Egyptian Journal of Anaesthesia 33 (2017) 315–321

HOSTED BY

ELSEVIER

Contents lists available at ScienceDirect

Egyptian Journal of Anaesthesia

journal homepage: www.elsevier.com/locate/egja

Research article

Different adjuvants to lidocaine in bier's block; comparison between ketamine, nitroglycerin, and magnesium

Ibrahim Abbas Yossef[a], Ahmed Zein Elabdein Mohamed[b,*], Gehad Fatehy Mohamed[c]

[a] El-Minia University, 156 Kornish el Nile, ZIP: 61512, Minia, Egypt
[b] El-Minia University, 21 Sarofim Street, ZIP: 61512, Minia, Egypt
[c] El-Minia University Hospital, Bneni-Mazar, Minia, Egypt

1. Introduction

Bier's block is a simple, safe, cheap, and trustable technique of regional anesthesia for operations performed on extremities but it has some obstacles such as pain of tourniquet, poor postoperative analgesia, and local anesthetic toxicity [1].

Lidocaine is the local anesthetic of choice in Bier's block because it is characterized by rapid onset, and it is associated with lowest incidence of side effects. Expansion of lidocaine use is opposed by its short duration, so different drugs were used to encounter this problem, prolong, and potentiate the effect of lidocaine such as muscle relaxant, neostigmine, ketamine, magnesium, nitroglycerin and opioids [2]. Ketamine blocks both of central and peripheral N-Methyl D-Aspartate (NMDA) receptors which are responsible of sensitization of central nervous system to painful stimuli. Peripheral NMDA receptors play important rule in transmission of tourniquet pain through the unmyelinated slow conducting C fibers, so blocking of these receptors will decrease tourniquet pain [3].

Nitroglycerin (NTG) is a vasodilator which is metabolized in the body into nitric oxide which has anti-inflammatory, and analgesic effects, and it could potentiate the analgesic effects of other drugs such as oral morphine in cancer pain [4], and lidocaine in Bier's block [5].

Magnesium sulphate was suggested to produce its antinociceptive effect by interference with NMDA receptors and calcium channels and it was used as an adjuvant to lidocaine in Bier's block for treatment of chronic limb pain [6].

The purpose of this study was to compare between ketamine, nitroglycerin, and magnesium when added to lidocaine in Bier's block as regards to onset of sensory, and motor block, sensory and motor recovery time, tourniquet pain, quality of anesthesia, time to 1st analgesic request, and side effects.

2. Patients and methods

This prospective, randomized, double blinded study was performed in El-Minia university hospital in the period from May 2016 to February 2017. After registration of the research in the registration unit of El-Minia university with registration number (1705233) and getting the approval of the local ethics committee in faculty of medicine El-Minia university on the study plan, written informed consent from all the patients included in the study were obtained.

Eighty-eight patients, of both sex, with ASA physical status I or II, planned for elective surgery on the forearm or the hand under Bier's block, aged 20–60 years, participated in this study. Patients with history of seizures, peripheral vascular disease, sickle cell anemia, peripheral neurological disease, infection in the site of operation, patients with hypersensitivity to the test drugs, lack of cooperation such as mental retardation or deafness, patients on anti-arrhythmic drugs, and patients who refused to participate in the study were excluded.

Preparation of the anesthetic solution was done by anesthesiologist not included in the study.

Patients were randomly classified into four equal groups each of 22 patients by computer generated randomization chart with the allocation ratio was 1:1 and the randomization card was placed in sealed opaque envelop for blindness.

Group (C) control group N = 22. They received 3 mg/kg lidocaine 2% with maximum dose of 200 mg diluted to 40 ml with 0.9% saline.

Group (K) ketamine group N = 22. They received 3 mg/kg lidocaine 2% with maximum dose of 200 mg plus 0.1 mg/kg ketamine diluted to 40 ml with 0.9% saline.

Group (N) nitroglycerin group N = 22. They received 3 mg/kg lidocaine 2% with maximum dose of 200 mg plus 200 μg of nitroglycerin diluted to 40 ml with 0.9% saline.

Group (M) magnesium group N = 22. They received 3 mg/kg lidocaine 2% with maximum dose of 200 mg plus 1.5 gm magnesium sulphate 25% diluted to 40 ml with 0.9% saline.

