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RESEARCH ARTICLE

Low Efficacy of Hypochlorous Acid Solution Compared to Povidone-iodine in Cataract Surgery Antisepsis

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Abstract:

Background:

Hypochlorous Acid Solution (HAS) is a non-irritating, odorless and transparent, pH-neutral substance having antimicrobial activity.

Objective:

The study aimed to compare the efficacy of HAS with a 10% povidone-iodine (PVI) solution for antisepsis in Phacoemulsification Cataract Surgery (PCS).

Methods:

Consecutive patients undergoing PCS in the Elbląg City Hospital, Poland, were enrolled in this prospective trial. In the morning just before surgery a swab was taken from the inferior conjunctival fornix of the eye that was to be operated. Patients were assigned to receive conjunctival irrigation with PVI or HAS in the operating room. Three minutes after lavage with PVI or HAS, conjunctival swabs were taken. During surgery the cornea and conjunctival sac were irrigated with Ringer's lactate. The last swab was taken before removing the eye speculum.

Results:

Overall, 110 patients completed the study; there were 59 patients in the PVI group and 51 patients in the HAS group. Conjunctival lavage with 10% PVI resulted in a decrease in bacterial load, while HAS application did not. In the HAS group a reduction in bacterial load was found after surgery. Patients after HAS irrigation reported significantly less discomfort associated with conjunctival lavage than with PVI. None of the patients developed postoperative endophthalmitis or any type of eye inflammation within the follow-up period.

Conclusions:

This study confirms the excellent antibacterial activity of a 10% povidone-iodine solution used for three minutes before cataract surgery. Conjunctival irrigation with Ringer lactate during PCS decreased the bacterial load of the conjunctival sac.

Keywords: Antisepsis, Cataract surgery, Conjunctival swabs, Endophthalmitis, Hypochlorous acid solution, Povidone-iodine.

Article History

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1. INTRODUCTION

Hypochlorous Acid Solution (HAS) is a non-irritating, odorless and transparent, pH-neutral substance having antimicrobial activity due to oxidizing properties. It is used as a disinfectant in ulcers, wounds and burns, in periodontal care

[1], peritoneal dialysis [2], and for breast implant pocket irrigation [3]. It has a broad spectrum antimicrobial efficacy against bacteria, viruses, spores, fungi. The aim of this study was to compare the efficacy of prepared diluted HAS (Microdacyn[®], Sonoma Pharmaceuticals, Petaluma, CA) with a 10% povidone-iodine (PVI) solution for antisepsis in Phacoemulsification Cataract Surgery (PCS).

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2. MATERIAL AND METHODS

Consecutive patients undergoing PCS at the Elblag City Hospital, Poland from April to May 2016 were enrolled in this prospective trial. The study adhered to the tenets of the Declaration Of Helsinki and written consent was obtained from all patients before enrollment in the study. The protocol was approved by the hospital's ethical board.

In the evening, a day before the surgery, the patients received topical tobramycin 0.3% with dexamethasone 0.1% and diclofenac sodium 0.1% in the eye that was to be operated, as per the standards of the hospital. In the morning before the surgery, a swab was taken from the inferior conjunctival fornix of the eye with a wet sterile cotton tipped applicator. A standardised swabbing technique was used for all study patients [4]. The swab was then inoculated in a bottle containing Stuart Transport Medium. Subsequently, microbes were cultured in blood, chocolate, Sabouraud glucose, Columbia-CNA, MacConkey, and Thioglycollate Agar. Each patient before surgery received topical tobramycin 0.3% with dexamethasone 0.1% and diclofenac sodium 0.1%. Three applications of lidocaine 2%, tropicamide 1% and phenylephrine 10% within 15 minute-breaks were applied to the operative eye 1 hour before surgery.

