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Topical Lidocaine Gel Versus Tetracaine Eye Drops for Panretinal Photocoagulation in Proliferative Diabetic Retinopathy

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Abstract: Panretinal photocoagulation (PRP) is a treatment for proliferative diabetic retinopathy (PDR). The procedure needs anesthetic agent to overcome the pain. Two widely used anesthetic agents are used in this study which are tetracaine 0.5% eyedrops and lidocaine 2% gel. This study aimed to compare the effectivity and efficacy of both anesthetic agents. A prospective randomized controlled trial was done to 40 eyes divided into two groups, group A was treated with tetracaine 0.5% eyedrop and group B with lidocaine 2% gel. Pain score was obtained subjectively from the patient and recorded during four stages of procedure. The results showed that the mean age was 56.5 years in Group A and 53.20 years in group B. Average procedure duration was 8.7 minutes in group A and 9.35 minutes in group B. Average 5 minutes pain level was 3.05 and 2.10 in group A and B consecutively. Average 10 minutes pain level was 2.65 and 2.45 in group A and B consecutively. Average during procedure pain level was 2.70 and 3.40 in group A and Group B, and average post procedure pain level was 1.20 in Group A and 1.55 in Group B. There was no significant difference between both groups' parameters. In conclusion, the use of both agents is interchangeable and shows no differences in efficacy and effectivity.
Keywords: panretinal photocoagulation; proliferative diabetic retinopathy; anesthetic agent; tetracaine; lidocaine

INTRODUCTION

Panretinal photocoagulation is a routine procedure for retinal neovascularization diseases including proliferative diabetic retinopathy (PDR).[1] The procedure uses laser to create thermal injury to the retinal tissue. The objective of this procedure is to decrease the level of vascular endothelial growth factor (VEGF),[2] however, this procedure is painful for the patient. Anesthetic then administered to relieve pain during the procedure. Different anesthetic and preparation options has now been available worldwide.[3-6]

Pain of panretinal photocoagulation starts from anesthetic administration. Most of local anesthetics available are acidic, thus, contribute to pain on application. Tetracaine and lidocaine are the most used anesthetic worldwide. Tetracaine is an ester of para-aminobenzoic acid (PABA) group of local anesthetics, available in 0.5% and 1% solution. It has a more acidic properties compared to lidocaine.[7-9]

Comparisons between different local anesthesia agents have several considerations. Anesthesia achieved when the anesthetic agent is bound to the nerve endings on the ocular surface; this contributes to the onset of action of the agent. Duration of action of the anesthetic agents is determined by the length of this bound stays. Different anesthetics also contributes to several potentials side effects.[9]

This research aimed to compare the effectivity and efficacy of tetracaine 0.5% eyedrops and lidocaine 2% gel for panretinal photocoagulations procedure in proliferative diabetic retinopathy patients.

METHODS

A prospective, randomized controlled trial was performed from October 2021 to October 2022 at Prof. Dr. R. D. Kandou Central General Hospital. Written informed consents were obtained from all patients before participation. The patients were assigned consecutively into group A (tetracaine 0.5% eye drop group) or group B (lidocaine 2% gel group). Inclusion criteria were proliferative diabetic retinopathy patient and clear media. Exclusion criteria were media opacities, known allergy to the anesthetic agents, and patient with neurological deficit.

Five minutes before the first evaluation, the eyes of group A were instilled with tetracaine 0.5% (Pantocaine® Cendo, Indonesia) and those in group B were instilled with lidocaine 2% gel (xylocaine ® aspen, Sweden). Group A used hydroxypropyl methylcellulose and group B used the lidocaine gel as contact lens lubricant during the procedure.

Laser used was Nidek Multicolor scan laser photocoagulator MC- 500 using the yellow (577 nm) laser, power range between 200–600 mW, duration was set between 0,2 to 0,5 seconds, spot size 200 μm with preferred interval between 0.2 to 0.5 seconds. Laser was done by two experienced vitreoretinal specialists.

Pain perception was measured using numeric rating scale with 0 meant no pain at all and 10 meant as painful as can be imagined. The pain perception was divided into four different periods: 1) during anesthetic administration; 2) during the contact lens insertion; 3) during treatment; and 4) after laser treatment. After all subjects were enrolled, pain scales data were gathered by one investigator who made the measurement and statistic test. Pain score difference was analyzed with independent t test, and significance was defined as $p<0.05$.

RESULTS

Forty eyes of forty patients were enrolled in this study. There were 20 eyes involved in each group. The age range were between of 30 to 83 with an average of 56.5±15.909 in group A and 53.20±14.537 years old. Group A consist of 12 males and eight females, meanwhile nine males and 11 females in group B. The average procedure duration was slightly higher in the group B with 9.35±2.412 minutes compared to 8.70±2.473 minutes in the group A but this difference was not statistically significant ($p= 0.878$). The average total shot was higher in group A compared to group B with 1272.10±449.527 and 1010.05±568.707 shots consecutively ($p=0.94$).

