BJUI
BJU International

A randomised single-blind comparison of the effectiveness of Tristel Fuse (chlorine dioxide) as an office-based fluid soak, with Cidex OPA (*ortho*-phthaldehyde) using an automated endoscopic reprocessor (AER) as high-level disinfection for flexible cystoscopes

Peter J. Gilling*, Rana M. Reuther*, Michael Addidle†, Michelle M. Lockhart‡, Christopher M. Frampton§ and Mark R. Fraundorfer*

*Department of Urology, Tauranga Hospital, Bay of Plenty District Health Board, Tauranga, †Pathlab, Tauranga, ‡Pharmaceuticol Ltd, Auckland, and §Department of Medicine, University of Otago, Christchurch, New Zealand

Objective

- To compare the effectiveness, safety and cost of Tristel Fuse (chlorine dioxide) with Cidex OPA (*ortho*-phthaldehyde; 1,2–benzenedicarboxaldehyde) in an automated endoscopic reprocessor (AER) for high-level disinfection of flexible cystoscopes.

Patients and Methods

- A randomised single-blind study comparing the high-level disinfectants Tristel Fuse as a simple office-based soak and Cidex OPA using an AER was performed. Participants were 'blinded' to the agent used for disinfection of the flexible cystoscopes.
- All patients had negative mid-stream urine at baseline, (MSU) no symptoms suggestive of urinary tract infection (UTI) on the day of investigation, no recent antibiotic use or current indwelling urinary catheter.
- Patients who underwent cystoscopic biopsy during the procedure were excluded.
- A urine analysis was done before and 3–5 days after cystoscopy and multiple equipment cultures were performed.
- The Urogenital Distress Inventory (UDI-6 + two questions from the 'long-form'), symptom and quality-of-life scores were assessed before and after cystoscopy as were ease-of-use assessments and a full cost analysis.

Results

- In all, 180 of 465 screened participants were randomised 1:1 and the mean age was 72.1 years, 17% were females and 57% of procedures were performed for bladder tumour surveillance.
- The urine analysis was positive in 5.4% of patients in each group and 29% (Tristel) vs 20% (Cidex) of patients had urinary leukocyturia (p = ns) after cystoscopy.
- The turnover (minutes per cycle) was 7.5 (Tristel) vs 26.7 (Cidex). The per-procedure costs were $11.67 (American dollars) for Tristel Fuse and $21.82 for Cidex OPA with fixed costs of $4788 for Tristel Fuse and $60 514 for Cidex OPA.

Conclusions

- Tristel Fuse appears to be as effective and more cost-effective than Cidex OPA for high-level disinfection of flexible cystoscopes. This has significant cost implications for the office urologist.

Keywords

chlorine dioxide, randomised trial, flexible cystoscopy, high-level disinfection, Cidex-OPA

Introduction

Flexible cystoscopy is normally an office-based procedure, undertaken to examine the bladder and urethra. It is usually a relatively quick procedure, but the throughput of patients is primarily determined by the time needed to disinfect the cystoscopes between cases. There are several methods and agents that can be used to provide high-level and non-corrosive disinfection of flexible cystoscopes.

The first step in cleaning flexible endoscopes is pre-cleaning and the removal of all biological material, this is necessary so

 | doi:10.1111/bju.12208
Published by John Wiley & Sons Ltd. www.bjui.org

that the disinfectant or sterilising agent can contact all cystoscope surfaces. Cleaning using an enzymatic detergent is the next step, which involves both flushing and brushing of the instrument channels. High-level disinfection, rather than sterilisation, is then appropriate for cystoscopes, as this process kills all organisms, except some bacterial spores that do not pose a risk for patients undergoing cystoscopy [1].

Tristel Fuse (Tristel Solutions Ltd, UK) is a high-level chlorine dioxide-based disinfecting and sporicidal solution used as a 5-min soak for the disinfection of flexible cystoscopes. The soak takes place in a dedicated decontamination tray, which is a moulded plastic bath in which the cystoscope is placed and into which the Tristel Fuse is poured. The tray has a lid and a microprocessor-controlled drain, which precisely times the duration of the soak. Tristel Fuse is supplied as two solutions (2.1% sodium chlorite and 5% citric acid) in a plastic envelope, separated by a plastic membrane to avoid mixing of the solutions until use. In preparation for use, the membrane is broken and the two solutions mix. This mixing produces chlorine dioxide as an aqueous solution [2,3]. At the end of the 5-min soak the cystoscope is removed from an empty bath as the Tristel Fuse disinfectant has already drained away and the scope is available for use without rinsing in accordance with the manufacturer's instructions. It is not yet USA Food and Drug Administration (FDA) approved.

