

The efficacy of the combination of 2% lidocaine and 0.5% bupivacaine as preemptive analgesia for post-operative pain in vitrectomy with or without scleral buckle under general anaesthesia

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ABSTRACT

Marlyna Afifudin, Hartono, Angela Nurini Agni - *The efficacy of the combination of 2% lidocaine and 0.5% bupivacaine as preemptive analgesia for post-operative pain in vitrectomy with or without scleral buckle*

Background: Post-operative pain is one of the main problems in the surgical services so that analgesia is very much needed, even intravenously given. The concept of preemptive analgesia in surgical intervention is the provision of analgesia before the occurrence of nociceptive stimulus. One of the agents for providing preemptive analgesia is local injection is local injection with local anesthetic, single or in combination.

Objective: This study was aimed to evaluate the efficacy of combination of lidocaine and bupivacaine as preemptive analgesia in vitrectomy with or without scleral buckle under general anesthesia.

Methods: Twenty eight patients who were scheduled for vitrectomy were included in this study. The patients were randomly classified into two equal groups. The surgery was conducted under general anesthesia for both groups, but in Group 1, subtenon anesthesia with local anesthetic was given as preemptive analgesia after induction anesthesia and before the start of surgery. Pain intensity was the primary outcome of this study. The pain intensity was measured in 3 hours and 24 hours after surgical procedure.

Results: The baseline characteristics between the two groups were similar. The pain intensity was lower in the treatment group, but the difference was not statistically significant (1.00 ± 1.71 vs 1.50 ± 2.16 , $p = 0.109$). The proportion of pain-free patients were similar between the two groups in 3 hours after procedure (65% vs 65%, $p = 1.00$). The proportion of pain-free patients were higher in the treatment group in 24 hours after procedure (100% vs 73%, $p = 0.222$, Fisher's Exact Test). The subtenon injection procedure was safe. There was insignificant difference in the incidence of side effects between the 2 groups.

Conclusion: This study did not show any additional benefit of subtenon injection for vitrectomy. The pain intensity was similar between two groups. There were no increases on side effects after the procedure.

Key words: vitrectomy - local anesthetic - post-operative pain - preemptive analgesia

ABSTRAK

Marlyna Afifudin, Hartono, Angela Nurini Agni - *Efikasi kombinasi 2% lidokain dan 0,5% bupivacain sebagai analgesik pre-emptif untuk nyeri pada pasca-operasi pada vitrektomi dengan atau tanpa scleral buckle di bawah anestesia general*

Latar Belakang: Nyeri pasca operasi merupakan salah satu masalah pada tindakan bedah sehingga amat diperlukan analgesia, bahkan dengan pemberian intravena. Konsep analgesia pre-emptif pada tindakan bedah adalah pemberian analgesia sebelum terjadinya rangsang pada reseptor nosiseptif. Salah satu cara untuk analgesia pre-emptif adalah suntikan lokal dengan anestetik sebagai preparat tunggal atau kombinasi.

Tujuan: Melakukan evaluasi daya guna kombinasi lidokain dan bupivakain sebagai analgesia preemtif pada operasi vitrektomi dengan atau tanpa skleral buckle.

Metode: Subyek penelitian adalah 28 pasien yang menjalani operasi vitrektomi. Subyek mengalami randomisasi secara blok untuk dibagi secara sama dalam 2 kelompok. Semua pasien menjalani anestesi general, namun pada kelompok 1 mendapat tambahan injeksi sub-tenon dengan kombinasi anestesi lokal sebagai analgesia preemtif. Luaran utama pada penelitian ini adalah intensitas nyeri pasca operasi. Intensitas nyeri diukur pada jam ke-3 dan jam ke-24 pasca operasi.

Hasil: Karakteristik dasar antara kedua kelompok adalah sebanding. Intensitas nyeri pada 3 jam pasca operasi adalah lebih rendah pada kelompok perlakuan, namun perbedaan tersebut tidak bermakna secara statistik ($1,00 \pm 1,71$ VS $1,50 \pm 2,16$, $p=0,109$). Proporsi bebas nyeri pada kedua kelompok adalah sebanding pada 3 jam pasca operasi (65% VS 65%, $p=1,00$). Proporsi bebas nyeri pada 24 jam pasca operasi di kelompok perlakuan adalah lebih tinggi dibanding pada kelompok kontrol, namun perbedaan tersebut tidak bermakna secara statistik (100% VS 73%, $p=0,222$, Fisher Exact Test). Tidak ada perbedaan dalam hal efek samping antara kedua kelompok.