2.1. Anesthetic technique

No sedatives or opioids were administered to the patients in the preoperative period. Standard monitoring was applied to the patients to measure non-invasive blood pressure, and heart rate every 5 min for the

Peer review under responsibility of Egyptian Society of Anesthesiologists.
* Corresponding author.
E-mail addresses: ibrahimabbasminia@yahoo.com (I.A. Yossef), ahmedzeen75@gmail.com (A.Z.E. Mohamed), Fatoma76@gmail.com (G.F. Mohamed).

http://dx.doi.org/10.1016/j.egja.2017.09.002
Received 4 June 2017; Received in revised form 27 August 2017; Accepted 6 September 2017
Available online 12 September 2017

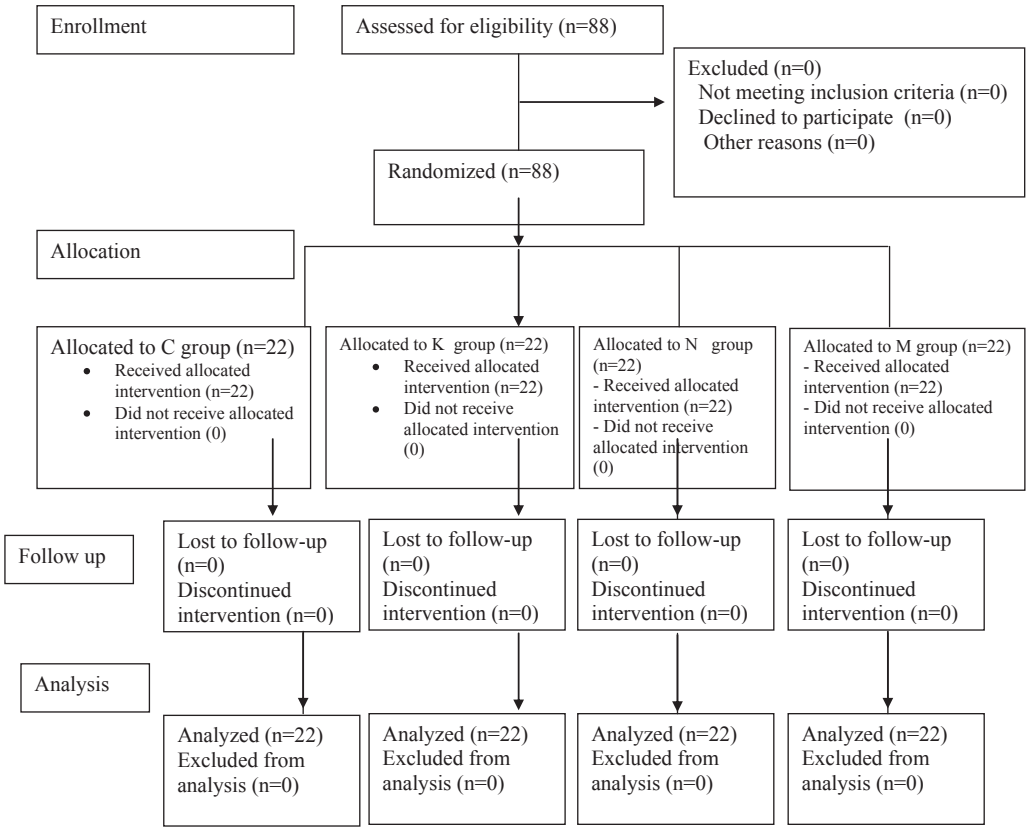

Fig. 1. Flow chart in the study.

1st quarter of hour then every 15 min till 2 h after deflation of the tourniquet.

22 gauge intravenous cannula was inserted in the most distal vein on the dorsum of the hand to be operated, it was used for lidocaine mixture injection, and another 20 gauge cannula was inserted in the other hand for fluids, antibiotics, and analgesics.

The arm to be operated upon was evacuated from blood by Esmarch bandage, then double tourniquet was applied on the upper arm with the proximal one was inflated to 300 mmHg. Complete cessation of arterial blood supply and venous return in this limb was confirmed by pallor of the hand absence of radial pulse, and absence of plethysmography of pulse oximetry.

Injection of 40 ml of the lidocaine solution with the adjuvant was done over 1 min and the time of complete injection of the solution was considered 0 time.

Sensation was examined by pin prick every 30 s in the 1st 10 min or until complete sensory loss to determine the sensory onset, and every 1 min after deflation of the tourniquet to determine sensory recovery time.

