by the health system at all levels of complexity [2].

Therefore, for this risk management, it is necessary knowledge on how to detect the health team, when considering the diversity of the tests descri-

bed in the literature [8, 9, 10]. Thus, this knowledge can foster the provision of appropriate planning and interventions, as well as the generation of prevention of protocols and early detection of dry eye risk, as well as point out perspectives for future investigations. Thus, this study aims to identify the best evidence for the methods used for the detection of dry eye in patients in intensive care unit.

Method

This study is an integrative review, based on the method proposed by Whittemore and Knalf (2005), who recommend the following steps: identification of the research question, literature search, evaluation of results, analysis of results and presentation of the review [11].

The next question was adopted to achieve the objective of this research: What are the methods used for the detection of dry eye in patients hospitalized in the intensive care unit?

The literature search was from April to June 2015, carried out by a pair of researchers on different computers, without communication, on the same day and time, using the same Internet network through proxy licensed use of the Federal University of Rio Grande do Norte/Brazil (www.capes.ufrn.br/port 3128), accessed via the portal capes journals (http://www-periodicos-capes-gov-br.ez18.periodicos.capes.gov.br/). The collection occurred by applying a protocol of search and access to databases: Science Direct (Elsevier), SCOPUS (Elsevier), Cumulative Index to Nursing and Allied Heath Literature - CINAHL, Public Medline, PUBMED, Medical Literature Analysis and Retrieval System Online - MEDLINE, Latin American and Caribean Health Science Literature Database - LILACS, Cochrane Library and Web of Science.

To articles survey, indexed descriptors in the Medical Subject Headings (MeSH) and Descriptors in Health Sciences (DeCS), in Portuguese, English and Spanish were used depending on the characteris-

tics of each database: (Ceratoconjuntivite Seca/ Keratoconjunctivitis Sicca/ Queratoconjuntivite Seca), 2# (Fatores de Risco/ Risk Factors/ Factores de Riesgo), 3# (Sindromes do Olho Seco/ Dry Eye Syndromes/ Sindromes de Ojo Seco), e 4# (Unidades de Terapia Intensiva/ Intensive Care Units/ Unidades de Cuidados Intensivos). The crosses were performed using the Boolean operator AND, as follows: 1# AND 2#; 1# AND 3#; 1# AND 4#;2# AND 3#; 3# AND 4#.

The following inclusion criteria were defined: articles available in full through the aforementioned proxy, in the selected databases, available in Portuguese, English or Spanish, answering the main question of this review. There were editorials, letters to the editor, the opinion of experts, abstracts, letters, reviews, book chapters, theses, and dissertations excluded.

The next step selected articles by applying Olsen Relevance Test (1995) that contains criteria for inclusion, exclusion and the guiding question of the review [12]. Repeated studies in the databases were excluded. There was the reading of the studies in full, and the information was extracted from an instrument containing information about the identification of the publication, the location of the study, the journal type, methodological aspects and method for detection of dry eye.

The initial research resulted in 19,586 articles. There were 217 articles included in the first selection by reading titles and abstracts. Of them, 131 were excluded by duplicating the database. Thus, 96 articles were listed for reading the full text, and out of them, 79 were excluded for not meeting the adopted guiding question or eligibility criteria. Thus, the final sample obtained was 17 articles. Levels of evidence used to classify the found scientific publications were considered in descending order according to the power of reliability and validity, according to the study designs [13].

Results

It is noteworthy that despite the studies composing the results are not unique to the intensive care unit, the tests and questionnaires used are apply to many individuals, especially patients hospitalized in the intensive care unit.

Table 1 shows the 17 studies identified. For the year of publication, there was an interval between 1996-2015, highlighting 35.3% of articles published in the last five years. Studies were predominantly identified from the United States (47%) and in English (100%), mainly in Scopus indexed database (41.2%).

Table 1. Distribution of studies on the language, indexed database, year, country, type of journal, type of study and methods for the detection of the dry eye used. Natal, 2015.

