INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY MARCH 2006, VOL. 27, NO. 3

ORIGINAL ARTICLE

Outbreak of Toxic Anterior Segment Syndrome Following Cataract Surgery Associated With Impurities in Autoclave Steam Moisture

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BACKGROUND. Toxic anterior segment syndrome (TASS), a complication of cataract surgery, is a sterile inflammation of the anterior chamber of the eye. An outbreak of TASS was recognized at an outpatient surgical center and its affiliated hospital in December 2002.

METHODS. Medical records of patients who underwent cataract surgery during the outbreak were reviewed, and surgical team members who participated in the operations were interviewed. Potential causes of TASS were identified and eliminated. Feedwater from autoclave steam generators and steam condensates were analyzed by use of spectroscopy and ion chromatography.

RESULTS. During the outbreak, 8 (38%) of 21 cataract operations were complicated by TASS, compared with 2 (0.07%) of 2,713 operations performed from January 1996 through November 2002. Results of an initial investigation suggested that cataract surgical equipment may have been contaminated by suboptimal equipment reprocessing or as a result of personnel changes. The frequency of TASS decreased (1 of 44 cataract operations) after reassignment of personnel and revision of equipment reprocessing procedures. Further investigation identified the presence of impurities (eg, sulfates, copper, zinc, nickel, and silica) in autoclave steam moisture, which was attributed to improper maintenance of the autoclave steam generator in the outpatient surgical center. When impurities in autoclave steam moisture were eliminated, no cases of TASS were observed after more than 1,000 cataract operations.

CONCLUSION. Suboptimal reprocessing of cataract surgical equipment may evolve over time in busy, multidisciplinary surgical centers. Clinically significant contamination of surgical equipment may result from inappropriate maintenance of steam sterilization systems. Standardization of protocols for reprocessing of cataract surgical equipment may prevent outbreaks of TASS and may be of assistance during outbreak investigations.

Infect Control Hosp Epidemiol 2006; 27:294-298

Many causes of sterile inflammation of the anterior chamber of the eye after cataract surgery have been identified. They include surgical trauma, lens design and finish, residues of sterilizing agents and polishing compounds used on lenses, inappropriately compounded or applied ocular medications, preservatives, antiseptics, denatured viscoelastic substances, residues of cleaning agents on instruments, talc from surgical gloves, fibers of cotton or cloth, endotoxin, and titanium flecks from the wear of surgical equipment.[1] Many of these causes have been eliminated as a result of improvements in manufacturing design and processing. Other causes continue to be episodically problematic, owing to inadvertent alterations in the compounding of medications or to the reprocessing of surgical equipment. Sometimes a cause is never identified because of the multiplicity of considerations and because the presence of relatively small amounts of material can produce clinically significant inflammation of the anterior chamber of the eye. When clinically significant, sterile inflammation of the anterior chamber of the eye develops within 24 hours after cataract surgery, it is called toxic anterior segment syndrome (TASS)[2]; when such inflammation is associated with cytotoxicity and corneal damage, it is called toxic endothelial cell destruction.[3]

In December 2002, an outbreak of TASS interrupted cataract surgery at 2 facilities: an outpatient surgical center (OSC) and its affiliated hospital. After an initial investigation,

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Received February 16, 2005; accepted February 22, 2005; electronically published February 22, 2006.

personnel were reassigned, new surgical equipment was purchased, and the protocol for reprocessing cataract surgery instruments was redesigned. After these changes were made, the outbreak of TASS improved, but it was not eliminated. Therefore, the problem was investigated further.

METHODS

Case Definition

Three elements were required for a case to be designated as TASS after cataract surgery: (1) inflammation characterized by hypopyon and fibrin in the anterior chamber, (2) inflammation that appeared within 24 hours postoperatively, and (3) minimal or no disturbance of the vitreous.