Patients were assigned to receive antiseptis with PVI or HAS, based on the time of surgery (odd weeks PVI, even weeks HAS). After topical application of sterile 2% lidocaine solution, subjects in the PVI group underwent periorbital disinfection using a gauze soaked with 10% PVI on the eyelids and surrounding skin. Periorbital disinfection was repeated after a few seconds and, subsequently, the skin was dried by wiping with sterile gauze. After application of sterile 2% lidocaine solution on the cornea, the conjunctival sac was vigorously irrigated with 10 mL of 10% povidone iodine solution. Subjects in the HAS group underwent periorbital skin disinfection, as well as conjunctival lavage using HAS. The patients were asked to rate their discomfort associated with conjunctival sac irrigation, particularly the perception of itching, stinging or burning. Three minutes after conjunctival sac lavage with PVI or HAS conjunctival swabs were taken

from both groups. The incubation time was identical in both groups and the laboratory staff was blinded.

PCS was conducted according to the standards of the department. During surgery the cornea and conjunctival sac were irrigated with Ringer's lactate. At the conclusion of the surgery 1 mg/0.1 mL intracameral cefuroxime was administered. Conjunctival swabs were taken before removing the eye speculum. After surgery the patients received a 0.3% tobramycin solution with dexamethasone 0.1% four times a day for one week, and diclofenac sodium 0.1% three times a day for four weeks. Follow-up was carried 3 months after surgery, particularly for symptoms of intraocular inflammation or endophthalmitis.

Sample size calculation was performed based on the estimates that an increase of 10% in the number of negative conjunctival cultures could be achieved with HAS (up to 90% of negative cultures) compared to an increase of negative cultures by 20% after PVI lavage. We considered the use of a two-tailed test with 80% power and a 5% level of significance. A sample size of 68 eyes (34 eyes in each arm) was considered sufficient to detect a difference of 10% in the number of negative cultures between groups as suggested by Sakpal *et al.* [5].

Statistical analysis was conducted using the Open Source Statistics for Public Health application [6]. The Wilson method was applied to calculate confidence intervals, as it provides more reliable coverage than the alternatives [7]. For analyzing differences among categorical data the Mid-P exact test was applied for fourfold tables, while the Chi Square for larger tables. Results with *p* levels under 0.05 were considered statistically significant.

3. RESULTS

Within the study, 59 eyes of 59 patients were assigned to the PVI group, while 51 eyes of 51 patients into the HAS group. Women represented 69.5% of the PVI group (41/59), and 64.7% of the HAS group (33/51). The mean age in the PVI group was 71.3 ± 8.7 years, and 70.5 ± 9.6 years in the PVI group.

Table 1. Bacterial distribution in the hypochlorous acid group (n=51) and povidone-iodine group (n=59) at different time points.

Bacterial Distribution	Before Surgery	Before Surgery	After HAS Lavage	After PVI Lavage	At The End of Surgery	At The End of Surgery
	HAS group	PVI group			HAS group	PVI group
CNS	3	7	9	0	2	0
Staphylococcus aureus	0	0	0	0	0	0
α -Hemolytic Streptococcus	0	0	0	0	1	0
β -Hemolytic Streptococcus	0	2	1	0	0	0
<i>Leuconostoc mesenteroides cremoris</i>	0	1	0	0	0	0
<i>Micrococcus spp.</i>	1	0	0	0	0	0
<i>Kocuria kristinae</i>	1	0	0	0	0	0
<i>Candida albicans</i>	0	1	0	0	0	0
Total positive swabs (confidence intervals)	4 / 7.8% (3.1–18.5%)	9 / 15.2% (8.2–26.5%)	9 / 17.6% (9.6–30.2%)	0 / 0.0%* (0.0–6.1%)	3 / 5.9%* (2.0–15.9%)	0 / 0.0% (0.0–6.1%)
Statistical significance	<i>P</i> = 0.24		<i>P</i> < 0.01		<i>P</i> < 0.05	

Abbreviations: CI - Confidence Interval; CNS - Coagulase-Negative Staphylococci, HAS - Hypochlorous Acid Solution, PVI - Povidone Iodine, * - a significant change from the previous time point.