Cidex OPA (*ortho*-Phthalaldehyde; 1,2–benzenedicarboxaldehyde) is a high-level disinfectant that is FDA approved for use with flexible endoscopes. It requires the endoscopes to be immersed for a minimum of 10 min at 20 °C using an automated endoscopic reprocessor (AER) and can be used over a maximum 14-day re-use period. At the end of the 10-min immersion in Cidex OPA, the cystoscope is rinsed in accordance with the manufacturer's instructions. Cidex OPA has been associated with anaphylaxis-like reactions in patients with bladder cancer undergoing repeated cystoscopies. The vapour may also be an irritant to the respiratory tract and eyes and may elicit an allergic reaction in workers if protective equipment is not used [4].

This 'in-use' study evaluated whether Tristel Fuse as a 5-min soak in a decontamination tray is as effective as Cidex OPA used in an AER, following a common standardised protocol for cleaning flexible cystoscopes.

Patients and Methods

The objectives of this study were to compare the effectiveness of Tristel Fuse with Cidex OPA for clinical efficacy, safety, cost-effectiveness and ease-of-use.

Outcomes

The clinical endpoints used included the rate of UTIs and leucocyturia as determined by a mid-stream urine analysis 3–7 days after cystoscopy in participants who have had flexible cystoscopy with a cystoscope that has been disinfected with either Tristel Fuse or Cidex OPA.

Other endpoints for the comparison included clinical, microbiological, cost-effectiveness, ease-of-use and safety endpoints.

Endpoints to assess storage/irritation symptoms were; the Short-Form Urogenital Distress Inventory (UDI-6) plus two questions from the 'long form' addressing the symptoms of Nocturia and Urgency, the AUA Symptom Index (AUA-SI 7) and the Single-Question Quality-of-Life (QoL) Score. These were assessed on the day of the procedure and 3–7 days afterwards.

Microbiological cultures were grown from equipment samples collected after the first and last disinfection on each Study clinic (as per SNZ HB 8149:2001; *Microbiological Surveillance of Flexible Hollow Endoscopes)*. These samples included sterile washings (10 mL normal saline) and sterile brushings of the working channel of the flexible cystoscopes, which were inoculated onto Blood Agar and MacConkey Agar and incubated aerobically. Further samples were taken from the AER (lid, rinsing solution and entry and exit ports) and the inner surface of the soaking tray and its exit port.

The total per-patient cost of high-level disinfection with the Tristel Fuse and the Cidex OPA systems was calculated from the per-procedure cost of the machine and tray and the cost of all disposables, irrigation fluids, nursing time and any scope damage caused by the disinfecting agents. The nursing time involved in disinfection was estimated from sample data collected in the study. The process of pre-cleaning the cystoscopes was not timed separately, as it was the same for both disinfectant groups. For Tristel Fuse the times involved in mixing the two components, adding the mixed solution to a plastic bottle, adding 5 L water and pouring the solution into the soaking tray, disinfecting and draining the tray were all assessed for a random selection of disinfections. For Cidex OPA, testing the Cidex OPA solution with a test strip, emptying the solution and replacing with a fresh solution and the disinfection cycle itself were all timed on a random selection of disinfection cycles.

The 'ease of use' of the disinfection systems was directly scored by the nurses on a Likert scale (scored from 1 to 5, 'very difficult to use' to 'very easy to use') using each of the systems on a random selection of events. Furthermore, the acceptability (scored 1 to 5, 'very unpleasant' to 'very pleasant') and the strength of any odour detected (scored from 1 to 5, 'undetectable' to 'very strong') was scored by the nurses during a random selection of disinfectant processes and by the surgeons during a random selection of cystoscopies.

Participant safety was assessed by capturing the number of and type of adverse events reported by the participants

regardless of whether these were likely to be related to the disinfectant. This included any allergic reactions in participants who were undergoing a repeat procedure. This data was specifically collected in the follow-up questionnaire completed 3–7 days after cystoscopy. Surgeon and nursing staff safety was measured by the incidence and severity of any allergic reaction, eye irritation or conjunctivitis reported by both the nurses and surgeons using the cystoscopes at 1–3 days after each study clinic.

Participants

Participants were eligible for inclusion in the study if they were booked to have a flexible cystoscope for surveillance or diagnostic purposes as per the usual clinical practice at the study site. All patients provided written informed consent, and had to have a negative MSU at baseline, have no symptoms of UTI on the day of investigation, have no specific indication for parenteral antibiotic prophylaxis (e.g. artificial heart valve), no current indwelling urinary catheter and no recent surgery of the urogenital tract. If the patient required a biopsy during the flexible cystoscopy they were also excluded from the study.