Motor block was assessed every 30 s in the 1st 10 min to determine the onset of motor block, then every 30 s after deflation of the tourniquet to determine motor recovery time. It was examined by the ability of the patient to move his wrist or fingers in flexion, extension, supination, or pronation.

After complete sensory and motor block, the distal tourniquet was inflated with 250 mmHg or 100 mmHg above the systolic blood pressure of the patient, and the proximal one was deflated, then the surgery was allowed to start. Severity of pain was evaluated either surgical or tourniquet pain at 5, 10, 15, 30, 45 min during the operation by VAS visual analogue scale graded from 0 = no pain to 10 cm = worst pain. Intraoperative fentanyl 1 μg/kg was given as a rescue analgesic when VAS was more than 3, to relieve pain of the tourniquet, and the total fentanyl dose was recorded.

At the end of the operation, the anesthesiologist deflated the tourniquet by repeated inflation, deflation technique in which 10 s of deflation followed by 1 min of re-inflation, and this was repeated three consecutive times.

Post operative pain was evaluated at 0.5, 1, 2, 4, and 8 h after tourniquet deflation by VAS and intravenous 30 mg ketrolac was given on request.

Time to 1st analgesic request was calculated from time of deflation of the tourniquet was recorded.

Side effects such as hypotension (20% decrease of baseline blood pressure), bradycardia (heart rate below 60 beat per minute), tinnitus, numbness, dizziness, hallucinations, excessive sedation and pain on injection were treated and recorded.

After the operation the anesthesiologist blinded with the type of adjuvant recorded the quality of anesthesia as follow: Excellent (4) where the patients were completely satisfied about the anesthesia without complaint, very good (3) where the patients slightly complained but continued without analgesics, good (2) where the patients slightly complained and continued with supplemental analgesics, bad (1) patients couldn't continue, and received general anesthesia.

2.2. Statistical analysis

2.2.1. Sample size calculation

Before the study, the number of patients required in each group was determined after a power calculation according to data obtained from pilot study. Pilot study reported a mean onset of sensory block of 3.5 min in group C, 2.5 min in group K, 2.4 min in group N and 2.6 min in group M; SD within each group was 1. A sample size of 20 patients in each group was determined to provide 90% power for one way ANOVA test at the level of 5% significance using G Power 3.19.2 software. 10% (2 patients) were added to each group for drop out.

Data were analyzed with Statistical Program SPSS version 21 (SPSS Inc., Chicago, IL, USA). Numerical results were expressed as mean ± SD, while categorical results were expressed as number and

Table 1
Demographic data, operative time, surgical site and tourniquet time.

Item	Group C (n = 22)	Group K (n = 22)	Group N (n = 22)	Group M (n = 22)	P value					
Age (Years)	31.4 ± 9.5	29.1 ± 8.2	29.6 ± 9.4	33.2 ± 10.7	0.470					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					0.424	0.531	0.531	0.862	0.156	0.212
Weight (kg)	70.6 ± 8.1	71.3 ± 7.8	69.5 ± 6.9	70.8 ± 6.6	0.873					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					0.754	0.622	0.929	0.421	0.823	0.560
Gender (Males/Females)	15/7	15/7	17/5	15/7	0.884					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					1	0.498	1	0.498	1	0.498
ASA (I/II)	18/4	20/2	18/4	17/5	0.676					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					0.380	1	0.709	0.380	0.216	0.709
Tourniquet time (Min)	49.7 ± 9.9	47.3 ± 10.6	48.9 ± 12.1	47.8 ± 11.9	0.892					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					0.478	0.813	0.574	0.636	0.882	0.745
Surgical site (Hand/Wrist/Fore arm)	7/6/9	7/7/8	7/9/6	8/8/6	0.945					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					0.934	0.549	0.621	0.765	0.811	0.939
Operative time (Min)	34.8 ± 12.9	35.7 ± 12.8	38.9 ± 12.1	35.04 ± 14.1	0.704					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					0.819	0.298	0.951	0.416	0.867	0.327

Numerical data are expressed as mean ± SD. Categorical data are expressed as number. One way ANOVA test for quantitative data between the four groups followed by *post Hoc* analysis between each two groups.
Chi square test for qualitative data between the groups.
P value < 0.05 is considered significant.

percentage. Results were tested for normal distribution by Kolmogorov-Smirnov test. One – way analysis of variance (ANOVA) was used to compare the numerical data between the four groups followed by *post Hoc* test for comparison between each two groups. Paired *t* test was used for comparison between different measurements of heart rate, and blood pressure within the same group. Categorical results were analyzed by Chi-square test. All tests are two-tailed and *P* value of < 0.05 was considered significant.

