TOXIC ANTERIOR SEGMENT SYNDROME AFTER CATARACT SURGERY: THE IMPLICATIONS FOR NURSING

Síndrome tóxica do segmento anterior após cirurgias de catarata: implicações para a enfermagem

Síndrome tóxico del segmento anterior después de cirugía de catarata: las implicaciones para la enfermería

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ABSTRACT: **Objective**: To describe the characteristics of the toxic anterior segment syndrome (TASS) and its implications for nursing actions. **Method**: It is a literature review through research in the MEDLINE (Medical Literature Analysis and Retrieval System Online) and LILACS (Latin American and Caribbean Center on Health Sciences Information) databases. **Results**: TASS is an acute ocular inflammatory reaction after ophthalmic surgeries, mainly cataract surgery. The clinical signs in the first 12 hours after the surgery include corneal edema, presence of cells in the anterior chamber, increased intraocular pressure, and irregular pupil. The main causes are related to noninfectious substances introduced into the patient's eye by products used during surgery or due to failures in cleaning and sterilization of surgical instruments. **Conclusion**: The implications for nursing consist of preventive measures, staff training, orienting the patients, and active epidemiological surveillance aimed at the early identification of warning signs of TASS.

Keywords: Cataract extraction. Perioperative nursing. Epidemiological surveillance. Sterilization. Endophthalmitis.

RESUMO: **Objetivo:** Descrever as características da síndrome tóxica do segmento anterior (TASS) e as implicações para as ações de enfermagem. **Método:** Trata-se de uma revisão da literatura por meio de pesquisa nas bases de dados *Medical Literature Analysis and Retrievel System Online* (MEDLINE) e Literatura Latino-Americana em Ciências da Saúde (LILACS). **Resultados:** A TASS é uma reação inflamatória ocular aguda após cirurgias oftálmicas, principalmente a cirurgia de catarata, cuja apresentação clínica nas primeiras 12 horas após o procedimento inclui sinais como edema da córnea, presença de células na câmara anterior (CA), pressão intraocular aumentada e pupila irregular. As principais causas estão relacionadas com substâncias não infecciosas introduzidas no olho do paciente a partir de produtos usados durante a cirurgia ou devido a falhas no processamento dos instrumentais. **Conclusão:** As implicações para a enfermagem consistem nas medidas de prevenção, treinamento de pessoal, orientação aos pacientes e vigilância epidemiológica ativa visando à identificação precoce de sinais indicativos da TASS.

Palavras-chave: Extração de catarata. Enfermagem perioperatória. Vigilância epidemiológica. Esterilização. Endoftalmite.

RESUMEN: **Objetivo**: Describir las características del síndrome tóxico del segmento anterior (TASS) y las implicaciones para las acciones de enfermería. **Método**: Se trata de una revisión de la literatura mediante búsquedas en las bases de datos MEDLINE y LILACS. **Resultados**: El TASS es una inflamación ocular aguda que se produce después de la cirugía oftálmica, especialmente la cirugía de cataratas, cuya presentación clínica en las primeras 12 horas incluye signos tales como edema corneal, la presencia de células en la cámara anterior, aumento de la presión intraocular y la pupila irregular. Las principales causas están relacionadas con sustancias no infecciosas introducidas en el ojo del paciente durante la cirugía o debido a fallas en el lavado y esterilización de instrumentos quirúrgicos. **Conclusión**: Implicaciones para la enfermería consisten en medidas de prevención, capacitación del personal, la orientación a los pacientes y la vigilancia epidemiológica activa encaminada a la identificación temprana de signos de advertencia de TASS.

Palabras clave: Extracción de catarata. Enfermería perioperatoria. Vigilancia epidemiológica. Esterilización. Endoftalmitis.

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INTRODUCTION

The toxic anterior segment syndrome (TASS) is an acute inflammatory reaction caused by noninfectious substances that enter the anterior chamber (AC) of the eye, damaging the intraocular structures, particularly the corneal endothelium and the trabecular meshwork[1-3].

Monson et al.[4] reported for the first time in 1992 three cases of intraocular inflammation after a cataract extraction surgery, with a pattern in the signs that appeared, as generalized corneal edema, corneal endothelium damage, reduced visual acuity, and dilated pupil. Because of the characteristics of all the observed signs, this type of inflammatory reaction started to be called toxic anterior segment syndrome[5].