Simpulan: Hasil penelitian tidak menunjukkan adanya manfaat tambahan pemberian injeksi sub-tenon. Intensitas nyeri adalah sebanding antara kelompok perlakuan dan kelompok kontrol. Prosedur injeksi sub-tenon adalah aman, dan tidak dihubungkan dengan peningkatan efek samping.

INTRODUCTION

Post-operative pain is one of the main problems in the surgical services.¹ Previous prospective study from Fekrat *et al.*² on 185 patients showed that 56% patients complained of post-operative pain, 48% required intravenous medication, and 27% required analgesic agent. Another study from Henzler *et al.*³ on 500 patients who underwent various eye surgeries showed that posterior segment surgery was more painful compared to the anterior segment surgery (RR = 4.5; 95% CI 3.01-6.791; $p < 0.0001$).

The concept of preemptive analgesia is the provision of analgesia before the occurrence of nociceptive stimulus. One of the agents for providing preemptive analgesia is local injection with local anesthetic^{4,5}. Drugs that stabilize the membrane (eg: local anesthesia) can prevent the formation of action potential of the pain pathway.⁶ Several clinical studies have been performed to know the efficacy of using local anesthetic agents in vitreoretinal surgery. The results of previous studies were still controversial and not conclusive yet.

Newsom *et al.*⁷ studied the use of local anesthesia in 1221 patients who underwent vitreoretinal surgery. The study showed that local anesthesia could be tolerated well. Pain was found in 9.4% patients with vitrectomy procedure. Roman *et al.*⁸ conducted research on pain during the operation in 109 patients who underwent various eye surgeries (cataracts, trabeculectomy, and vitrectomy) under subtenon local anesthesia. The

result obtained showed that 97.3% patients reported no pain during the operation. Novel study from Barakat *et al.*⁹ and Lai *et al.*¹⁰ did not show any benefit of local anesthesia in vitreoretina surgery, on the contrary.

The main objective of this study was to find out the efficacy of combination of 2% lidocain and 0.5% bupivacain as preemptive analgesia in vitrectomy with and without sclera buckle.

METHODS

The design of this study was double-blind randomized clinical trial. Parallel design was used to test the hypothesis. The subjects were randomly allocated into two groups. One group received the combination of 2 ml 2% lidocain and 2 ml 0.5% bupivacain by subtenon injection in addition to general anesthesia, while the other group only received general anesthesia.

The samples of our study were adult patients who underwent vitrectomy with or without a scleral buckle. The inclusion criteria were: (1) patients who underwent vitrectomy surgery with or without scleral buckle (2) age above 18 years old, (3) cooperative, (4) there was no interference of liver and kidney disturbance or history of anaphylaxis with local anesthesia, and (5) were willing to participate in the study. The exclusion criteria were verbal or visual disturbance to VAS interpretation. The sample size calculation showed that the minimal requirement was at least 14 patients for each group.

Patients who met the inclusion criteria underwent random block allocation. First group received additional subtenon injection treatment, while the second group received general anesthesia only. Post-surgery pain measurement was conducted with VAS (visual analogue scale). VAS has been widely used to assess pain intensity. The administration of subtenon local injection was conducted by initially creating slices of conjunctiva, and tenon capsule along the 2 mm length, starting approximately 6 mm from the limbus in the inferotemporal quadrant. Blunt cannula was inserted into the retrobulbar space, and the injection of the mixture of 2 ml of 2% lidocain and 2 ml 0.5% bupivacain was performed.

Throughout the operation, several recordings were performed: (1) length of anesthesia, (2) duration of operation, and (3) the incidence of oculocardiac reflex during surgery. Duration of anesthesia and surgery were measured in minutes. The oculocardiac reflex was defined as 20% decrease in heart rate due to muscle-twitch ocular muscle. Additional analgesic was given when asked by the patient as the inability to withhold pain.

The data were analyzed with SPSS. Fisher's exact test and Mann Whitney U test were used to test the hypothesis.

