



Aqueous Chlorhexidine for Intravitreal Injection Antisepsis

A Case Series and Review of the Literature

Rohan Merani, MBBS, MMed,^{1,2,3,4} Zachary E. McPherson, BMedSci,⁵ Alan P. Luckie, MBChB,⁶ Jagjit S. Gilhotra, MBBS, MMed,^{7,8} Jim Runciman, MBBS,⁸ Shane Durkin, MBBS, MMed,⁸ James Muecke, MBBS,⁸ Mark Donaldson, MBBS,⁹ Albert Aralar, MBBS,⁹ Anupam Rao, BMed,¹⁰ Peter E. Davies, MBBS, MPH^{5,11}

Purpose: To determine the incidence of endophthalmitis in a large clinical series using aqueous chlorhexidine for antisepsis before intravitreal injection and to review the ophthalmic literature regarding chlorhexidine efficacy and safety.

Design: Multicenter retrospective case series.

Participants: All patients receiving intravitreal injections from 7 retinal specialists.

Methods: An audit of intravitreal injections performed by retinal specialists who exclusively used aqueous chlorhexidine 0.05% or 0.1% for prophylaxis of infective endophthalmitis was undertaken. The incidence of endophthalmitis was determined from August 1, 2011, to February 28, 2015. A literature review was performed to critically appraise the ocular safety and efficacy of aqueous chlorhexidine.

Main Outcome Measures: Incidence of endophthalmitis after intravitreal injections.

Results: A total of 40 535 intravitreal injections were performed by 7 retinal specialists across 3 centers. Chlorhexidine was well tolerated, and only 1 patient with a suspected allergic reaction was noted. Three cases of endophthalmitis were identified with 1 culture-positive case. The 0.0074% (1 in 13 512) per-injection rate of endophthalmitis in this series compares favorably with previous series in which povidone-iodine has been used.

Conclusions: Aqueous chlorhexidine was associated with a low rate of postinjection endophthalmitis and was well tolerated by patients. *Ophthalmology* 2016;■:1–7 © 2016 by the American Academy of Ophthalmology

The most commonly used antiseptic for ophthalmic procedures is povidone-iodine (PI), and in a 2010 survey of retinal specialists, 758 of 761 respondents (99.6%) reported using PI before intravitreal injection.¹ Povidone-iodine has been long established as the gold standard for antiseptic prophylaxis for intraocular procedures, with Speaker and Menikoff² reporting a postoperative endophthalmitis rate of 0.06% using PI compared with 0.24% using silver protein solution, albeit in a nonrandomized study. Numerous studies have recommended the use of PI before intravitreal injection.^{3–5} Chlorhexidine is an alternative antiseptic that was first used in ophthalmology as a disinfectant for soft contact lenses,^{6,7} and it has been used for the treatment of acanthamoeba keratitis for more than 20 years.⁸ In the United States, concerns regarding its ocular toxicity have limited the use of chlorhexidine.^{5,9} Despite being well tolerated, the manufacturers explicitly warn against the use of aqueous chlorhexidine on the ocular surface (Figs 1 and 2).

Some patients experience iodine sensitivity or allergy, often after prolonged application of full-strength PI on the skin.^{9,10} Although true immunoglobulin-E-mediated

allergy is rare,¹¹ in 1 report 6.6% of patients developed mild to moderate eye irritation after the use of PI as antisepsis for intravitreal injections.¹² Povidone-iodine causes hyperemia and punctate epitheliopathy in a significant number of patients.^{9,13} Before the study period, we observed that patients who reported iodine allergy or intolerance to PI seemed to experience less postinjection discomfort when chlorhexidine was used for antisepsis.

In a meta-analysis that included both retrospective and prospective studies, 197 cases of endophthalmitis of 350 535 (0.06%; 1/1779) intravitreal injections were identified.¹⁴ In a more recent review including only large retrospective studies, 144 cases of endophthalmitis were identified of 510 396 (0.03%; 1/3544) intravitreal injections.¹⁵ Povidone-iodine was used for antisepsis in all the included studies in both of these large reviews.

In other areas of medicine, chlorhexidine has gained favor over PI, although in many studies alcohol-based chlorhexidine has been used, rather than the aqueous form that we describe in the present series. Chlorhexidine has been shown to be more effective than PI in reducing postoperative surgical

site infections.¹⁶ Superiority also has been demonstrated in vaginal hysterectomy,¹⁷ which is somewhat analogous to intravitreal injection, in that the procedure is performed on a mucosal surface where fluids can potentially affect the viability of biocides. In 2 nonophthalmic studies, synergy has been demonstrated when PI and chlorhexidine have been used sequentially on the skin.^{18,19}

The aims of the present study were to determine the rate of endophthalmitis in a large series in which aqueous chlorhexidine was used for preinjection antisepsis and to review the ophthalmic literature regarding chlorhexidine efficacy and safety.