3. Results

Eighty-eight patients were assessed for eligibility to participate in the study, all of them were randomized, allocated into 4 groups, and all of them continued the study to be analyzed as shown in (Fig. 1).

There was no significant difference between the four groups as regards demographic data, ASA classification, duration of surgery, site of the surgery, and duration of tourniquet (Table 1).

There was no significant difference between the four groups or within each group as regards the heart rate changes (Fig. 2), mean blood pressure Fig. 3, at any time of the research.

As regards the characteristics of the block, it was found that the onset of sensory block was more rapid in the nitroglycerin group (2.27 ± 0.5 min) followed by magnesium group (2.33 ± 0.4 min), ketamine group (2.43 ± 0.5 min), and finally the control group (4.65 ± 0.8 min). This difference was significant to the control group but there was no significant difference between the other three groups. Onset of motor block was significantly faster in nitroglycerin group (3.25 ± 0.4 min), magnesium group (3.35 ± 0.5 min), and ketamine group (3.6 ± 0.6 min) in comparison to the control group (5.91 ± 1.1 min) while there was no significant difference between the three groups. Sensory recovery time after tourniquet deflation was significantly earlier in the control group (13.26 ± 5.7 min) when compared to the other groups as nitroglycerin group (27.35 ± 7.8 min), ketamine group (28.7 ± 10.4 min), and

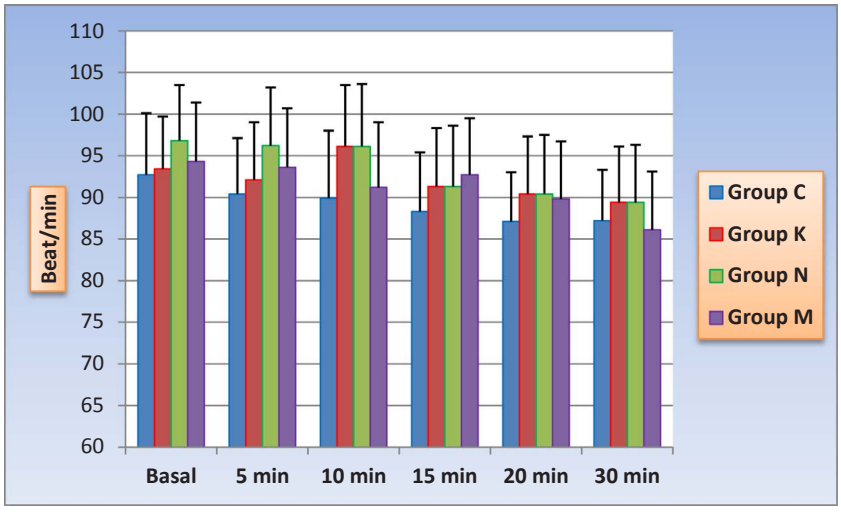

Fig. 2. Heart rate changes between the four groups. Values are presented as mean ± SD. There was no significant difference between the four groups nor within the same group.

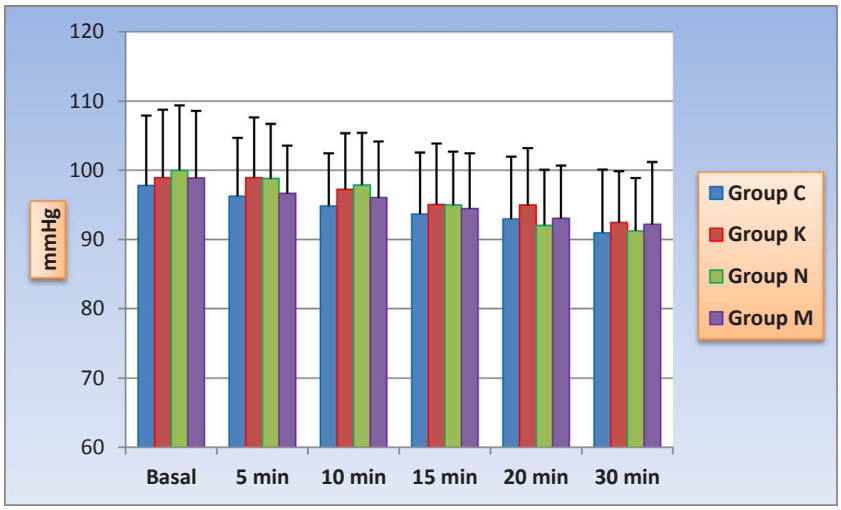

Fig. 3. Changes in mean blood pressure (mmHg). Values are presented as mean ± SD. There was no significant difference between the four groups. There was no significant difference within the same group.

