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PROFESSIONAL DIRECTIONS

Enzymatic Detergents: Are They the Primary Cause of TASS?

Introduction

Surveyors for the Centers for Medicare and Medicaid Services (CMS) routinely advise health-care facilities to adhere to the labeling of reusable medical instruments (Hillman, 2016). This labeling routinely includes the manufacturer's recommendation, if not the requirement, to use enzymatic detergents prior to sterilization to clean reusable ophthalmic instruments used to perform cataract and other intraocular surgeries. A joint statement released in December 2015 does not endorse this cleaning recommendation, however, notwithstanding the reusable instrument's labeling (ASCRS, AAO, & OOSS, 2015). This joint statement was approved by the American Society for Cataract and Refractive Surgery (ASCRS), the American Academy of Ophthalmology (AAO), and the Ophthalmic Outpatient Surgery Society (OOSS).

Instead, these three organizations have concluded that enzymatic detergents should not be required to clean intraocular surgical instruments (Hillman, 2016). This stance is based on a concern that residues of the enzymes used in these detergents could remain on the surfaces and in the lumens of these surgical instruments after cleaning and incomplete water rinsing, potentially elevating the risk of toxic anterior segment syndrome – or TASS (Hillman, 2016).

A fourth organization, the American Society of Ophthalmic Registered Nurses (ASORN), did not approve the December 2015 joint statement, questioning the merit of its conclusions (ASORN communication). ASORN continues to advise adherence to the device's labeling, which may include use of an enzymatic detergent to enhance cleaning effectiveness. Presenting as sporadic cases or outbreaks, TASS is an acute, sterile inflammation of the anterior segment of the eye that can result in blindness.

Methods and Objectives

To review reports, guidelines, publications, and studies to evaluate whether enzymatic detergents have been confirmed to be the primary cause of TASS following cataract and other intraocular surgeries, or whether other confounding factors might be as significant a risk factor for TASS.

Key Findings

- Risk factors for TASS include, but are not limited to, the improper cleaning and sterilization of intraocular surgical instruments.
- Studies reporting enzymatic detergents to be the primary cause of TASS outbreaks are lacking.
- Studies reporting enzymatic detergents to be associated more strongly with TASS than several other possible risk factors, including short-cycle sterilization, are similarly lacking.

Results

This review identified the improper cleaning and sterilization, or "reprocessing," of (reusable) intraocular surgical instruments to be a risk factor for TASS (Hillman, 2016; ASCRS, AAO, & OOSS, 2015; Mamalis & Edelhauser, 2013). As discussed in the joint statement approved in December 2015 by ASCRS, AAO, and OOSS (ASCRS, AAO, & OOSS, 2015), both the inappropriate use of enzymatic detergents and their incomplete removal during (water) rinsing have been linked to outbreaks of TASS (Hillman, 2016). However, this review did not identify the enzymes in these detergents to be either the primary cause of TASS outbreaks or a more significant contributor to TASS than several other documented risk factors, whether or not related to instrument reprocessing.

Reports indicate that TASS also has been associated with impurities in the moisture of the steam used to achieve sterilization (Hellinger et al., 2006) – often short-cycle sterilization, which a significant number of ambulatory surgery centers (ASCs) use to steam sterilize intraocular instruments (AAO, 2015). Whereas the longer cycle of gravity displacement steam sterilizers may

reach a temperature of 121°C for 30 minutes, short-cycle (prevacuum) steam sterilizers instead use a higher temperature (e.g., 137°C) during a significantly shorter exposure time (e.g., as short as 3 minutes). "Flash" sterilization of unwrapped instruments for immediate, emergency use and a process that some organizations may define as "immediate-use steam sterilization," or IUSS, are two examples of what this review defines as a short-cycle sterilization process (AAO, 2015; Lipner, 2015).

Although a rapid short-cycle process sterilizes instruments quickly, allowing repeated use throughout the day, this benefit can be offset by possible drawbacks resulting from the cycle's rapid heating and cooling phases, including potential damage to delicate surgical instruments and wear/fatigue that shortens their use-life (AAO, 2015; Lillis, 2015; Timmons & Goodman, 2016). Like both the labeling of some of these surgical instruments and a healthcare facility's policies and procedures, guidelines may emphasize the potential limitations associated with short-cycle sterilization processes, particularly flash sterilization (AAO, 2015; Lillis, 2015; Timmons & Goodman, 2016).

Due to a lack of published data, this review could not determine whether damage to delicate intraocular instruments following their repeated exposure to a rapid sterilization cycle might be a more direct cause of TASS than is documented (or than the use of enzymatic detergents to enhance instrument cleaning). However, the potential for factors such as ordinary wear and tear, pitting, flaking, spotting, staining, chipping, and/or corrosion of intraocular instruments to contribute to the inadvertent introduction into the eye of microscopic debris cannot be ruled out as a potentially significant risk factor for TASS.