Data Collection

Epidemiological information was recovered by interviewing the surgical team members and by reviewing medical records, pharmacy records, procedures at the sterile field in the operating room, equipment reprocessing protocols and procedures, and infection control surveillance data from 1995 through 2002. Product information was obtained directly from manufacturers.

Microbiological Analysis

Anterior chamber aspirates were sent to the clinical microbiology laboratory in sterile, preservative-free saline. Specimens of each aspirate were cultured aerobically and anaerobically. The aerobic culture media were trypticase soy agar with 5% sheep blood, chocolate blood agar, and trypticase soy broth. Aerobic cultures were incubated for 48-96 hours at 37°C with 5% carbon dioxide. The anaerobic culture media were Centers for Disease Control and Prevention anaerobic laked blood agar with kanamycin and vancomycin, Centers for Disease Control and Prevention blood agar with phenylethyl alcohol, and Centers for Disease Control and Prevention anaerobic blood agar. Anaerobic cultures were incubated for 5 days at 37°C.

Water Content Analysis

Water samples were analyzed using inductively coupled plasma–atomic emission spectroscopy, ion chromatography, pH meter, and conductivity studies. Spectroscopy was performed on a P-400 spectroscope (PerkinElmer). Ion chromatography was performed on a DX500 system (Dionex) using an anion exchange analytical column and guard column (Dionex AS14 and AG14) with conductivity detection. The eluent was a solution of sodium carbonate (3.5 mmol/L) and sodium bicarbonate (1.0 mmol/L). These analyses were performed according to the validated methods of the Steris Corporation. The assay for endotoxin was performed using the *Limulus* amebocyte lysate kinetic turbidimetric method (Pyros Kinetix, V1.01; Associates of Cape Cod).

RESULTS

Outbreak

TASS developed in 1 of 6 patients undergoing cataract surgery at the OSC on December 9, 2002; in 4 of 7 patients undergoing cataract surgery at the OSC on December 10, 2002; and in 1 of 2 patients undergoing cataract surgery at the hospital on December 11, 2002. By comparison, between January 1996 and the end of November 2002, only 2 possible cases of TASS occurred after 2,436 cataract operations performed at the OSC, and none occurred after 277 cataract operations performed at the hospital.

Cataract surgery was suspended on December 12, 2002, and the recent cataract operations of December 9-12, 2002, were reviewed. The patients of 2 of 3 surgeons were affected, and the lot numbers of medications and irrigants used at the OSC and the hospital were different. The only identified change in personnel and instrument reprocessing was the introduction of a new scrub technician to the surgical team on December 9, 2002. Unlike the rest of the surgical team, the new person used latex-free (neoprene) gloves. This scrub technician and latex-free gloves were excluded from further cataract surgery. When surgery was resumed on December 19, 2002, TASS developed in 2 of 5 patients who underwent cataract surgery at the OSC, but the postoperative course was uncomplicated in the patient who underwent cataract surgery at the hospital. The epidemic period was defined as December 9-19, 2002.

Cohort Investigation

All patients with TASS improved after receipt of topical corticosteroid therapy. The first patient was given 1 empirical injection of intravitreal antibiotics on the second day postoperatively while awaiting culture results for a vitreal aspirate obtained immediately before the injection. No other antibiotic therapy was given to this patient or to the other patients. Corrected vision in the affected eye following resolution of TASS was 20/20 to 20/25 for all patients, except for one whose corrected visual acuity of 20/40 was attributed to underlying macular degeneration.

Anterior chamber aspirates from patients 1 and 4 showed no growth in aerobic or anaerobic bacterial culture during 4 days of incubation.

Associations between characteristics of cataract surgery and cases of TASS during the epidemic period are summarized in Table 1. None of the 8 cases of TASS was the first cataract surgery of the day. Instruments were reprocessed on the same day of surgery in 7 of the 8 cases.