Several eye surgeries can be affected by this type of adverse event, such as posterior vitrectomy[6,7], corneal transplant[8], and combined surgeries of posterior vitrectomy and cataract extraction[9]. However, the latter is the one that most commonly presents this type of postoperative complication.

Despite the frequency that researches about this topic have been published in the world, only one study has been released in Brazil reporting the occurrence of TASS[10]. This gap can be attributed to the difficulty in the diagnosis of these cases by ophthalmologists and nurses working in the ophthalmology area or in the area of prevention and control of health-care-associated infections (HAIs).

The nursing staff must actively participate in the process of identifying adverse events after cataract surgeries and intervene preventively in the actions under its responsibility. Thus, this study aimed to present the phenomenon of TASS, its epidemiology, and its implications for nursing actions.

METHOD

This is a review of scientific literature about the epidemiological aspects, clinical characteristics, and factors associated with TASS. A search in the databases MEDLINE (Medical Literature Analysis and Retrieval System Online) and LILACS (Latin-American and Caribbean Center on Health Sciences Information) was performed. The data were collected from January to July 2014, with no limitation regarding the study's publication period, using the following keywords in Portuguese, English, and Spanish, respectively: *síndrome tóxica do segmento anterior, inflamação do segmento anterior*; toxic anterior segment syndrome, anterior segment inflammation; and *síndrome tóxico del segmento anterior* and *inflamación del segmento anterior*, and adopting the Boolean operator "OR".

We selected studies focused on factors associated with TASS, including its epidemiological aspects and clinical characteristics, to identify factors on which the nursing staff can act. Editorials and commentaries were excluded.

The variables investigated in the review included the following components: incidence, clinical signs and symptoms, evolution, treatment, factors associated to TASS, and prevention measures.

RESULTS

Incidence and clinical characterization

Most of the selected articles are case reports in which it was not possible to identify the incidence, but five of them reported 0.98% incidence of TASS, on average, ranging from 0.07 to 2.13% (Table 1).

As for its clinical characterization, great variation is observed between the reported cases. The most common signs are corneal edema, deposition of cells, fibrin in the AC, flare[14,16,17] (Tyndall effect, in which small particles that are impossible to be seen with the naked eye are viewed through a beam of light), and mydriasis[1,2,4,14]. Other less common signs are irregular and/or nonreactive pupil[1,2,4], high intraocular pressure (IOP)[3,4,15,18], and hypopyon[16,18-20].

The time frame to detect these signals is 12–36 hours, and, in most cases, they are detected in the first 12 hours with at least four of the manifestations described earlier[1-3,14].

The affected patients do not show a characteristic symptomatology. In some cases, they may have low visual acuity (LVA)[1,4,19,21] and, rarely, pain[2,18].

As for the morphological characteristics, the affected corneas are characterized by the low density of the endothelial cells, the high coefficient of variation of cell areas, and the low average percentage of hexagonal cells[17].

Evolution and treatment

The evolution of cases with TASS has usually a favorable prognosis[15,18,19,22], however, most severe cases, more than half, on average, evolve to the need for corneal transplant surgery[1-3,20,23,24]. Another complication of the syndrome is the elevation of IOP, which may demand

Table 1. Incidence of toxic anterior segment syndrome according to different authors and countries. São Paulo, 2014.

Country	Year of publication	Surgeries performed	Number of cases	Incidence (%)
South Korea[1]	2008	801	15	1.87
USA[11]	2006	2,713	2	0.07
India[12]	2011	26,408	60	0.23
Turkey[13]	2010	1,742	14	0.80
Pakistan[14]	2013	18,140	15	0.80
Turkey[15]	2012	893	19	2.13

USA: United States of America.

antiglaucomatous surgery when it is impossible to control it by drug therapy[1-3].

The treatment is usually pharmacological based on the concomitant use of steroid eye drops, antibiotics, and 5% NaCl[1,15,25,26]. In some cases, additional surgical procedures are needed, such as washing the AC, replacing intraocular lens (IOL), and anterior or posterior vitrectomy[3,18,19].

Factors associated with the toxic anterior segment syndrome

In 2006, eight cases of TASS were reported in the United States of America (USA). Despite adjustments in the cleaning procedures and sterilization of surgical instruments, among other measures, other patients had the TASS clinical status. After additional measures have been adopted, other cases were not reported. Several hypotheses have been raised, but the causes have not been identified[27].