RESULTS

Data were obtained from 28 patients who underwent vitrectomy surgery with or without scleral buckle. Both groups underwent the same peri-operative procedure, except the subtenon injection after general anesthesia in the treatment group. Data were obtained from 18 male and 10 female respondents with average age of 45.47 ± 13.33 years (18-74 years). The main surgical indication in this study was retinal detachment, 78.6% in the treatment group and 64.3% in the control group. Type of operation in most cases was a combination of vitrectomy and scleral buckle. Most patients had intact cornea. The duration surgical procedure was significantly longer in the treatment group compared to the control group ($135.7 \pm 108.5 \pm 40.08$ vs 32.07 , Mann Whitney U

Test, $p = 0.048$). The average intraocular pressure was slightly higher in the treatment group compared to control group, but the difference was not statistically significant (13.0 ± 4.18 vs 11.7 ± 2.99 , $p = 0.359$). TABLE 1 shows the baseline characteristics of both groups.

Proportion of patients who were pain-free after 3 hours operation procedure was similar between the treatment group and control group (65% vs 65%, $p = 1.00$). No patients in the two groups who required additional analgesics. The 24-hour observation post-surgery showed that no patients in the treatment group experienced pain. No member of the treatment group feel excruciating pain or had sleep disturbance due to pain 24 hours post-operation.

Proportion of pain-free in the treatment group was higher than that in the control group for 24 hours post-operation (100% vs 73%, $p = 0.222$, Fisher's Exact Test). The proportion of patients who were free from the excruciating painful feeling was higher in the treatment group (100% vs 86, $p = 0.135$, Fisher's Exact Test). Proportion of patients who were free from sleep disturbance due to pain was also much higher in the treatment group compared to that in control (100% vs 86%).

Result of our research indicated that there was no difference in pain intensity between the treatment group and control group. Proportion of pain-free and pain impact (feel excruciating pain and had sleep disturbance) did not differ in meaning between the two groups. Research showed that there was no additional benefit of subtenon injection to reduce post-surgery pain after vitrectomy. TABLE 3 shows that there were no significant difference in pain intensity and pain impact in both groups after 24 hours post-operation.

The procedure of subtenon injection did not provide significant side effects. There was no difference of side effects between treatment group and control group. There were 2 cases of oculocardiac reflex in the treatment group. The occurrence of oculocardiac reflex was probably due to surgical procedure, and not associated with the administration of local anesthetic.

TABLE 1. Baseline characteristics of the treatment group and control group

Variable	Treatment group	Control group	<i>p</i>
Gender	9 (64.3%)	9 (64.3%)	0.653
- Male	5 (35.7%)	5 (35.7%)	
- Female			
Age (years)	47.79±10.47	43.44±15.47	0.382
Chronic disease			
- Yes	3 (21.4%)	8 (57.1%)	0.142
- No	11 (78.6%)	6 (42.9%)	
Diagnosis			
- Retinal detachment	11 (78.6%)	9 (64.3%)	0.137
- Vitreous bleeding			
- Retinal detachment and vitreous bleeding	0	4 (28.6%)	
- PDR	1 (7.1%) 2 (14.3%)	1 (3.6%) 3 (10.7%)	
Procedure			
- Vitrectomy	2 (14.3%)	4 (28.6%)	0.324
- Vitrectomy and scleral buckle	12 (85.7%)	10 (71.4%)	
Corneal status			
- Intact	13 (92.9%)	12 (85.7%)	0.50
- Non intact	1 (7.1%)	2 (14.3%)	
Duration of procedure	135.7±40.08	108.5±32.07	0.048*
IOP (mmHg) pre-surgery	13.0±4.18	11.7±2.99	0.359

TABLE 2. The measurement of efficacy of subtenon injection in 3 hours post operation

Variable	Treatment group	Control group	<i>P</i>
Mean VAS	1.00±1.71	1.50±2.16	0.109
Pain impact (severity)			
- None	9 (64.3%)	8 (52.3%)	0.788
- Few	4 (28.6%)	4 (33.3%)	
- Moderate	1 (7.1%)	2 (13.3%)	
Sleep disturbance			
- None	11 (78.6%)	9 (64.2%)	0.318
- Few	2 (14.5%)	3 (21.4%)	
- Moderate	1 (7.2%)	2 (14.2%)	
- Severe	0	0	