Table 2
Onset time of sensory and motor block, and sensory, and motor recovery time after deflation of the tourniquet (min).

Item	Group C (n = 22)	Group K (n = 22)	Group N (n = 22)	Group M (n = 22)	P value					
Onset of sensory block (Min)	4.65 ± 0.8	2.43 ± 0.5	2.27 ± 0.5	2.23 ± 0.4	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	< 0.001*	< 0.001*	0.728	0.248	0.418
Onset of motor block (Min)	5.91 ± 1.1	3.6 ± 0.6	3.25 ± 0.4	3.35 ± 0.5	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	< 0.001*	< 0.001*	0.103	0.242	0.639
Sensory recovery time (Min)	13.26 ± 5.7	28.7 ± 10.4	27.35 ± 7.8	29.73 ± 8.6	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	< 0.001*	< 0.001*	0.591	0.682	0.344
Motor recovery time (Min)	18.04 ± 5.5	36.22 ± 11.5	35.13 ± 7.9	36.32 ± 9.2	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	< 0.001*	< 0.001*	0.682	0.970	0.655

Data are expressed as mean ± SD.
One way ANOVA test for quantitative data between the four groups followed by *post Hoc* analysis between each two groups.
P value < 0.05 is considered significant.
* Significant to control group.

magnesium group (29.73 ± 8.6 min) without significant difference between them. Motor recovery time was significantly more rapid in the control group (18.04 ± 5.5 min) in comparison to the other three groups where it was (35.13 ± 7.9 min) in nitroglycerin group, (36.22 ± 11.5 min) in ketamine group, and (36.32 ± 9.2 min) in magnesium group without significant difference between the three test groups (Table 2).

As regards the tourniquet pain which assessed by the VAS it was significantly higher in the control group more than the adjuvant groups at all study times. There was no significant difference between the three adjuvant groups (Table 3). Intraoperative fentanyl doses required to overcome tourniquet pain was significantly higher in the control group (57.8 ± 20.6 μg) when compared to the adjuvant groups as it was (35 ± 8.3 μg) in nitroglycerin group, (30.6 ± 11.9 μg) in ketamine group, and (29.9 ± 9 μg) in magnesium group. There was no significant difference between the three adjuvant groups (Table 5).

As regards postoperative pain which was assessed by VAS it was significantly higher in the control group more than the adjuvant groups at all the study times (Table 4), and the time to 1st analgesic request was more prolonged in magnesium group (2.77 ± 0.9 h), followed by ketamine group (2.7 ± 0.6 h), nitroglycerin (2.3 ± 0.7 h), and control group (1.6 ± 0.7 h). There was significant difference between the three adjuvant groups and the control group without significant difference between them (Table 5).

As regards the quality of anesthesia evaluated by the anesthesiologist it was noticed that more patients in the ketamine group (59.09%) experienced excellent quality of anesthesia, while in nitroglycerin group the percentage was (54.5%) magnesium group (50%), and control group (18.2%). Four patients in the control group experienced bad quality of anesthesia and they received general anesthesia while no one in the adjuvant groups received general anesthesia (Table 6).

As regards the side effects, there was one patient in nitroglycerin group suffered from hypotension after deflation of the tourniquet and he was treated with fluids, four patients complained from pain with injection in magnesium group, no one of the patients complained from bradycardia, excessive sedation or hallucinations (Table 7).

4. Discussion

The mechanism of action of Bier's block was suggested to be that the injection of lidocaine distal to the site of vein occlusion creates a hydrostatic pressure in the venous system distal to the occlusion makes lidocaine to spread through the small venules to act on the major nerve trunks or the peripheral nerve endings [7].

This study compared between ketamine 0.1 mg/kg, nitroglycerin 200 μg, and magnesium 25% 1.5 gm as adjuvant to lidocaine 2% in Bier's block and it found that all of the three adjuvants accelerated the onset of sensory and motor block, prolonged the sensory and motor recovery time, decreased tourniquet pain, intraoperative fentanyl

Table 3
Tourniquet pain (VAS) in the four groups.