Members of the industry and the American Society of Cataract and Refractive Surgery (ASCRS) developed a task force. The first actions were posting an online questionnaire on the practices of eye care services and notification of cases of TASS. This questionnaire was answered by centers in several countries, including the USA, Italy, Spain, Romania, Mexico, Argentina, and Brazil.

The result of the analysis of these questionnaires was supplemented by data obtained through interviews and direct observation in visits to ophthalmology centers in the USA. Of the 68 questionnaires included in the study, 909 cases were identified in 50,114 performed surgeries and 367 cases were reported during the visits to the American centers after 143,919 surgeries from 2005 and 2009. The noncompliance most observed in these visits were the inadequate rinsing of the phacoemulsification probe and the irrigation and aspiration devices and the reuse of single-use devices, such as cannulas and "Sleeves" infusion gloves[28].

Continuing this work, a retrospective analysis of the same database referring to the 2009–2012 period was performed. In this period, the participating centers reported to have performed approximately 69,000 surgeries with the detection of 1,454 cases of TASS, with the washing and sterilization process and the reuse of single-use devices being the most common nonconformities observed[29].

Rose[30] reported six cases in which it was not possible to determine the etiology. However, with the implementation of precleaning of phacoemulsification probe and irrigation and aspiration (I/A) handpieces immediately after the surgery, no new cases were reported over 2 years, which suggests a causal link between the cleaning failure and the occurrence of TASS in cataract surgeries.

Other works could point out some products as the possible causes of TAAS (Table 2).

Cleaning and sterilization process

The misuse of *ortho*-phthalaldehyde solution was the cause indicated in the report of a case in which this solution was used to soak the instruments before being subjected to sterilization by Ethylene Oxide (EtO)[26].

Another report suggested the glutaraldehyde solution as the cause of an outbreak of six cases, five of which have evolved to the need for corneal transplant. This solution was used in the processing of instruments as an autoclave pretreatment without rinsing[2]. Similar to this report, the use of a surgical instrument sterilized in glutaraldehyde solution was pointed out as the likely cause of TASS in a child after cataract surgery[22].

Table 2. Products mentioned as causes of toxic anterior segment syndrome in the literature, according to country, year of the study, and number of cases. São Paulo, 2014.

Place	Year of the study	Number of cases	Mentioned products
South Korea[1]	2008	15	Ethylene oxide gas
Turkey[2]	2006	6	Glutaraldehyde
USA[3]	2006	8	Remnants of ointment
USA[11]	2006	8	Sulfate
India[12]	2011	60	BSS with altered pH
Pakistan[14]	2013	15	Lactated Ringer with high pH
Turkey[15]	2012	19	Ethylene oxide gas
USA[18]	2000	10	IOL
Israel[19]	2010	2	Viscoelastic solution
USA[20]	2010	2	Trypan blue
Netherlands[21]	2011	3	Viscoelastic solution
China[22]	2010	1	Glutaraldehyde
USA[25]	2006	1	IOL
South Korea[26]	2010	1	*Ortho*-phthalaldehyde
USA[31]	2008	112	Endotoxins in BSS
USA[32]	2004	16	Enzymatic detergent

USA: United States of America; BSS: balanced salt solution; IOL: intraocular lens.

Clouser[32] described the investigation of three cases that arose several hypotheses, including the fact that the enzymatic solution was not changed at the appropriate frequency, but only when it was visibly dirty. Another hypothesis was the possibility of evaporation of the water from the enzymatic detergent bath in the tanks of the ultrasonic washer and consequent increase in its concentration. However, an experimental study that simulated an inadequate rinsing of the instruments does not support this hypothesis, concluding that even a high amount of detergent remnants could not be the main cause of TASS[33], as shown in the study of Parikh et al.[34].

Ari et al.[15] described the clinical course of 19 cases, and the analysis of the data from the surgeries led the authors to suspect that the EtO sterilization of the kits for anterior vitrectomy was the cause.

Another study that examined 15 case records also indicated EtO sterilization as the most likely cause. After using steam sterilization, instead of EtO for processing instruments, no more cases were reported in the next 2 years[1]. However, this hypothesis did not prove to be reliable according to a study that evaluated the intraocular reaction caused by EtO in rats and found that it is not associated with TASS[35].