Methods

Study Design

Seven retinal specialists from 3 Australian centers (centers 1, 2, and 3) were identified from members of the Australia New Zealand Society of Retinal Specialists who had *exclusively* used aqueous chlorhexidine antiseptic prophylaxis for intravitreal injection for a period of 1 year or more. An audit of billing and practice data of patients receiving intravitreal injections was performed. This retrospective study was approved by the Royal Australian and New Zealand College of Ophthalmologists Human Research Ethics Committee.

After a presentation detailing the safety, efficacy, and superior tolerability of aqueous chlorhexidine compared with PI for intravitreal injection (Dr. Alan Luckie, Oceania Retinal Association Meeting, August 2011, Queenstown, New Zealand), the ophthalmologists in the present study increasingly began using chlorhexidine rather than PI before intravitreal injection. The audit period commenced on the date each surgeon began exclusive use of chlorhexidine (between August 1, 2011, and January 1, 2013) through to February 28, 2015. Chlorhexidine gluconate 0.1% (Pfizer Australia, West Ryde NSW) was used in centers 1 and 3 (Fig 1), and chlorhexidine acetate 0.05% (Baxter Healthcare Pty Ltd, Old Toongabbie, NSW, Australia) was used in center 2 (Fig 2).

All cases of endophthalmitis were confirmed with a chart review. In each practice, protocols are in place to ensure that patients who fail to return for their scheduled visits are not lost to follow-up. Thus it is unlikely, but not impossible, that a patient could have developed endophthalmitis and been treated elsewhere without the knowledge of the practice and the treating ophthalmologist.

Ophthalmologists were also asked to report any patients who were found to be intolerant to chlorhexidine for any reason or requested to be switched back to PI. All intravitreal injections in the study period were considered for inclusion. Intravitreal injections of antibiotic or injections associated with another procedure (e.g., vitrectomy, cataract surgery) were excluded. "Endophthalmitis" was defined as any inflamed eye that was clinically suspected as having infective endophthalmitis and underwent an intravitreal antibiotic injection.

Intravitreal Injection Technique

All surgeons used their own technique for their intravitreal injections (summarized in Table 1). All surgeons flushed chlorhexidine across the conjunctiva, eyelids, and lashes. All surgeons in this study performed bilateral injections on the same day when required by the patient. Surgeon E used lidocaine gel for 2 months of the study period during which 1 case of endophthalmitis occurred. Surgeons E and G reapplied

chlorhexidine after speculum insertion just before injection. Surgeons A and D did not use a speculum.

Literature Review Technique

A Medline search from 1946 to present was performed combining the term "chlorhexidine" AND "eye OR ocular OR ophthalmic OR ophthalmology." Further specific searches were done combining "chlorhexidine" with "toxicity," "safety," "allergy," "resistance," and "efficacy."

Results

A total of 40 535 consecutive intravitreal injections were performed. Three cases of endophthalmitis were identified (0.0074%, 1/13 512), of which only 1 was culture positive. The surgeon-specific data are summarized in Table 2.

One case of suspected allergy to chlorhexidine was documented. The patient developed itching with associated conjunctival hyperemia and eyelid swelling after 2 consecutive injections, and had a more severe reaction the second time. This occurred in center 1 where 9266 injections were performed for 931 patients. Apart from this case, no other patient requested to be switched back to PI. Although patients' pain scores were not formally assessed, the surgeons observed that patients who were switched over from PI to chlorhexidine frequently described less postinjection discomfort with chlorhexidine.

All 3 patients who developed endophthalmitis were undergoing treatment for neovascular age-related macular degeneration. They presented 3 to 4 days postinjection with visual acuity down to hand movements. Chlorhexidine 0.05% was used in 2 cases, and 0.1% was used in 1 case. A lid speculum was used in all 3 cases. A vitreous tap was performed in all cases followed by injection of vancomycin 1 mg in 0.1 ml and ceftazidime 2.25 mg in 0.1 ml. One patient subsequently underwent pars plana vitrectomy. Further details are summarized in Table 3.

Discussion

In the present series, 3 cases of endophthalmitis were identified of 40 535 intravitreal injections (0.0074%, 1/13 512) in which aqueous chlorhexidine 0.05% or 0.1% was used for preinjection antisepsis rather than PI. In a recent review of large retrospective series (>10 000 injections) in which PI was used for antisepsis, an endophthalmitis rate lower than 0.0074% was found in only 3 of 18 studies.¹⁵

Mechanism of Action

Chlorhexidine is a topical antiseptic that was first described in 1954.²⁰ It is a cationic biguanide that binds to and disrupts the bacterial cell wall followed by damage to the cytoplasm's semipermeable membrane leading to cytoplasmic damage and cell death.^{21,22} Compared with PI, chlorhexidine exhibits more sustained antimicrobial activity and is not readily neutralized by organic matter.^{21,22} Because PI is brown, it is easy to identify the area where it is been applied, unlike chlorhexidine, which is colorless when applied.

Download English Version:

<https://daneshyari.com/en/article/5705536>

Download Persian Version:

<https://daneshyari.com/article/5705536>

[Daneshyari.com](https://daneshyari.com)