Item	Group C (n = 22)	Group K (n = 22)	Group N (n = 22)	Group M (n = 22)	P value					
5 min	1 ± 0.4	0 ± 0	0 ± 0	0 ± 0	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	< 0.001*	< 0.001*	1	1	1
10 min	1.3 ± 0.5	0 ± 0	0 ± 0	0 ± 0	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	< 0.001*	< 0.001*	1	1	1
15 min	2 ± 0.6	1 ± 0.4	1 ± 0.3	1 ± 0.4	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	< 0.001*	< 0.001*	1	1	1
30 min	3 ± 0.9	1.3 ± 0.6	1.3 ± 0.4	1.4 ± 0.5	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	< 0.001*	< 0.001*	1	0.599	0.599
45 min	3.6 ± 1.1	1.4 ± 0.5	1.3 ± 0.4	1.6 ± 0.5	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	< 0.001*	< 0.001*	0.629	0.335	0.149

Data are expressed as mean ± SD. $P < 0.05$ is considered significant.
One way ANOVA test for quantitative data between the four groups followed by post Hoc analysis between each two groups.
* Significant to control group.

Table 4
Postoperative pain (VAS) in the four groups after tourniquet deflation.

Item	Group C (n = 22)	Group K (n = 22)	Group N (n = 22)	Group M (n = 22)	P value					
0.5 h	2.1 ± 0.4	1.3 ± 0.4	1.2 ± 0.3	1.2 ± 0.4	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	< 0.001*	< 0.001*	0.382	0.382	1
1 h	2.6 ± 1.2	1.2 ± 0.3	1.3 ± 0.4	1.2 ± 0.4	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	< 0.001*	< 0.001*	0.627	1	0.627
2 h	2.8 ± 1.3	1.5 ± 0.4	2 ± 0.6	1.6 ± 0.5	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	0.001*	< 0.001*	0.037*	0.673	0.094
4 h	3 ± 1.3	1.8 ± 0.6	2 ± 0.8	1.8 ± 0.5	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	< 0.001*	< 0.001*	0.441	1	0.441
8 h	3 ± 0.8	1.4 ± 0.7	1.6 ± 0.6	1.5 ± 0.6	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	< 0.001*	< 0.001*	0.332	0.627	0.627

Data are expressed as mean ± SD. $P < 0.05$ is considered significant.
One way ANOVA test for quantitative data between the four groups followed by post Hoc analysis between each two groups.
* Significant to control group.

Table 5
Time to 1st analgesic request (hours) and intra operative fentanyl consumption (μg).

Item	Group C (n = 22)	Group K (n = 22)	Group N (n = 22)	Group M (n = 22)	P value					
Time to 1st analgesic request (hr)	1.6 ± 0.7	2.7 ± 0.6	2.3 ± 0.7	2.77 ± 0.9	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	0.002*	< 0.001*	0.074	0.752	0.036*
Fentanyl consumption (μg)	57.8 ± 20.6	30.6 ± 11.9	35.0 ± 8.3	29.9 ± 9.0	< 0.001*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					< 0.001*	< 0.001*	< 0.001*	0.279	0.863	0.210

Data are expressed as mean ± SD.
One way ANOVA test for quantitative data between the four groups followed by post Hoc analysis between each two groups. $P < 0.05$ is considered significant.
* Significant to control group.

supplementation, decreased postoperative pain, prolonged the time to 1st analgesic request, and improved the quality of anesthesia without serious side effects. There was no significant difference between the three drugs as regards any measurements in the research.

These results coincide with El Metwally et al. [8], who compared between 200 μg nitroglycerin and 0.1 mg/kg ketamine as additives to lidocaine 2% in 75 patients scheduled for hand surgery with bier's block and they found that both of them could improve the quality of Bier's block, decreased tourniquet pain, and improved postoperative analgesia. They found that nitroglycerin was associated with faster onset of sensory and motor block while ketamine was associated with better tolerance to tourniquet pain. They found that nitroglycerin had no

Table 6
Quality of anesthesia by the anesthesiologist.

	Group C (n = 22)	Group K (n = 22)	Group N (n = 22)	Group M (n = 22)	P value					
Bad	4 (18.2%)	0 (0%)	0 (0%)	0 (0%)	0.007*					
Good	9 (40.1%)	6 (27.27%)	5 (22.7%)	3 (13.63%)	C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
Very good	5 (22.6%)	3 (13.63%)	5 (22.7%)	8 (36.36%)						
Excellent	4 (18.2%)	13(59.09%)	12(54.54%)	11 (50%)	0.02*	0.02*	0.01*	0.73	0.17	0.53

Data are expressed as number and percentage. Chi square test for qualitative data between the groups. $P < 0.05$ is value considered significant.
* Significant to control group.