Randomisation

Each study day was allocated to one of the two disinfectant groups, either Tristel Fuse or Cidex OPA, in a 1:1 ratio. Study days were randomly allocated rather than the individual participants, as the logistics of individually allocating each participant would have created an unnatural clinical environment that would not reflect standard practice. Each successive study clinic was assigned a unique identification number upon randomisation once patient eligibilities and bookings for the day were confirmed. In this manner the study clinic was not randomly allocated until all bookings for the clinic had been made.

Sample Size

It was intended to enrol 180 participants in this study. This allowed for ≈10% of participants not completing the study (not returning for the 3–7-day visit) and so provided a minimum of 80 participants completing the study in each group. This sample was estimated on the basis of showing non-inferiority (not >10% worse) of the Tristel Fuse compared with Cidex OPA for the incidence of MSU detected UTIs. This endpoint was judged to be the least sensitive (and therefore requiring the largest sample size) of the patient-related outcomes in this setting. The calculation was based on data that suggested that the rate of UTIs after cystoscopy was between 2% and 10% [6]. We assumed a UTI rate after cystoscopy of 2.5% for Cidex OPA, therefore if the rate for Tristel Fuse is ≤5% then there would be an 80% chance that the upper limit on the 95% one-tailed CI of the difference would be <10%.

Statistical Analyses

All participants who were randomised and had the cystoscopy on the designated day were analysed as belonging to the group to which they were randomised. All study days correctly used the randomised disinfection process.

Baseline clinical and participant features were summarised by randomised group using means, medians, standard deviations (SD), ranges, frequencies and percentages as appropriate. The UTI rate as assessed by the MSU analysis was compared between the randomised groups and the 95% CI of the difference calculated using exact methods. The levels and changes in the secondary efficacy measures were compared between randomised groups using repeated measures ANOVA. Costs were estimated from fixed and variable cost components and summarised as means. Individual cost components (e.g. timings) are summarised as means and ranges. The 'ease of use' measures are compared between groups using Mann–Whitney *U*-tests. Microbiological data was summarised by randomised groups as frequencies and percentages. Safety data was summarised by randomised groups as frequencies and percentages overall and listed within relatedness and severity subgroups.

Results

In all, 44 study clinics were randomised, 23 to Tristel Fuse and 21 to Cidex OPA. On three occasions two clinics were held on the same day, one in the morning and one in the afternoon. In total, the site screened 465 patients of whom 184 met the entry criteria and were randomised (Fig. 1). The main reasons for failing the entry criteria were either a UTI at baseline, being on concomitant antibiotics or in patients who had indwelling catheters. The 184 participants were enrolled at the study site (Urology Outpatients Department, Tauranga Hospital) over a

Fig. 1 Diagram of patient disposition.

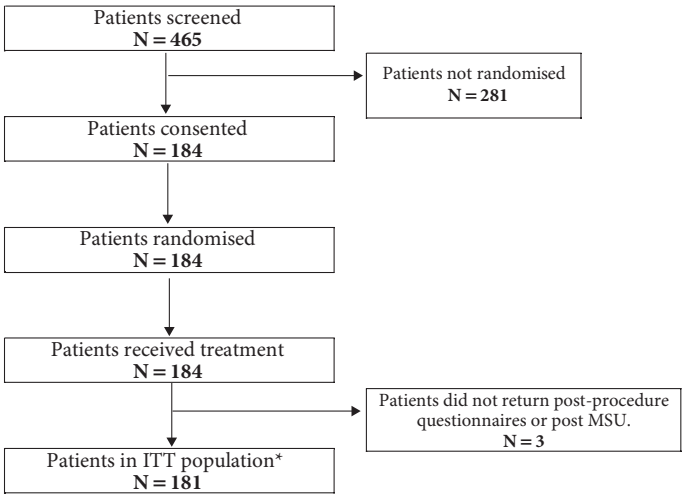

Table 1 Demographic and baseline characteristics.