No cases of TASS were associated with surgeon C (Table 1). Review of his operating technique showed that he used a much larger volume of balanced saline solution for irrigation of the anterior chamber intraoperatively than did the other 2 surgeons. He also routinely applied a larger amount of

TABLE 1. Identifying Features of Cases of Toxic Anterior Segment Syndrome (TASS) Associated With 21 Cataract Operations, December 9-19, 2002

Feature	No. of Cataract Operations	TASS Cases, No. (%)
Surgeon		
A	6	2 (33)
B	11	6 (55)
C	4	0 (0)
Total	21	8 (38)
New scrub technician	9	6 (67)
Location		
Outpatient surgical center	18	7 (39)
Hospital	3	1 (33)
First cataract surgery of the day	5	0 (0)
Instruments reprocessed on the day of surgery	8	7 (88)

topical anti-inflammatory medication postoperatively than did his colleagues, who each applied the same amount. However, surgeon B, who routinely used the smallest volume of balanced saline solution intraoperatively, had the highest number and frequency of TASS cases (6 of 11 operations); surgeon A, who used an intermediate volume of balanced saline solution, had lower number and frequency of TASS cases (2 of 6 operations).

Potential causes of TASS common to all cataract operations performed during the outbreak were the surgical equipment and the manufacturing sources of the perioperative medications, viscoelastic substances, implanted lenses, and cleaning solutions. Because cataract operations were performed infrequently at the hospital, cataract surgical equipment used there was borrowed from the OSC, where it was cleaned and sterilized. A review of instrument reprocessing at the OSC showed that there were opportunities for contamination with substances toxic to the eye. Before steam sterilization, some cataract surgical equipment was cleansed with tap water and enzymatic detergent, and some equipment was exposed to soiled, nonophthalmologic surgical equipment and instrument milk.

The lot numbers of the cleaning solution, medications, and viscoelastic substances used at the hospital and the OSC were different. After telephone communication with the manufacturers, we could not identify a definite increase in the number of reports of potential problems associated with the use of their products.

The results of this initial investigation led to a working hypothesis that the outbreak was related to toxic contamination of the surgical instruments, the onset of which coincided with the introduction of a new member to the surgical team. The effect of the suspected instrument contamination was promoted by reprocessing on the day of surgery. Mitigating factors included increasing the volume of balanced saline solution used for intraoperative irrigation and increasing the intensity of postoperative topical anti-inflammatory therapy.

Interventions

The new scrub technician and the use of latex-free gloves remained excluded from cataract surgery. Potentially contaminated equipment that might be difficult to clean completely because of small-bore lumina and small surface irregularities was replaced or substituted with single-use disposable items. Exposure to tap water, enzymatic detergent, and nonophthalmologic surgical equipment was eliminated during instrument reprocessing. Instruments were cleansed with only sterile water, nonlinting cloths, and soft brushes before steam sterilization.

Outcomes Following Initial Investigation and Intervention

Cataract surgery was resumed on January 20, 2003. A case of TASS occurred on February 4, 2003, after 44 operations. This case occurred after a surgery performed at the OSC by surgeon C. In addition, after resuming surgery on January 20, 2003, each of the 3 surgeons observed 1 or more cases during which fibrin debris appeared on the implanted lens on the first postoperative day, without inflammatory changes typical of TASS.

Second Investigation, Interventions, and Outcome

Attention was turned to the quality of water and steam provided for sterilization by the autoclave steam generator. Endotoxin was not identified in the condensates of steam that entered the autoclaves. Samples of feedwater and autoclave steam condensates collected at the OSC in February 2003 showed carryover of sulfate, silica, copper, zinc, and nickel in the condensates, some of which were implicated in prior outbreaks of TASS (Table 2).[6] Similar testing of feedwater and autoclave steam condensates obtained from the hospital in February 2003 showed no such carryover (Table 2).