TABLE 3. The measurement of efficacy of subtenon injection in 24 hours post-operation

Variable	Treatment group	Control group	<i>p</i>
Mean VAS	0.00	0.81±1.834	0.492
Pain impact (severity)	14	12 (86%)	0.135
- None	(100%)	1 (7%)	
- Few	0	1 (7%)	
- Moderate	0	0	
Sleep disturbance			
- None	14	12 (86%)	0.135
- Few	(100%)	0	
- Moderate	0	1 (7%)	
- Severe	0	1 (7%)	

DISCUSSION

There was no difference in pain intensity between the treatment group who received subtenon injection and control group. Proportion of pain-free patients was higher in the treatment group after 24 hours, but the difference was not significant. The previous study showed that the role of preemptive analgesia was still controversial. Systematic study from Ong *et al.*¹¹ showed that the results for preemptive analgesia in many cases were still variable. Result of meta-analysis concluded that the provision of local preemptive anesthesia was significantly lower total consumption of analgesic post-operation. The meta-analysis did not show the benefits of local injection to decrease pain intensity.

Our study showed that the mean VAS and the proportion of pain-free patients between the two groups were similar. The mean value of VAS in the treatment group was very low, 1.00±1.71 (scale of 0-10). This indicated the success of achieving analgesia in the patients. Similar results were shown by a research by Kristin *et al.*¹², where the average value of VAS in the group who had combination of general and local anesthesia was 1.00 (scale of 0-10). Average value of VAS in the group that only received general anesthesia was 3.00 (scale of 0-10).

This study showed that the proportion of pain-free patients was 65% 3 hours post-operation. Similar research by Clarke *et al.*¹³ showed that a number of success ranging between 56%-72% cases. Proportion of patients who were pain-free in both groups were similar (65% vs 65%, *p* = 1.00). The insignificant difference between group who received local injection and control group may be explained by several reasons, namely: (1) less adequate afferent blockade, (2) pain intensity and type of operation, (3) inflammatory mediators, and (4) individual reaction post-operation. Research by Aida *et al.*¹⁴ concluded that certain types of operations were associated with the higher success of preemptive analgesia. In this study, vitreoretinal operations might not provide major noxious stimuli like the major operation of the body in general (mastectomy, leg surgery, or peritoneal operation). This was reflected in the average VAS of the control group that was 1.50±2.16 (scale of 0-10). The insignificant difference can also be caused by the effective delivery of post-operative tramadol. Tramadol is a central analgesic that stimulate the opioid receptor, it has potent inhibitory effect by increasing serotonin and norepinephrine reuptake.¹⁵ In this study, post-operative pain intensity might be higher when tramadol was not given as a post-operative routine procedure.

Our study was similar with the study by Mason *et al.*¹⁶ on 46 vitrectomy patients. The study showed that the addition of local anesthesia block did not affect the measurement of pain incidence.

This is shown by similar research by Bahcecioqlu *et al.*¹⁷, which indicated that the local anesthesia did not provide additional benefits in the vitreoretinal operation. Controversial result was obtained from

TABLE 4. The incidence of side effects between two groups

Side effects	Treatment group	Control group	<i>p</i>
Nausea			
- 3 hours	7/14 (50%)	8/14 (57%)	0.705
- 24 hours	10/14 (71.4%)	9/14 (64%)	0.695
Vomiting			
- 3 hours	6/14 (42.8%)	8/14 (57%)	0.706
- 24 hours	10/14(71.4%)	8/14 (57%)	0.440

the study of Guise¹⁸ who showed that subtenon block was very effective. Calenda *et al.*¹⁹ evaluate the effectiveness of the subtenon injection compared to standard analgesic medication for posterior segment surgery with general anesthesia. The result showed that the average VAS in the subtenon injection group was lower than the control group. The needs for additional rescue analgesic was also lower in the subtenon injection group.

The subtenon injection procedure was very safe. There was no difference in the incidence of nausea and vomiting between the two groups. The high incidence of nausea and vomiting in both groups can be caused by the administration of post-operative tramadol. One of the main side effects of tramadol is nausea.²⁰

CONCLUSION

This study did not show any additional benefit of subtenon injection for vitrectomy. The pain intensity was similar between the two groups. There was no increase in side effects after the procedure.

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