Table 7
Side effects of the test drugs.

Item	Group C (n = 22)	Group K (n = 22)	Group N (n = 22)	Group M (n = 22)	P value					
Hypotension	0	0	1 (4.5%)	0	0.105					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					–	0.148	–	0.148	–	0.148
Bradycardia	0	0	0	0						
Pain on injection	0	0	0	4 (18.1%)	0.006*					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					–	–	0.036*	–	0.036*	0.036*
Excessive sedation	0	0	0	0	–					
Hallucination	0	0	0	0	–					
					C vs k	C vs N	C vs M	K vs N	K vs M	N vs M
					–	–	–	–	–	–

Data are expressed as number and percentage. Chi square test for qualitative data between the groups. $P < 0.05$ is value considered significant.
* Significant to magnesium group.

hypotensive effects as it had short half life and tourniquet was not deflated till 30 min.

Kumar et al. [9], compared ketamine 0.5 mg/kg versus dexmedetomidine 1 μg/kg as additives to lidocaine in Bier's block on 72 patients scheduled for hand and forearm surgeries and they found that ketamine delayed onset of tourniquet pain, reduced postoperative analgesics with better pain satisfaction with minimal side effects. They noticed that the patients were more sedated in ketamine group than the control group which was not noticed in our study because of the high dose (0.5 mg/kg) they used in comparison to the low dose(0.1 mg/kg) used in our study. Sen et al. [5], who were the 1st one who added 200 μg nitroglycerin to lidocaine in Bier's block on 30 patients scheduled for hand surgeries and they found that it accelerated the onset of sensory, and motor block, prolonged its duration, improve quality of anesthesia, decreased tourniquet pain, and decreased the postoperative analgesic consumption without side effects. They explained these effects by its potent vasodilator effect which facilitates the diffusion of local anesthetic through small venules and peripheral nerve endings. The analgesic effects of nitroglycerin was obtained through its metabolite nitric oxide (NO) which increases cyclic guanosine monophosphate in the cell which results in central and peripheral modulation of pain or its direct stimulation of peripheral nerve fibers simulating the action of acetyl choline [10].

Abbasivash et al. [11], found that adding 200 μg of nitroglycerin to lidocaine in Bier's block accelerated the duration of sensory and motor block, prolonged the duration of postoperative analgesia, and decreased intensity of tourniquet pain without any side effects. Honarmand et al. [12], examined three different doses (200 μg, 300 μg, 400 μg) of nitroglycerin added to lidocaine and they found that nitroglycerin accelerated the onset of sensory, and motor block, prolonged the postoperative analgesic duration, decreased the analgesic requirements, and improved the satisfaction of the patients. They found that the best dose was the 400 μg nitroglycerin but we used 200 μg instead because of the fear of hypotension and it was our 1st experience with nitroglycerin added in Bier's block.

Asadi and Mehri [13] studied the effect of adding nitroglycerin 200 μg to lidocaine in intravenous regional anesthesia in patients underwent elective surgeries in the forearm and they found that nitroglycerin was effective in enhancement of the quality of anesthesia, accelerated the onset time of sensory, and motor block, prolonged recovery time, and decreased opioids requirements without significant affection of the blood pressure. This could be explained by the short duration of nitroglycerin and the tourniquet was not deflated till 1 h passed.

Bansal et al. [14], compared the effect of adding 1.5 gram magnesium sulphate versus 200 μg nitroglycerin as adjuvant to lidocaine in intravenous regional block on seventy-five patients scheduled for hand and forearm surgeries and they found that both of magnesium and nitroglycerin accelerated the onset of sensory and motor block, prolonged the duration of sensory and motor block, and decreased the postoperative analgesic request without any side effects.

Turan et al. [15], investigated the effects of adding 10 ml of 15% magnesium sulphate to lidocaine and they found that it accelerated the onset of both sensory and motor block, prolonged the duration of block, decreased fentanyl consumption, decreased tourniquet pain, and improved quality of anesthesia. Magnesium sulphate augments the action of lidocaine in Bier's block through many ways. It has a vasodilator effect which permits better spread of the local anesthetic, it blocks both of the NMDA receptors and calcium channels which were suggested to be responsible of tourniquet pain, and its peripheral analgesic effects.