A review of maintenance records showed that the autoclave steam generator, which was purchased for the OSC in 1995, had been supplied throughout its lifetime with softened city water. During its first 5 years of use, it was flushed and drained weekly. In 2000, the responsibility for maintenance was outsourced. The frequency of flushing and draining was decreased to once every 4-8 weeks. Current recommendations for maintenance of an autoclave steam generator advise supplying the system with pure water[7] or flushing and draining the system daily[8] to prevent the accumulation and carryover of impurities in feedwater. The hospital autoclaves received steam from a facility-wide boiler that allowed for regular monitoring and chemical adjustment of boiler water to prevent buildup and carryover of impurities of feedwater. Further investigation identified buildup of residues in the boiler of the autoclave steam generator at the OSC.

Beginning March 4, 2003, cataract surgical equipment was steam sterilized only at the hospital, and compliance

TABLE 2. Results of Water Quality Measurements, by Date, Location, and Source of Water

	February 2003						
	OSC		Hospital		June 2003, OSC		
Impurity	Feedwater	Autoclave Condensate	Feedwater	Autoclave Condensate	Feedwater	Autoclave Condensate	Expected[a]
Dissolved solids	543	254	...	...	1	2	<33
Chloride	20.1	9.68	...	...	<1	<1	<1
Nitrate	<1	2.37	...	...	<1	<1	<1
Sulfate	155	119	183	<1	<1	<1	<1
Silica	8.77	8.89	22	<0.2	<0.2	<0.2	<0.2
Copper	0.77	1.57	0.1	<0.1	<0.1	<0.1	<0.1
Zinc	0.12	0.86	<0.1	<0.1	<0.1	<0.1	<0.1
Nickel	<0.1	8.56	...	...	<0.1	<0.1	<0.1

NOTE. Data are the amount of each impurity found in the water, expressed as milligrams per liter. OSC = outpatient surgical center.

[a] Autoclave steam moisture.[4,5]

with the revised reprocessing protocol was maintained. The autoclave steam generator at the OSC was replaced. A system was installed to supply the new generator with deionized, ultrafiltered water. Analyses of feedwater and autoclave steam condensates were repeated in June 2003 (Table 2). Steam sterilization of cataract surgical equipment resumed at the OSC after June 2003. From March 2003 through June 2004, more than 1,000 cataract operations were performed without complication.

Ultrasonic rinsates from 2 sources—cataract surgical equipment retired after the outbreak of December 2002 and corresponding equipment purchased in 2003 and recycled throughout the summer of 2003—were collected using sterile, deionized water heated to 50°C. Analysis of these rinsates identified increased concentrations of sulfate in the specimens collected from the retired equipment (Table 3).

DISCUSSION

The actual incidence of sterile inflammation of the anterior chamber of the eye after cataract surgery is uncertain but low, with estimates ranging from 2% to less than 0.1%.[6,9] One estimate is that, of the more than 1.4 million cataract operations performed annually in the United States, 0.62% are complicated by corneal edema or corneal transplantation that requires rehospitalization.[9] Several clusters of cases of TASS occurring after cataract surgery are reported annually to centers with active research interests.[10] Recent outbreaks have been linked to a new intraocular lens[11] and to the use of a plasma gas sterilizer.[6]

Establishing the cause of a TASS outbreak is challenging because of the multiplicity of considerations. The initial investigation of the outbreak in the present study led to the hypothesis that the outbreak was due to an unrecognized contamination of the cataract surgical equipment. Many potential causes of contamination were identified, and all were addressed by revising the instrument reprocessing protocol.