Before conjunctival lavage 7.8% (95% confidence interval (CI): 3.1–18.5%) swabs in the HAS group and 15.2% (95% CI: 3.1–18.5%) swabs in the PVI group showed bacterial growth, not statistically different ($P = 0.24$). The bacterial distribution is presented in Table 1, and coagulase-negative staphylococci were preeminent. Conjunctival lavage with 10% PVI resulted in a decrease in bacterial load ($P < 0.01$), while HAS application did not decrease the rate of positive conjunctival swabs ($P = 0.07$). In the HAS group significantly less positive cultures were found at the end of surgery than immediately after HAS lavage ($P = 0.04$). A statistically significant difference in positive cultures between the PVI and HAS group was noted immediately after lavage ($P < 0.01$) and towards the end of the surgery ($P < 0.05$)

Patients undergoing HAS lavage reported significantly less discomfort associated with conjunctival lavage (Table 2). None of the patients developed postoperative endophthalmitis or any type of eye inflammation within the follow-up period.

Table 2. Subjective evaluation of discomfort associated with conjunctival lavage.

–	HAS	PVI
no discomfort	37	5
low intensity	12	10
medium intensity	2	30
severe intensity	0	14
–	p<0.01 ($\chi^2=62.81$; df=3)	

Abbreviations: HAS - hypochlorous acid solution, PVI - povidone iodine

4. DISCUSSION

The European Society of Cataract and Refractive Surgery recommends the use of 5–10% PVI to the cornea, conjunctival sac and periocular skin for a minimum three minutes prior to PCS [8]. The use of PVI in ophthalmic surgery has disadvantages, including conjunctival irritation [9], toxicity to the corneal epithelium [10, 11], as well as to the corneal endothelial cells in animal studies [12, 13]. With that, self-reported allergies to PVI or iodine were reported. True “iodine allergy” shows that it lacks a scientific basis [14], however, in these situations 0.05% aqueous chlorhexidine might be used [8]. The increase in the rate of positive cultures after HAS lavage, which was not statistically significant, could be attributed to uncertainty of microbiological testing [15]. A less probable explanation is contamination of the HAS solution. Contamination of hospital disinfectants was reported, particularly if they were used in low concentrations [16]. As our study presented significantly lower antimicrobial activity of HAS compared to PVI, it should not be taken into consideration for perioperative antisepsis.

Interestingly, the rate of positive cultures at the conclusion of surgery in the HAS group was significantly lower than after conjunctival lavage with HAS. This finding is particularly important, as it is believed that even after proper antisepsis, bacteria move onto the operative field during surgery, enter the eye and might cause infection [17]. We believe that the reduction in bacterial load during surgery might be attributed to repeated flushing of the cornea and conjunctiva with Ringer lactate.

A significant limitation of the current study is the use of

10% PVI. Currently, most commonly a 5% solution is applied for conjunctival sac irrigation [18 - 20]. Thus, our work has a more theoretical than practical value. To date, no study has reported a complete bactericidal effect of the PVI application on the ocular surface. [17, 21]. The lowest rate of culture positive swabs found after 5% PVI for three minutes was three percent [18]. Our study reported complete sterilization of the ocular surface after PVI application, which might be attributed to use of a 10% PVI solution, low group size and uncertainty of testing.

Our work revealed that patients undergoing PVI irrigation reported lower comfort compared to those receiving HAS lavage. Similarly, Ridder *et al.* noted that a single topical application of 60 μ l PVI 5% results in an increased subjective discomfort and dry eye symptoms in healthy eyes for up to four hours, as well as in a decrease in visual acuity, contrast sensitivity and corneal staining [11]. A limitation of our study is the use of topical lidocaine 2%, as the use proxymetacaine was shown to provide better comfort to the patient particularly in applanation tonometry [22]. Another option is performing an additional regional block, however, PCS with topical anesthesia is usually well tolerated [23]. Finally, some recommend topical application of PVI in a lower concentrations. Nevertheless, according to the ESCRS guidelines a minimum 5% solution is recommended, unless repetitive PVI irrigation is performed during surgery [19].