Narang et al. [16], in their study on 30 patients scheduled for upper limb surgery under Bier's block, evaluated the effect of adding 1.5 gram of magnesium to 9 ml of lidocaine 2% diluted to 36 ml and they found that it improved the quality of anesthesia, hastened the onset, and decreased tourniquet pain but increased the pain of injection caused by magnesium.

This study was limited by the small number of patients who were included in the study.

5. Conclusion

Ketamine, nitroglycerin, and magnesium when added to lidocaine in

Bier's block improved the quality of anesthesia, decreased tourniquet pain, decreased postoperative pain, increased time to 1st analgesic request without side effects. Nitroglycerin was associated with the most rapid onset of sensory, and motor block.

Conflict of interest

The Authors declared no conflict of interest.
The fund of the research was from the university budget.

References

[1] Celik H, Abdullayev R, Akcaboy EY, Baydar M, Gogus N. Comparison of tramadol and lornoxicam in intravenous regional anesthesia: a randomized controlled trial. Rev Brasilica De Anesth 2016;66(1):44–9.
[2] Choyce A, Peng P. A systematic review of adjuncts for IVRA for surgical procedures. Can J Anesth 2002;49(1):32–45.
[3] De Kock MF, Lavandhome PM. The clinical role of NMDA receptor antagonist for the treatment of postoperative pain. Best Pract Res Clin Anesth 2007;21:85–98.
[4] Lauretti GR, Perez MV, Rels MP, Pereira NL. Double-blind evaluation of transdermal nitroglycerin as adjuvant to oral morphine for cancer pain management. J Clin Anesth 2002;14:83–6.
[5] Sen S, Ugur B, Aydin ON, Ogurlu M. The analgesic effect of nitroglycerin added to lidocaine on intravenous regional anesthesia. Anesth Analg 2006;102:916–20.
[6] Tamer RM, Glynn CJ. Magnesium Bier's block for treatment of chronic limb pain: a randomized, double blind, cross-over study. Pain 2002;99:235–41.
[7] Brill S, Middleton W, Brill G, Fisher A. Bier's block: 100 years old and still going strong. Acta Anaesthesiol Scand 2004;48:117–22.
[8] El Metwally KF, Hegazy NA, Aboelseoud AA, Alshaer AA. Does the use of ketamine or nitroglycerin as an adjuvant to lidocaine improve the quality of intravenous regional anesthesia. Saudi J Anesth 2010;4(2):55–62.
[9] Kumar A, Sharma DK, Datta B. Addition of ketamine or dexmedetomidine to lignocaine in intravenous regional anesthesia: a randomized controlled study. J Anesthesiol Clin Pharmacol 2012;28(4):501–4.
[10] Hashimoto S, Kobayashi A. Clinical pharmacokinetics and pharmacodynamics of glyceryl trinitrate and its metabolites. Clin Pharmacokinet 2003;42:205–21.
[11] Abbasivash R, Hassani E, Aghdashi NM, Shirvani M. The effect of nitroglycerin as an adjuvant to lidocaine in intravenous regional anesthesia. Middle East J Anesthesiol 2009;20:265–9.
[12] Honarmand A, Safavi M, Fatemy A. The analgesic effect of three different doses of nitroglycerin when added to lidocaine for intravenous regional anesthesia in trauma patients. Ulus Travma Acil Cerrahi Derg 2011;17:497–503.
[13] Asadi HK, Mehri D. The analgesic effect of nitroglycerin added to lidocaine on quality of intravenous regional anesthesia in patients undergoing elective forearm and hand surgery. Acta Cirurgica Bras 2013;28(1):19–25.
[14] Bansal P, Baduni N, Bhalla J, Mahawar B. A comparative evaluation of magnesium sulphate and nitroglycerin as potential adjuncts to lidocaine in intravenous regional anesthesia. Int J Crit Ill Injury Sci 2015;5(1):27–31.
[15] Turan A, Memis D, Karamanlioglu B, Guler T, Pamukcu Z. Intravenous regional anesthesia using lidocaine and magnesium. Anesth Analg 2005;100:1189–92.
[16] Narang S, Dali JS, Agarwal M, Garg R. Evaluation of the efficacy of magnesium sulphate as an adjuvant to lignocaine for intravenous regional anesthesia for upper limb surgery. Anesth Inten Care 2008;36(6):840–4.