Participant characteristic	Tristel Fuse	Cidex OPA	Total
Number of patients	94	87	181
Gender, M : F, n	74:20	74:13	148:33
Mean (range) age, years	72.6 (36–90)	72.3 (43–89)	72.5 (36–90)
Indication for cystoscopy, surveillance : diagnosis, n	55:39	48:39	103:78
Mean (SD) baseline scores:			
Urinary symptoms AUA-SI 7	11.0 (7.7)	11.2 (8.3)	11.1 (8.0)
QoL	2.6 (1.7)	2.8 (1.7)	2.7 (1.7)
UDI 6	5.0 (4.1)	5.3(4.4)	5.1 (4.2)
UDI 2	2.8 (1.7)	3.2 (1.8)	3.0 (1.7)

Table 2 Clinical efficacy outcomes.

Clinical efficacy measures	Tristel Fuse		Cidex OPA		*P*
	Before	After	Before	After	
Mean (SD):					
AUA-SI 7 (Max 35)	11.0 (7.7)	10.8 (8.7)	11.2 (8.3)	11.2 (8.4)	0.684
QoL (Max 6)	2.6 (1.7)	2.3 (1.7)	2.8 (1.7)	2.9 (1.9)	0.087
UDI 6 (Max 18)	5.0 (4.1)	4.9 (4.3)	5.3 (4.4)	5.5 (4.3)	0.582
UDI 2 (Max 6)	2.8 (1.7)	2.7 (1.8)	3.2 (1.8)	3.1 (1.9)	0.749

Max, maximum score.

14-month period from 17 September 2009 to 24 November 2010. Participants were randomised depending on which day they underwent their cystoscopy and this resulted in 97 participants being randomised to the Tristel Fuse group and 87 to Cidex OPA. Three patients did not return for their 3–7-day assessment and were not able to be contacted after the study clinic; these three were from Tristel Fuse study clinics.

The demographic and other baseline characteristics of the 181 participants are provided by randomised group in Table 1.

The rate of UTIs as determined by a MSU test 3–7 days after cystoscopy was assessed. In all, 10 participants returned a positive MSU culture 3–7 days after cystoscopy (>10^5 CFUs/mL urine for a recognised urinary pathogen), with seven (3.9%) of these having an elevated white cell count (>10×10^6/L) commensurate with a positive urine culture. Three were in the Tristel group and four were in the Cidex OPA group. The difference in the UTI rate between Tristel Fuse and Cidex OPA was – 1.4% (95% CI 5.6–3.5%), indicating that Tristel Fuse is well within the non-inferiority range of +10% in terms of UTIs.

The mean (SD) symptom and QoL scores before and after cystoscopy for are shown in Table 2, and the *P*-values reflecting the comparison of the changes indicate no significant differences between the two disinfectants.

The microbiology results from the equipment washings are shown in Table 3, as the number of positive cultures and the total number of samples taken. Only one positive culture was identified and this was identified as *C. Albicans* and came from the inner tray rim used for Tristel Fuse.

Table 3 Microbiology efficacy outcomes.

Sample description	Positive cultures, n/N	If positive, specify organism cultured
Washing of cystoscope	0/88	
Brushing of cystoscope	0/88	
Glass lid (Cidex OPA)	0/42	
Rinsing solution (Cidex OPA)	0/21	
Drainage outlet (Cidex OPA)	0/21	
Inner tray rim (Tristel Fuse)	1/46	*C. Albicans*
Exit port (Tristel Fuse)	0/46	

The results of the timings of the relevant individual components of the two disinfectant processes are shown in Table 4. For Tristel Fuse, on average the mixing takes ≈0.5 min, adding the water, pouring and draining ≈1 min each, and the disinfection cycle ≈5 min. The full process took on average, 7.5 min. For Cidex OPA the full disinfection cycle takes ≈27 min, with only a very small contribution from using the test strip. The full Cidex OPA disinfection cycle takes about four times the duration of a Tristel Fuse disinfection cycle.

The costs are shown in Table 5. The cost per disinfection is based on a cost of ≈$20/h (American dollars) for technician time and six disinfections per day. The per-procedure costs were $11.67 for Tristel Fuse and $21.82 for Cidex OPA with fixed costs of $4788 for Tristel Fuse and $60 514 for Cidex OPA.

Table 4 Timings.

Timings	Mean (range)
Tristel Fuse, n = 38	
Mix components, s	30.9 (18–40)
Add with water and pour, s	60.6 (34–101)
Disinfection cycle, s	290.4 (61–315)
Drain, s	65.7 (40–298)
Total, min	7.5 (6.9–8.3)
Cidex OPA, n = 18	
Test strip, s	31.4 (15–67)
Disinfection cycle, min	26.0 (25–28)
Total, min	26.8 (25.5–27.6)

Table 5 Costings of the two methods.