Characteristics	N	%
Language		
English	17	100
Indexed database		
Scopus	7	41-2
ScienceDirect	5	29-4
Pubmed	3	17-6
Cochrane	1	5-9
Web of Science	1	5-9
Cinahl	0	0-0
LILACS	0	0.0
Year		
2013	3	17-6
2010	3	17-6
2008	3	17-6
2015	1	5.9
2014	1	5-9
2012	1	5-9
2006	1	5-9
2003	1	5.9
2002	1	5-9
1997	1	5-9
1996	1	5-9

Characteristics	N	%
Country		
US	8	47-0
India	2	11-7
Canada	1	5-9
Korea	1	5-9
England	1	5-9
Japan	1	5-9
Nigeria	1	5-9
Thailand	1	5-9
Taiwan	1	5-9
Type of Study		
Control Case	6	35-3
Clinical work	3	17-6
Cohort	3	17-6
Experimental Study	2	11-8

Characteristics	N	%
Type of Study		
Transverse	2	11-8
Systematic Review	1	5-9
Methods		
Schirmer Test	13	76-5
Bengal Rose staining test	9	52-9
Fluorescein staining test	8	47-0
Test Film Tear Breakup Time	7	41-2
Questionnaire Ocular Surface Disease Index (OSDI)	2	11-8
Meibomian gland dysfunction test	2	11-8
Green Lissamine test	2	11-8
Mcmonnies' Questionnaire (MMI)	1	5-9
Film Evaporation Rate Tear test	1	5-9
Phenol Red test	1	5-9

The selected studies were classified as level of evidence between II and IV, highlighting that most of the published studies (35.3%) were classified as evidence level IV. Regarding the most common detection methods, the Schirmer test was in 76.5% of the studies, followed by 47.0 % of Bengal Rose, fluorescein staining in 47%, and tear film breakup time in 41.2% of publications.

Table 2 shows the details of the items that were extracted and synthesized for results composition.

Table 2. Characterization of the selected articles on the title/ publication year, evidences level/type of study and methods for the detection of dry eye.

Title/Year	Evidence Level/ Type of Study	Population/Sample	Methods for the detection of dry eye
Punctal occlusion for dry eye syndrome [14]/2013	Level I/Clinical Trial	7 randomized clinical trials, including 305 participants (601 eyes) in adults and the elderly.	-Bengal rose staining test -Fluorescein staining test -Green lissamine test -Schirmer test
Influence of eye position on the schirmer tear test [15]/2013	Level II/Clinical Trial	20 adult volunteers who had no dry eye during an eye examination.	-Schirmer test -Bengal rose staining test
The comparison of efficacies of topical corticosteroids and nonsteroidal antiinflammatory drops on dry eye patients: a clinical and immunocytochemical study [16]/2003	Level II/Clinical Trial	32 adult patients with keratoconjunctivitis with or without Sjögren's syndrome were included in the study. Participants were randomized into three groups.	-Schirmer test -Test film tear breakup time (TBUT) -Fluorescein staining test -Bengal rose staining test
Impaired functional visual acuity of dry eye patients [17]/2002	Level II/Clinical Trial	Adult patients and elderly patients with dry eye, including dry eye non-Sjögren syndrome (non-SS, N=10, dry eye Sjögren syndrome (SS, N=12, and normal controls (n=8).	-Schirmer test-Bengal rose staining test

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Title/Year	Evidence Level/ Type of Study	Population/Sample	Methods for the detection of dry eye
Tear film evaporation-effect of age and gender [18]/2010	Level II/Experimental Study	217 volunteers adults and elderly who perform routine visit were part of this research.	-Film evaporation rate tear test (TBUT)
The efficacy of eye care for ventilated patients: outline of an experimental comparative research pilot study [19]/1996	Level II/Experimental Study	6 elderly patients were the pilot study sample.	-Schirmer test -Bengal rose staining test
Dry eye in the beaver dam off spring study: prevalence, risk factors, and health related quality of life [20]/2014	Level III/Cohort	3275 adult and elderly participants were included in this study.	-Test film tear breakup time (TBUT) -Bengal rose staining test
Ethnic differences in dry eye symptoms: effects of corneal staining and length of contact lens wear [21]/2013	Level III/Cohort	395 adult patients who use contact lens.	-Fluorescein staining test
Evidence for the major contribution of evaporation to tear film thinning between blinks investigative [22]/2010	Level III/Cohort	39 adults who are not wearing contact lens which were not pregnant or breastfeeding.	-Questionnaire ocular surface disease index (OSDI)
Dry Eye: a protein conformational disease [23]/2015	Level IV/Control Case	50 adult patients with dry eye by aqueous deficiency and 46 healthy adult volunteers were recruited.	-Schirmer test
Children with dry eye type conditions may report less severe symptoms than adult patient [24]/2012	Level IV/Control Case	45 children and 45 adults with different dry eye conditions were included in this study.	-Test film tear breakup time lacrimal (TBUT) -Fluorescein staining test -Schirmer test
Comorbidities of dry eye disease: a nationwide population-based study [25]/2010	Level IV/Control Case	The study group consisted of 12,007 patients who sought outpatient care for the treatment of dry eye in 2005 and 2006. In total, there were 36,021 patients randomly selected in the comparison group.	-Schirmer test -Test film tear breakup time (TBUT) -Fluorescein staining test
Case control study of dry eye and related ocular surface abnormalities in Ibadan [26]/2008	Level IV/Control Case	56 eyes of 78 subjects treated at an eye clinic. Subjects with a score of 4-9 were considered case group and a score from 0 to 3 in the rose bengal test were included as control group.	-Meibomian gland dysfunction test -Test film tear breakup time (TBUT) -Fluorescein staining test -Bengal rose staining test -Phenol red test -Schirmer test
Prevalence of dry eye at high altitude: a case controlled comparative study [27]/2008	Level IV/Control Case	There were 100 subjects composing the case group, and 100 were composing the control group, residing in Leh (high altitude region) and New Delhi (low region), respectively.	-Mcmonnies' questionnaire (MMI) -Questionnaire ocular surface disease index (OSDI)