CONCLUSION

This study confirms the excellent antibacterial activity of a 10% povidone-iodine solution used for three minutes before cataract surgery. Due to significantly lower antimicrobial activity of HAS compared to PVI, the commercially available HAS solution should not be taken into consideration for perioperative antisepsis in PCS. Conjunctival lavage with Ringer lactate during cataract surgery decreased the bacterial load of the conjunctival sac.

LIST OF ABBREVIATIONS

HAS	=	Hypochlorous Acid Solution
PCS	=	Phacoemulsification Cataract Surgery
PVI	=	Povidone-iodine

ETHICS APPROVAL AND CONSENT TO PARTICIPATE. HUMAN RIGHTS

The study was approved by the hospital’s IRB on Mar 1, 2016.

HUMAN AND ANIMAL RIGHTS

No Animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Each participant signed an informed consent to participate in the study.

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None.

CONFLICTS OF INTEREST

Dr. Kanclerz, Dr. Grzybowski and Dr. Olszewski report no conflict of interest..

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REFERENCES

- [1] Jorgensen MG, Aalam A, Slots J. Periodontal antimicrobials-finding the right solutions. *Int Dent J* 2005; 55(1): 3-12. [http://dx.doi.org/10.1111/j.1875-595X.2005.tb00025.x] [PMID: 157 47646]
- [2] Cabralda T, Wadhwa NK, Suh H. Use of Amuchina 50% solution versus povidone-iodine 10% solution for transfer-set change in peritoneal dialysis patients. *Adv Perit Dial* 1998; 14: 142-4. [PMID: 10649712]
- [3] Hu H, Sleiman J, Johani K, Vickery K. Hypochlorous acid *versus* povidone-iodine containing irrigants: Which antiseptic is more effective for breast implant pocket irrigation? *Aesthet Surg J* 2018; 38(7): 723-7. [http://dx.doi.org/10.1093/asj/sjx213] [PMID: 29190321]
- [4] Winn W Jr, Allen S, Janda W, *et al.* Introduction to Microbiology Part II: Guidelines for the Collection, Transport, Processing, Analysis, and Reporting of Cultures From Specific Specimen Sources. *Koneman's Color Atlas and Textbook of Diagnostic Microbiology*. Lippincott Williams & Wilkins 2006; pp. 66-110.
- [5] Sakpal TV. Sample size estimation in clinical trial. *Perspect Clin Res* 2010; 1(2): 67-9. [PMID: 21829786]
- [6] Open Source Statistics for Public Health. <https://www.openepi.com>
- [7] DasGupta A, Tony Cai T, Brown LD. Interval Estimation for a Binomial Proportion. *Stat Sci* 2001; 16: 101-33. [http://dx.doi.org/10.1214/ss/1009213286]
- [8] Barry P, Cordoves L, Gardner S. 2013. www.esccrs.org/endophthalmitis/guidelines/ENGLISH.pdf
- [9] Zamora JL. Chemical and microbiologic characteristics and toxicity of povidone-iodine solutions. *Am J Surg* 1986; 151(3): 400-6. [http://dx.doi.org/10.1016/0002-9610(86)90477-0] [PMID: 3513654]
- [10] Jiang J, Wu M, Shen T. The toxic effect of different concentrations of povidone iodine on the rabbit's cornea. *Cutan Ocul Toxicol* 2009; 28(3): 119-24. [http://dx.doi.org/10.1080/15569520903080511] [PMID: 19694608]