Item	Frequency	Cost, $ (American dollars)
Tristel Fuse		
Cost of Tristel Fuse	Each disinfection	8.16
Stella disinfection tray	Once	4 771
5-L plastic bottle	Once	20.39
Sterile gloves	Each disinfection	0.84
20-mL syringe	Each disinfection	0.22
Tap water	Each disinfection	0
Cidex OPA		
Cidex test strip*	Daily	2.40
Medivator AER machine	Once	60 514
Cidex OPA solution	Every 14 days+	939.50
Sterile gloves	Each disinfection	0.84
Ethanol rinse	Each disinfection	0.32

**Tests if current Cidex OPA solution still valid; +Or earlier if the Cidex OPA solution fails testing with test strips.*

The ease-of-use and odour ratings were not significantly different between groups. There were no serious adverse events or deaths during this study. There were no instances of nurses or surgeons experiencing any adverse events. There were a total of 34 adverse events reported by participants. There were 13 reported among 12 participants in the Cidex OPA group, with all but one being considered mild. All were considered possibly or probably related to the procedure of flexible cystoscopy. There were 21 reported among 13 participants in the Tristel Fuse group, with 15 considered mild, three moderate and three severe. In all, 14 were considered possibly or probably related to the study procedure. The symptoms described were typical and expected in a small proportion of patients after a transurethral procedure of this type (e.g. mild symptoms of pain on urination, dysuria, change in urinary frequency) and none were considered related to the disinfection process.

Discussion

There is a need for an effective, safe and non-corrosive office-based soak for flexible cystoscopes worldwide. Although Tristel Fuse is a new agent compared with Cidex OPA for chemical disinfection of flexible cystoscopes, the present study confirms that the two high-level disinfectants studied provide equivalent microbiological sterilization of flexible cystoscopes when used following the manufacturers recommendations [5]. No positive cultures of the instruments themselves were noted. The positive culture from the decontaminating tray is unlikely to be of any clinical significance and probably represented contamination. The number of UTIs was consistent with known data from other studies and showed no association with disinfection type [6]. The adverse events noted were expected and typical after flexible cystoscopy. Importantly, there were no events felt to be related to the disinfectants themselves. Patient reported LUTS were not increased after cystoscopy in either of the randomised groups. Surgeon and nurse data on safety, acceptability and ease-of-use were comparable.

The costs, both fixed and per-procedure, favoured Tristel Fuse suggesting that this product maybe more cost-effective in this setting. Given that the agent is microbiologically equivalent to Cidex OPA, user-friendly and that the patient throughput is more rapid, it may become an agent of choice for high-level disinfection of flexible cystoscopes.

Conflict of Interest

Peter J. Gilling and Mark R. Fraundorfer were study investigators for this paper and were funded by Tristel Solutions Ltd UK. All the other authors have no conflicts of interest to declare.

References

1 **Clemens JQ, Dowling R, Foley F et al.** Joint AUA/SUNA White Paper on Reprocessing of Flexible Cystoscopes. *J Urol* 2010; 184: 2241–5

2 **Isomoto H, Urata M, Kawazoe K et al.** Endoscope disinfection using chlorine dioxide in an automated washer-disinfector. *J Hosp Infect* 2006; 63: 298–305

3 **Coates D.** An evaluation of the use of chlorine-dioxide (Tristel One-Shot) in an automated washer/disinfector (Medivator) fitted with a chlorine dioxide generator for decontamination of flexible endoscopes. *J Hosp Infect* 2001; 48: 55–65

4 **Cooke RP, Goddard SV, Whymant-Morris A, Sherwood J, Chatterly R.** An evaluation of Cidex OPA(0.55% ortho-phthalaldehyde) as an alternative to 2% gluteraldehyde for high-level disinfection of endoscopes. *J Hosp Infect* 2003; 54: 226–31

5 **Rutala WA, Weber DJ.** Sterilization, high-level disinfection, and environmental cleaning. *Infect Dis Clin North Am* 2011; 25: 45–76

6 **Johnson M, Merrilees D, Robson W et al.** Oral ciprofloxacin or trimethoprim reduces bacteriuria after flexible cystoscopy. *BJU Int* 2007; 100: 826–9

Correspondence: Peter J. Gilling, Suite 6, Promed House, 71 Tenth Avenue, Tauranga 3140, New Zealand.

e-mail: peter@urobop.co.nz

Abbreviations: AER, automated endoscopic reprocessor; AUA-SI 7, AUA Symptom Index 7; FDA, USA Food and Drug Administration; MSU, mid-stream urine; QoL, quality of life; UDI-6, Short-Form Urogenital Distress Inventory.