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Title/Year	Evidence Level/ Type of Study	Population/Sample	Methods for the detection of dry eye
Dry eye diagnosis [28]/2008	Level IV/Control Case	Two groups of subjects with dry eye and 32 normal individuals were recruited into the study including 41 without symptoms or signs of anterior eye disease.	-Schirmer test -Test film tear breakup time (TBUT) -Bengal rose staining test -Fluorescein staining test -Green lissamine test
Prevalence of dry eye in bangkok, Thailand [29]/2006	Level VI/Clinical Trial	550 volunteers adult and elderly who came for a routine eye examination.	-Test film tear breakup time(TBUT) -Fluorescein staining test -Meibomian gland dysfunction test -Schirmer test
Prevalence of dry eye among the elderly [30]/1997	Level VI/Cohort	2,520 elderly residents of Salisbury, Maryland. Data derived from the Health Care Financing Administration Medicare database.	-Bengal rose staining test -Schirmer test

Discussion

Several methods should be employed to examine the tear dynamics fully because of the multifactorial nature of the dry eye disease [31]. Thus, when the diagnosis is not established at an earlier stage, it may result in various implications [5, 9]. Thus, the results of this study allowed the scientific knowledge of the different methods used for the detection of dry eye, which are essential, especially for patients in intensive care unit.

For the detection of dry eye, some studies reported the performance of tests and questionnaires as required. Its diagnosis is made after the measurements methods. After careful reading, there was not consensus on what and what order the tests should be performed. According to Kantor (2010), it is not easy to determine the incidence and prevalence of dry eye because there is no single diagnostic test to differentiate people with dry eye. Also, there is no consensus on the combination of tests that must be used to define the clinical disease [32].

In a cross-sectional study, the dry eye was evaluated by scoring a questionnaire (Mcmonnies' questionnaire) associated with the following diagnostic tests: Meibomian gland impairment test, tear film breakup time test, Bengal Rose staining test, lissamine color test and Schirmer test [33].

From the analysis of the articles by the level of evidence, there is a large portion of studies (76.5%) describing the Schirmer test as a method to detect dry eye. Out of the 13 studies found, six presented evidence level II, one study with a level of evidence III and six studies with level of evidence IV. Only three studies thoroughly described the test performance.

In two studies evidence level VI and evidence level VI, the test is described by its steps performance. This test placed a dry filter paper strip measuring 35 x 5mm in the region of the lower bag at the junction of the side and middle thirds, avoiding touching the cornea for 5 minutes. After this, the strips are removed, and some tears are recorded in millimeters from the pre-calibrated strips [24, 29]. In the study of Laight (1996) [19], evidence level II, it is advised that preferably during the test, the lid must remain open. However, in another study with evidence level IV, the closing of the eyes during the test was reported [24].

Studies indicate the test division as Schirmer I test, used without anesthesia and evaluating the basal

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secretion coupled tear to the reflection trigeminal, and the Schirmer II test that evaluates the basal component only when anesthesia is used [15]. The types of tests were mentioned in three studies with evidence level II and in one study with evidence level IV.