An outbreak investigation published last year reported a strong association between cases of TASS at a California surgery center and the bacterial contamination of two steam sterilizers (Sorenson, Sorenson, & Evans, 2016). This report suggested that the outbreak might have been caused by heat-stable bacterial cell antigens (endotoxins) in the steam. These antigens likely originated from biofilms from the walls of each autoclave's water reservoir, which the investigators cultured; according to this report, the antigens may have contaminated the surgical instruments during sterilization. This report also found eighteen other autoclaves used by nearby surgery centers to be similarly contaminated with bacterial biofilms. No additional cases of TASS were identified once this California surgery center replaced the two implicated steam sterilizers.

Similarly, in 2007 a clinical professor in British Columbia reported an association between a TASS outbreak and endotoxin contamination due to a short-cycle sterilization process. The outbreak was terminated by resolving bacterial growth identified in the steam sterilizer's water reservoir, as well as limiting use of short-cycle sterilization (Lipner, 2007). According to the professor, "If you're short of time or you're flashing instruments, then it can certainly kill bacteria, but it doesn't deactivate endotoxin. If you get a sufficient load of endotoxin in a susceptible individual you can get TASS" (Lipner, 2007).

The potential for TASS attributable to damaged surgical instruments is reportedly not limited to thermal sterilization processes (CDC, 1998). Certain oxidizing chemicals that may be used to achieve low-temperature sterilization (for example, a peracetic acid vapor) may degrade the brass components of some intraocular instruments, potentially causing copper and zinc deposits, toxic to the eye, to form during the sterilization process. Reports have linked TASS to the formation of these metallic precipitates in the cannulas of small-lumened intraocular instruments (CDC, 1998).

Factors unrelated to instrument cleaning or sterilization or to instrument damage also have been linked to TASS, including the improper use of irrigation solutions that contain preservatives, ophthalmic viscosurgical devices, and certain anesthetics, ointments, and other eye medications (CDC, 2008).

Discussion

As reported in the joint statement approved in December 2015 by ASCRS, AAO, and OOSS (ASCRS, AAO, & OOSS, 2015), using enzymatic detergents to clean intraocular instruments can be a risk factor for TASS. These detergents are not the only risk factor for TASS, however. Nor have enzymatic detergents been scientifically documented to be either the primary cause of TASS outbreaks or a more significant contributor to TASS than other documented risk factors, including the sterilization process. One study that investigated the effects of enzymatic detergents on the eye concluded that results "do not support residual enzymatic detergents on (ophthalmic) surgical instruments as a cause for TASS" (Leder et al., 2012).

Moreover, a TASS outbreak may be caused by more than one factor, without investigators determining or isolating the primary cause (Moyle, Yee, Burns, & Biggins, 2013). Studies investigating a single cause or risk factor for TASS – for example, the use of enzymatic detergents – may be poorly controlled and

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generally cannot eliminate the confounding effects of other possible contributing factors. In short, controlled scientific studies assessing the relative contribution to TASS of an enzymatic detergent, compared to one or more other risk factors including both the sterilization process and wear and tear to the intraocular instruments, have not been published.

Short-Cycle Sterilization

Generally delicate and expensive, intraocular surgical instruments may be reused several times a day, on different patients. To accommodate the time constraints posed by a demanding workflow, ASCs and other healthcare facilities performing intraocular surgery may use short-cycle sterilization to process these instruments, achieving a temperature as high as 137°C for a sterilization time as short as 3 minutes (CMS, 2015). Examples of intraocular instruments include phacoemulsification handpieces, cannulas, and both irrigation and aspiration handpieces.

In response to a large outbreak of TASS in 2006, ASCRS – which is one of the three groups that approved the joint statement in December 2015 (ASCRS, AAO, & OOSS, 2015) – formed a task force to investigate the outbreak's likely cause(s), as well as to provide recommendations for safely reprocessing intraocular instruments (ASCRS, 2006). This task force reported later that year that the short time allotted to clean and sterilize the instruments between patient cases was a risk factor for TASS (ASCRS, 2006; CBC News, 2006; Holland, Morck, & Lee, 2007; Guttman, 2006; Dalton, 2007).

No "Proven Benefit"?