Hellinger et al.[11] investigated the causes of an outbreak of eight cases focusing on the quality of the water used in the cleaning and sterilization process. These authors concluded that, although the outbreak was possibly multifactorial in its etiology, sulfate was one of the impurities found in the water of the autoclave's reservoir, which may be pointed out as the main factor associated with those cases.

In an experimental study in partnership with the Food and Drug Administration (FDA), in which the ability of metals to produce intraocular inflammation was evaluated, the results confirmed this hypothesis[35], but this study used much higher concentrations than those found in the study by Hellinger et al.[11].

Supplies and medicines used during surgeries

Kutty et al.[31] presented the results of an investigation in which tests were conducted to detect and quantify toxins and microbial contaminants in the solutions used in the hospital, which were the following: lubricants, anesthetics,

balanced salt solution (BSS), polyvinylpyrrolidone–iodine (PVP-I), and anti-inflammatories, among others. Of the products tested, the BSS had high level of endotoxins of, on average, 0.908 endotoxin units per milliliter (EU/mL), therefore greater than the recommended limit, which is 0.5 EU/mL[36]. The products of the tested brand were taken out of the market, which resulted in the discontinuation of outbreaks. Until then, there were 112 cases.

Buchen et al.[36] conducted an experiment in an animal model to assess the maximum level of endotoxins in the solutions for intraocular use capable of inducing ocular inflammation after eye surgeries. The study showed that an endotoxin concentration in the range of 0.25–0.75 EU/mL may have the capacity to promote deposition of cells on the IOL surface, flare, and deposition of cells in the AC but no corneal edema.

Reinforcing these findings, another experimental study investigated the minimal concentration of endotoxins capable of causing TASS in the eyes of rats and found that a concentration of 0.23 EU/mL can cause an inflammatory reaction in the anterior segment of the eye[37].

Considering these findings, the FDA changed the recommendations for maximum levels of endotoxin in products used in cataract surgery, from 0.5 to 0.2 EU/ml[38].

Sengupta et al.[12] reported 60 cases of TASS. In 31 of them, the etiology remained unknown, but there were two clusters of cases in which the causes were identified as the pH of 6.0 (cluster of 12 cases) of BSS and a specific batch of Ophthalmic Viscosurgical Device (OVD) (cluster of 17 cases).

Other reports also suggested the OVD as a likely cause of TASS in patients undergoing implantation of a type of IOL that does not require the removal of the crystalline lens[19,21]. Although an investigation that supports this hypothesis has not been performed. It was reinforced by the fact that the OVD was longer in contact with the AC tissues of the eye, particularly the iris and corneal endothelium.

Unlike these studies, Mathys et al.[39] observed in approximately 20 patients remnants of OVD between the posterior capsule and the IOL, and that, in a period of 2 months, when these remnants were removed for analysis, there was no inflammatory reaction.

An experimental study analyzed the cytotoxitity of the cannulas used for OVD injection. After filling the lumens with OVD, cannulas were pre-cleaned in an ultrasonic washer with enzymatic detergent, rinsed with pressurized water pistols and sterilized. The samples were submitted to the cytoxoticity test, which showed no cytotoxic effect. In a group of samples that were not rinsed, alterations in the cells morphology were observed. Although not considered toxic, such alterations may suggest an inducer or precursor of the phenomenon of TASS.[40]

Intraocular dyes and antibiotics used during surgery and ointments used in bandage at the end are also mentioned as potential causes of TASS. Buzard et al.[20] reported two cases related to the use of trypan blue dye of a generic brand, which, after laboratory analysis, proved to be almost three times more toxic than the trademark used as control.

Werner et al.[3] reported the clinical characteristics of TASS that had in common remnants of oily substance found on the surface of the explanted IOLs, from ophthalmic ointment used under the bandage after surgery. The ophthalmic ointment was identified as the etiology of the cases that evolved mostly for the replacement of the IOL, and, in four of the eight cases, there was a need for corneal transplant.

Although the ointment has been strongly associated as the cause, other studies have shown an inert reaction of that product. Chen et al.[41] reported the case of a patient who had ointment remains deposited on the surface of the IOL for over a year without causing inflammatory reaction, similar to other two other studies that reported the ointment remains on the AC of the eye as not being enough to cause inflammatory reaction[42,43].