The measurement methods are different for each type of Schirmer test. An evidence level II study defines as 10 mm to score Schirmer without anesthesia and 5 mm to Schirmer test with anesthesia [29]. Another evidence level IV study evaluates, Schirmer less than or equal to 5 mm in five minutes without the use of anesthetic as a diagnosis of dry eye [24]. In the literature, there is a study inferring the diagnosis of dry eye with Schirmer less than 10 mm without the use of anesthetic [34]. In this sense, it is emphasized that the test is useful for evaluating dry eye, but dry eye diagnosis or exclusion cannot be based only on this test. It is considered the simplest test to assess the production of the aqueous tear [35].

The most frequently second test (52.9%) was the Bengal Rose, found in nine studies. Out of these studies, 5 had evidence level II, two studies had evidence level III and 2 had evidence level IV. Authors describe that 1% Bengal Rose dye is placed in the conjunctival sac. The vital dye staining intensity on the ocular surface is graded from 0-9 according to the criteria proposed by Bijsterveld, which is used as the standard for vital evaluation staining of the exposed area of the cornea and conjunctiva for coloring Bengal Rose [17]. In another evidence level II study, it is mentioned that the condition of the conjunctival epithelium is obtained through a graduated scale of coloration that provides ordinal data with 0 to 3 values (0=absent, 1=slightly present 2= moderate coloration, 3=gross coloration) [19].

Zeev, Miller and Latkany (2014) in his study indicates that the Bengal Rose staining is a valuable tool in the evaluation of dry eye, but it is best used as a supplement due to its lack of sensitivity and specificity and the ability to occur in patients as-

ymptomatic. Moreover, it is important to note that this dye is toxic to the corneal epithelium. Without anesthesia, it may cause discomfort upon instillation and therefore, it is less commonly used than the fluorescein staining test [36].

The staining test with fluorescein was the third most frequently cited (47%). Its division in the results as the level of evidence was: 4 studies of evidence level III and four studies in the evidence level IV. The fluorescein is useful in the evaluation of dry eye because its application can determine the corneal epithelial and conjunctiva integrity. The normal epithelium does not stain. However, when the mucosal layer is absent, the dye penetrates and stains the epithelium. Evaluation after 2 minutes is recommended for premature examination of the surface may underestimate the degree of damage [37]. In a study evidence level IV, the test was graded as 0 (no staining), 1 (slight coloration limited to less than one-third of the cornea), 2 (moderate staining of less than 1/2 of the cornea) or 3 (severe staining half or more of the cornea) [24].

Another study reports that there may be problems with the use of fluorescein as the preservative can cause some toxicity on the surface or the means of verifying the intraocular pressure; a procedure sometimes performed before the test that can cause subtle epithelial damage. Ideally, to evaluate a patient in the dry eye condition properly, he must be evaluated before using any eye drops or performing other evaluation [36]. This same study states that the Bengal Rose staining test is more aggressive for the ocular region.

The tear film breakup time test also cited by 41.2% of the studies is for applying the dye fluorescein. After instillation, the patient is instructed to blink once and finally keep the eye open. This test was mentioned in two studies evidence level II, one study evidence level III, and four studies evidence level IV. In normal patients, a dry spot by evaporation appears on the tear layer on the surface of the cornea in a time less than 10 seconds. Patients with

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aqueous-deficient (lacrimal glands) and oil layer disorders (Meibomian glands) have the time reduced significantly [38]. Thus, this result is confirmed with other studies that report the time of rupture considered within the larger normal value or equal to 10 seconds [29, 39, 40]. Also, the study describes that this test should be done without anesthetic, although many health professionals evaluate with eye drops or strips combination with anesthetic eye drops [36].

Besides these tests, the results reported the Meibomian gland dysfunction test, which determines the condition of the Meibomian glands. The examiner must visually evaluate the eyelid margin for each patient on both upper and lower eyelids with a slit lamp. Digital pressure is constantly applied to the upper and lower tarsus and, after that, the Meibomian gland and the degree of obstruction should be evaluated [26, 29, 31, 41].

This evaluation was found in studies evidence level II and IV. In a study evidence level II, the presence of obstruction of Meibomian gland was recorded as follows: grade 0, clear secretion and without obstruction; grade 1, translucent serous when compressed the margin of the eyelid; grade 2 white sticky discharge or serous when compressed the margin of the eyelid and grade 3, no secretion by compressing the edge of the eyelid [29]. Another study states that the simplest method to assess the Meibomian glands involves quantifying the clogged holes of the gland and quality of the expressed oil secretion classification. Meibometry, a technique in which a margin of the eyelid oil sample is removed with a strip and quantified by densitometry can measure the deficiency of oil in the eyelid margin quantitatively. The thickness of the lipid film of oil can be assessed by interferometry [35].