- [11] Ridder WH III, Oquindo C, Dhamdhare K, Burke J. Effect of povidone iodine 5% on the cornea, vision, and subjective comfort. *Optom Vis Sci* 2017; 94(7): 732-41. [http://dx.doi.org/10.1097/OPX.0000000000001091] [PMID: 28609 415]
- [12] Naor J, Savion N, Blumenthal M, Assia EI. Corneal endothelial cytotoxicity of diluted povidone-iodine. *J Cataract Refract Surg* 2001; 27(6): 941-7. [http://dx.doi.org/10.1016/S0886-3350(00)00750-1] [PMID: 11408 145]
- [13] Alp BN, Elibol O, Sargon MF, *et al.* The effect of povidone iodine on the corneal endothelium. *Cornea* 2000; 19(4): 546-50. [http://dx.doi.org/10.1097/00003226-200007000-00028] [PMID: 1092 8775]
- [14] Krohne TU, Allam J-P, Novak N, Holz FG. "Iodine allergy" : A medical myth with risks for the ophthalmological patient. *Ophthalmologie* 2016; 113(12): 1023-8. [http://dx.doi.org/10.1007/s00347-016-0359-9] [PMID: 27601148]
- [15] Jarvis B, Hedges AJ, Corry JEL. Assessment of measurement uncertainty for quantitative methods of analysis: comparative assessment of the precision (uncertainty) of bacterial colony counts. *Int J Food Microbiol* 2007; 116(1): 44-51. [http://dx.doi.org/10.1016/j.ijfoodmicro.2006.12.037] [PMID: 1731 6860]
- [16] Keah KC, Jegathesan M, Tan SC, *et al.* Bacterial contamination of hospital disinfectants. *Med J Malaysia* 1995; 50(4): 291-7. [PMID: 8668045]
- [17] Koerner JC, George MJ, Meyer DR, Rosco MG, Habib MM. Povidone-iodine concentration and dosing in cataract surgery. *Surv Ophthalmol* 2018; 63(6): 862-8. [http://dx.doi.org/10.1016/j.survophthal.2018.05.002] [PMID: 2977 8494]
- [18] Halachmi-Eyal O, Lang Y, Keness Y, Miron D. Preoperative topical moxifloxacin 0.5% and povidone-iodine 5.0% *versus* povidone-iodine 5.0% alone to reduce bacterial colonization in the conjunctival sac. *J Cataract Refract Surg* 2009; 35(12): 2109-14. [http://dx.doi.org/10.1016/j.jcrs.2009.06.038] [PMID: 19969216]
- [19] Ferguson AW, Scott JA, McGavigan J, *et al.* Comparison of 5% povidone-iodine solution against 1% povidone-iodine solution in preoperative cataract surgery antiseptics: a prospective randomised double blind study. *Br J Ophthalmol* 2003; 87(2): 163-7. [http://dx.doi.org/10.1136/bjo.87.2.163] [PMID: 12543744]
- [20] Carrim ZI, Mackie G, Gallacher G, Wykes WN. The efficacy of 5% povidone-iodine for 3 minutes prior to cataract surgery. *Eur J Ophthalmol* 2009; 19(4): 560-4. [http://dx.doi.org/10.1177/112067210901900407] [PMID: 19551669]
- [21] Grzybowski A, Kanclerz P, Myers WG. The use of povidone-iodine in ophthalmology. *Curr Opin Ophthalmol* 2018; 29(1): 19-32. [http://dx.doi.org/10.1097/ICU.0000000000000437] [PMID: 28984 794]
- [22] Birchall W, Kumar V. A comparative study of proxymetacaine-fluorescein and lignocaine-fluorescein use during applanation tonometry. *Br J Ophthalmol* 2001; 85(4): 477-9. [http://dx.doi.org/10.1136/bjo.85.4.477] [PMID: 11264141]
- [23] Malik A, Fletcher EC, Chong V, Dasan J. Local anesthesia for cataract surgery. *J Cataract Refract Surg* 2010; 36(1): 133-52. [http://dx.doi.org/10.1016/j.jcrs.2009.10.025] [PMID: 20117717]