Table 1. Demography and pain scores of patients

Parameters	Tetracaine	Lidocaine	p-value
Mean age (years)	56.5±15.909	53.20±14.537	0.663
Male to female ratio	12:8	9:11	NA
Average procedure duration (minutes)	8.70±2.473	9.35±2.412	0.878
Average total shot	1272.10±449.527	1010.05±568.707	0.94
Average 5 minutes pain level	3.05±1.572	2.10±1.553	0.904
Average 10 minutes pain level	2.65±1.531	2.45±1.638	0.578
Average during procedure pain level	2.70±2.029	3.40±2.137	0.497
Average post procedure pain level	1.20±1.196	1.55±0.999	0.234
Adverse event	0	0	NA

The pain level was evaluated in 5 minutes, 10 minutes, during the procedure, and after the procedure. At the 5 minutes after instillation, group A reported higher pain scale (3.05±1.572) compared to group B (2.10±1.553), albeit, the difference was not significant (p=0,904). The average pain level at 10 minutes was also higher in group A (2.65±1.531) compared to group B (2.45±1.638) with not significant difference (p=0.578). The average procedure pain level was higher in group B (3.40±2.137) compared to group A (2.70±2.029) with no significant difference (p=0.497). The average after procedure pain level was higher in group B compared to group A (1.20±1.196 compared to 1.55 0.999) and was not statistically significant (p=0.234). No adverse event was documented during the procedure in both groups.

DISCUSSION

The patients were consecutively divided into two groups and reached 20 patients in each group. Average age in both groups was above 50 years old. Blindness in diabetic retinopathy patient with age of 50 and above increased globally almost two-fold in one decade between 1990 to 2010. As the disease progress, age becomes the contributing factor to the increasing severity of diabetic retinopathy. There were more males than females in group A and more females than males in Group B. However, gender difference has no significant association with diabetic retinopathy severity.[10]

The average duration for laser procedure in both groups was not statistically different. However, the total numbers of shots were higher in group A. The total one session shots in this study were relatively lower compared to a couple of studies in China and Japan with Asian patients.[11,12] The total number of laser shots depends on the patient's endurance. Laser treatment in our healthcare center is usually divided into several sessions to share the patient burdens and to anticipate any inflammation after the therapy.

The pain level was not significantly higher in group A in the first 5 minutes and 10 minutes, and was higher in group B during and post procedure pain level. Both anesthetic agents had passed their onset of action time in five minutes. Tetracaine has an onset of action of 10-20 seconds, meanwhile lidocaine has 3.02 minutes for onset of action.[8,9] The difference in pain level might not related to this factor because the first pain evaluation was at 5 minutes. The pain levels in the 5 and 10 minutes were higher in group A compared to group B, but group A showed decrease in pain level in the 10-minute evaluation compared to the 5-minute evaluation. The higher pain score in group A might be related to the acidic profile of tetracaine. Tetracaine in fact is more acidic than lidocaine with an average pH of 4.54 compared to lidocaine with 6.37 pH which was closer to physiological ocular surface pH.[7,8,13]

The pain level during procedure was increased a little bit in group A with about 0.05 increment compared to 10-minute evaluation. This difference was smaller compared to group B

with 0.95 increase in pain score. The pain level decreased in both groups after the procedure with 1.50 and 1.85 decrement in group A and group B consecutively. The average procedure duration was 8.70±2.473 minutes in group A, and 9.35±2.412 minutes in group B. If the duration was added with 10 minutes waiting time before the procedure, patient in group A should have almost ended its anaesthetic effect at the end of the procedure. This was unexpected regarding the duration of action of lidocaine was longer than tetracaine. Lidocaine has a one-hour duration of action which is longer than tetracaine with only 20 minutes duration.[9]

Beside the anesthetic agent, the procedure difference between both groups also lies in the contact lens lubricant of choice. Group A had viscoelastic hydroxypropyl methylcellulose (HPMC) as the contact lens lubricant which was recognized to have a good surface tension profile. This type of HPMC has been known as a good protector of ocular surface epithelial cells.[14] On the other hand, tetracaine has been reported to have side effect of corneal compromise including ultrastructural damage to the cell membrane, loss of microvilli, and desquamation of superficial epithelial cells.[9] The use of dispersive viscoelastic as ocular epithelial protector is a mitigation effort to this risk. However, lidocaine 2% Gel in group B also contains hydroxypropyl methyl cellulose. Lidocaine 2% gel is known with its good preservation to the exposed epithelial surface.[15]

CONCLUSION

Tetracaine 0.5% eyedrops has the similar effectivity and efficacy as lidocaine 2% gel in the procedure of panretinal photocoagulation in proliferative diabetic retinopathy patients. The use of both anesthetic agents is interchangeable and shows no differences in efficacy and effectivity.

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Conflict of Interest

No conflict of interest in this study.

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