Another test used is green lissamine, observed in studies of evidence II and IV. The green color on the ocular surface determines dead or devitalized cells when suggestive of dry eye. Several indices are available for the evaluation of coloration, such as Bijsterveld Van index, Oxford Grading Scale and the scheme Collaborative Longitudinal Evaluation of Keratoconus (CLEK) [42]. This test resembles the Bengal Rose staining but causes much less eye irritation [43].

The Ocular Surface Disease Index (OSDI) is a questionnaire that beyond the level of evidence IV, it was performed in a study evidence level III. The questionnaire is psychometric, tested, a validated and reliable instrument for the measurement of dry eye disease severity. The questionnaire has 12 questions divided into three sub-ranges: a related vision range, an ocular symptoms range, and an environmental sensors range. The three sub-ranges have 5, 4 and three questions. All items of the questionnaire have equal scores. Scores do not vary with the item, but according to the duration in which the problem persists [27].

This questionnaire can range from 0 to 100; higher scores represent greater disability. Based on OSDI score, the ocular surface is defined as normal (0-12), mild (13-22), moderate (23-32), or severe (33-100) [44]. It is noteworthy that although the OSDI is not routinely used in clinical practice, it has been shown to be valid and reliable to quantify the impact of dry eye on the quality of life [44].

The phenol red test, presented in a study evidence level IV is used to provide an index of the lacrimal volume, which is related to the secretory rate of tear and, therefore, detects dry eye disease by aqueous deficiency. A cotton thread with phenol red is used, a sensitive substance to pH changes from yellow to red in contact with the neutral pH of tears. The end of the cotton thread is gently placed on the lower lid (as in Schirmer test), and wet wire length is measured after 15 seconds. Using a cutoff value of 6 mm for the diagnosis of dry eye, this test shows less variation among patients and is reportedly better in the detection of the dry eye of Schirmer test. However, there is no universal consensus on its value about the Schirmer test. As the test has only a short period, the effects of environ-

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mental conditions such as humidity are minimized. The diagnosis of dry eye is inferred with a cutoff value of 10 millimeters [35].

Furthermore, one study also performed the rate of evaporation of the tear film, measured separately for each eye. Humidity sensors and evaporimeter closed temperature are closed used inside a sealed chamber held in place in the eye to measure the change in humidity, in which the measurements are performed with open and closed eyes. The evaporation from the ocular surface is calculated as the difference between the evaporation rate during measurement with a closed eye and the evaporation rate during the measurement taken with the eyes open. The tear film evaporation rate is then calculated for two relative humidity, ranging from 25-35% (30% average humidity) and 35-45% (average 40% moisture) [18].

Finally, the McMonnies' Questionnaire (MMI) was identified in a study of level IV, presenting 14 questions that focus on clinical risk factors for dry eye. These domains are derived from the literature and includes age, gender, history of use of contact lenses, the symptoms of dry eye (stinging, foreign body sensation, feeling of dryness and fatigue), prior treatment for dry eye, secondary symptoms (associated environmental stimuli), systemic diseases, dryness of mucous membranes and systemic medications. The MMI uses a scoring system of 0 to 45. Scores above 14 are consistent with the diagnosis of dry eye. The closer the score is 45, the more definite diagnosis of dry eye [27].

Conclusion

It was found that the main methods for the detection of dry eye identified in the literature are: Schirmer test, Bengal Rose staining test, fluorescein staining test and tear film breakup-up time. For its execution and analysis, the first test cited is a practical test, and the trained nursing professionals can accomplish it, so its use in hospitalized patients in ICU can minimize future eye damage.

There were 17 articles on levels of evidence II to IV, of which most of them were classified as level IV. Thus, it is seen the need for studies with better levels of evidence on the subject as well as with the participation of nursing in these procedures, because it is a profession in direct and continuous contact with patients. However, it is noted that all sector staff should participate in an effective way, to consider the need for multidisciplinary integration.

Furthermore, a consensus on the most appropriate test for dry eye detection highlights that it is necessary as well as their measurements, as it is seen some differences between the studies. Also, it is emphasized that the results of this research will be of great value to managers, health professionals and especially for ICU patients, to provide a better quality of life.

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