The joint statement issued nine years later, in 2015, concluded that "based on the documented risk of TASS associated with enzyme detergent use, without proven benefit for endophthalmitis prevention, enzymatic detergent should not be required for routine decontamination of ophthalmic intraocular instruments" (ASCRS, AAO, & OOSS, 2015). This statement did not resolve, however, two questions germane to discussions and investigations about the use and safety of enzymatic detergents for cleaning intraocular instruments:

1. Might more complete water rinsing of these instruments (using sterile distilled or sterile deionized water, as recommended) significantly reduce, if not eliminate, the risk of TASS associated with enzymatic detergent residues remaining on their surfaces and in their cannulas following sterilization?
2. Might the relative risk of TASS associated with using enzymatic detergents to clean intraocular instruments be no greater than that which is associated with some other risk factors, such as a short steam sterilization cycle or the short time between patient cases?

More precise determination and measurement of the relative contribution of different risk factors for TASS is important to ensure that effective measures are developed and implemented to prevent future outbreaks. While the use of a detergent without enzymes could plausibly reduce the risk of TASS attributed specifically to enzyme residues, improved safety might alternatively be achieved by using an enzymatic detergent for cleaning, as commonly instructed by the manufacturers of intraocular instruments, while ensuring more robust and complete rinsing of the instrument with water to remove all remaining residues. The three organizations' 2015 joint statement (ASCRS, AAO, & OOSS, 2015) might concur, reporting that TASS outbreaks have been linked to incomplete (water) rinsing, which raises the unresolved question: Which is a more significant risk factor for TASS: incomplete water rinsing of the instrument, or the use of an enzymatic detergent to clean it?

Also, to be evaluated is whether the use of some nonenzymatic detergents to clean intraocular instruments could, plausibly, inadvertently introduce a different but possibly important risk factor for TASS – for example, damaging the instrument due to material incompatibility or ineffective cleaning. The cost-effectiveness of the detergent is also an important consideration for an ASC deciding which product to use. Some studies report that enzymatic detergents may be more effective than other types of detergents for cleaning soiled surgical instruments (CDC, 2008). Indeed, the labeling of many different types of reusable surgical instrumentation recommends using enzymatic detergents to enhance cleaning effectiveness.

The Labeling of Ophthalmic Instruments

As noted, CMS surveyors routinely advise healthcare facilities to adhere to a reusable surgical instrument's labeling, including its cleaning instructions (Hillman, 2016), which often include using enzymatic detergents (ASCRS, AAO, & OOSS, 2015). The 2015 joint statement endorsed by ASCRS, AAO and OOSS, however, recommends that "contrary to some manufacturers (instructions for use), it is our position that enzymatic detergent should not be required for intraocular instruments for several reasons" (ASCRS, AAO, & OOSS, 2015). While a recommendation that deviates from an instrument's reprocessing

labeling is certainly not unprecedented, it can create a "slippery slope" and cause confusion among healthcare staff about which instructions to follow or disregard.

Moreover, the FDA instructs manufacturers of reusable instruments to "recommend only cleaning agents or classes of agents (e.g., detergents such as quaternary ammonium compounds and enzymatic detergents) that were used during the cleaning validation studies, that have been demonstrated to be compatible with the device, and are effective in cleaning the device" (FDA, 2015). Therefore, use of untested detergents to clean intraocular surgical instruments may not be advisable, as these products may be less effective or may be incompatible with the delicate instruments' materials and cause damage, which may increase the risk of TASS. Echoing this stance, the ASCRS in 2007 published a guideline advising that the detergent and instrument manufacturers' directions for use be followed "to ensure proper use of the detergent and to ensure compatibility with the instruments" (Hellinger et al., 2007). Several other organizations discussing the sterilization of surgical instruments have recommended that critical reprocessing steps, including cleaning, "must be followed regardless of the specific sterilization cycle employed; a safe process does not include short-cuts or work-arounds" (AAMI et al., n.d.).

Summary and Conclusions

While the improper cleaning of intraocular instruments is recognized as a risk factor for TASS, this review found, however, that using an enzymatic detergent to clean intraocular instruments has not been shown to be either the primary cause of TASS or a more significant contributor to this inflammatory reaction of the eye than other documented risk factors, such as bacterial contamination of the water reservoirs of steam sterilizers, short-cycle sterilization, and damage to the intraocular instruments. More research is recommended to better quantify the relative risk of enzymatic detergents causing TASS, compared to these other risk factors, and to develop additional mitigations validated for the prevention of TASS.

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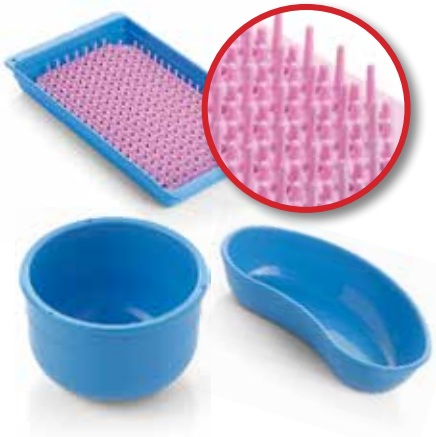

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