Other factors

Jehan et al.[18] reported 10 cases and investigated through questionnaires sent to the surgeons involved. The authors claimed that IOL was the probable cause because all cases used the same type and the same brand, besides the fact that such IOL has been taken out of the market by the own manufacturer after other reports of adverse events. Also regarding the type of IOL, Moshirfar et al.[25], despite having considered other possible causes, suggested the possibility that a specific model of IOL was the cause.

Kim et al.[44] did a report of a case in which a patient evolved to a characteristic clinical condition of TASS after cataract surgery in both eyes. The collection and analysis of materials to assess the IgE and IgG levels present in the vitreous found a higher value than expected. The authors postulated that the probable cause is a hypersensitivity of unknown etiology.

Nursing actions to prevent toxic anterior segment syndrome

Nursing can play an important role in preventing TASS, as long as the professionals are aware of the main factors involved in its causality.

The cleaning and sterilization process has often been mentioned as a factor associated with the occurrence of TASS[1,2,11,15,22,26,32]. In Brazil, as in many other countries, the nursing team is responsible for processing instruments. Therefore, ensuring the completion of the correct procedures, the nurses can contribute significantly to reduce the chances of occurrence of TASS. On the basis of the recommendations found in the literature, we can summarize the main preventive measures regarding the handling of surgical instruments, namely:

- to keep the employees of the Surgical Center and of the Material and Sterilization Center aware of possible adverse events and how to prevent them[45,46];
- to acquire sufficient quantity of instruments to allow sufficient time for cleaning and sterilization[45,46];
- to not reuse single-use products[46,47];
- to wash the instruments immediately after use to prevent OVD from drying in the lumens. If the immediate washing is not possible, a pre-rinsing still in the operation room is recommended[45,46];
- to wash ophthalmic instruments separately from other instruments[48];
- to promote abundant rinsing of instruments and of the I/A handpieces[45,47,48] with purified water[49], preferably using high-pressure rinse gun;
- to dry the instruments with filtered compressed medical air[45,49]; and
- to never sterilize the instruments with chemical solutions, such as glutaraldehyde, *ortho*-phthalaldehyde, and peracetic acid[46].

Other forms of nursing activities are the standardization and the training for dilution of drugs that are administered into the eye during surgery to prevent the administration of toxic doses[50] or medications with preservatives[47,51]. In addition, it is essential to maintain detailed records on the use of materials, solutions, and medicines[45] capable of causing TASS, such as BSS[12,31], OVD[19,21], Lactated Ringer[14], trypan blue[20], and IOL[18,25] so that further investigation in case of outbreaks could be possible.

Although a mild and transitory inflammatory process characterized by the eye's AC reaction is common after cataract surgery[52,53], it is necessary to be aware of it because it is a warning sign of TASS[51]. In this sense, an active surveillance system that intends to monitor this sign in cataract postoperative period could have it as an indicator for early detection of this type of adverse event. The active search for new cases and continuous surveillance can be added to this measure, as attitudes that will allow us to know the endemic levels and favor the early detection of outbreaks[52].

For the success of this active search, the involvement of all medical staff is necessary. They should be oriented and encouraged to report any suspected cases to the nurse responsible for the prevention and control of HAIs[54].

Among the general recommendations found in the literature regarding adverse event surveillance, the following stand out:

- monitoring of postoperative inflammatory reactions[51];
- investigating all episodes of outbreaks, for the enlightenment of the etiology[51];
- orienting patients to return immediately to the clinic in case of LVA or pain[51];
- establishing the registration of drugs and solutions used in the surgeries to enable tracing[46,51]; and
- developing effective communication regarding the changes in the purchase of solutions and medicines to ensure that new products will be properly used[51].

FINAL CONSIDERATIONS

The TASS is a worrisome event because of its severity and multi-causal nature. In addition to issues related to the failure to diagnose it and underreporting, the limitation of the investigation methods makes it difficult to determine its causes.

The main recommendations for preventing new cases consist of staff training, implementation of best practices for medical device processing, and adoption of a system of records on the use of materials, solutions, and medicines used in eye surgery, in addition to the establishment of an active surveillance system aiming at early identification and management of cases of TASS.

Next to the important role of the ophthalmologist, it was identified in the literature the role of nursing in the measures for preventing the phenomenon, from the processing of materials and the provision of inputs to the epidemiological surveillance and the orientation to the patient.

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