After changes in the instrument reprocessing protocol were instituted, the reappearance of TASS (at a decreased frequency) led to the recognition of a potentially novel cause of postoperative inflammation. The possibility that carryover of impurities in the autoclave steam moisture contributed to this outbreak of TASS was suggested by the following: (1) documentation of impurities (particularly sulfates, copper, zinc, nickel, and silica) in autoclave steam moisture, (2) termination of the TASS outbreak after avoidance of the original autoclave steam generator in the OSC for sterilization of cataract surgical equipment, and (3) documentation of increased sulfate levels on the surface of cataract surgical equipment that was retired after the outbreak in December 2002. Interventions introduced after the initial investigation could be expected to attenuate this cause of TASS, as they appeared to do, but they could not be expected to fully eliminate the problem. Despite these observations, the possibility exists that this TASS outbreak was multifactorial in etiology and that one or more contributing factors were eliminated by revisions of the instrument reprocessing protocol.

On the basis of the water and rinsate analyses, sulfate was the impurity in the autoclave steam moisture that may have contributed to the appearance of TASS in this outbreak. This finding may explain the relatively benign course of these TASS cases, compared with those attributed to copper and zinc.[6]

TABLE 3. Concentrations of Impurities in Instrument Rinsate, by Set of Instruments

Impurity	Old Instruments[a]	New Instruments[b]
Zinc	0.75	0.38
Copper	0.06	0.03
Sulfate	4.92	0

NOTE. Data are expressed as milligrams per liter.

[a] Denotes instruments used in 2002 and retired after an outbreak of toxic anterior segment syndrome.

[b] Denotes instruments newly purchased in 2003.

There are, however, no previous reports of sulfates causing ocular inflammation in clinical or experimental settings, and methods for quantifying sulfate accumulation on surgical equipment have not been validated.

We learned several lessons from this outbreak. First, during the course of the investigation, we discovered that the instrument reprocessing protocol for cataract surgery had evolved over the years to accommodate other surgical activities in the OSC and the ever-present need to reduce costs by minimizing the inventory of equipment and increasing the speed of recycling by bundling of processes. This evolution led to the exposure of cataract surgical equipment to unnecessary, potentially harmful cleaning agents and to contaminated, nonophthalmologic surgical equipment.

Second, manufacturers of equipment and materials widely used in cataract surgery have recognized inconsistencies among users in how they manage and reprocess the equipment. The development of uniform standards for instrument reprocessing and materials management for cataract surgery would allow for the introduction of consensus-generated, evidence-based guidelines for best practices and for easier recognition of causes of TASS outbreaks.

Third, suboptimal management and maintenance of autoclave steam generators can result in carryover of feedwater impurities in autoclave steam moisture to surgical equipment. In this outbreak, contamination may have resulted in clinically significant inflammation of a small, sensitive body compartment. This previously unreported complication of steam sterilization, however, will require further study before it can be conclusively implicated in this outbreak of TASS or in other incidents of unexplained inflammation occurring after steam sterilization. Although the findings of our investigation were sufficiently compelling to lead to replacement of the autoclave steam generator and installation of a system to purify feedwater, the findings were not sufficient to conclude that the deposition of impurities of steam on cataract surgical equipment caused this TASS outbreak or that the impurities could be expected to cause inflammation in other clinical settings. Further research will be required, perhaps using animal models, as were used to demonstrate ocular toxicity after the reprocessing of surgical equipment with a plasma gas sterilizer.[6]

In conclusion, an outbreak of TASS after cataract surgery involved 3 surgeons at 2 affiliated facilities. During the course of the investigation, multiple opportunities for contamination of cataract surgical equipment, resulting from an evolution of practices in the instrument reprocessing area of a busy ambulatory surgical center, were identified. Impurities in autoclave steam moisture, resulting from the suboptimal management and maintenance of an autoclave steam generator, were also identified. The outbreak of TASS subsided after procedures were introduced to optimize cataract surgical equipment reprocessing and after impurities were eliminated from the autoclave steam. The finding that small quantities of impurities in steam may produce disease has potential implications that will require further investigation for the use of steam sterilization in clinical and research settings.

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Potential conflicts of interest: J.E.T. and M.J.R. are employed by Steris Corporation and own shares in Steris Corporation. All other authors have no conflict of interest to disclose.

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