

ORIGINAL ARTICLE

A COMPARATIVE STUDY OF TWO DIFFERENT DOSES OF DEXMEDETOMIDINE AS ADJUNCT TO LIDOCAINE IN INTRAVENOUS REGIONAL ANESTHESIA

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ABSTRACT

The aim: To compare the different doses of dexmedetomidine as adjuvant to lidocaine in intravenous regional anesthesia.

Materials and methods: Ninety patients participated in this study in Al-Yarmook teaching hospital in period between January 1st 2016 – July 1st 2016, divided randomly in to 3 groups. Group 1: received lidocaine diluted with normal saline; Group 2 – lidocaine with dexmedetomidine 0.5 µg/kg; Group3 -lidocaine with dexmedetomidine 1 µg/kg. Statistical analysis was done by IBM SPSS program version 20 and Microsoft excel version 2010, the means were compared by ANOVA methods and Dunnett t3, significance between groups were recorded if p value less than 0.05.

Results: Dexmedetomidine was effective in decreasing the sensory block onset time and motor block onset time and prolongation of the motor and sensory recovery with no significant hemodynamic changes than is often shown by the lidocaine alone, it also prolongs the time interval for analgesic requirement after the operation. For the group 3 it was faster than in group 2 and faster than in group 1 significantly (p value < 0.001) to form a sensory block onset and motor block onset; and it took significantly more time to recover the sensation than in group 1 (p value <0.001) and 2 (p value <0.002), and more time for motor recovery than in group 1 (p value < 0.001). Group 3 had the longest time to call for the analgesia after operation than group 2 and 3 (p value < 0.001); and group 2 also had longer time for the same process than group 1 (p value < 0.001).

Conclusions: A variety of adjuvants have been used in IVRA to decrease tourniquet pain, improve block quality, and prolong analgesia after cuff deflation. Opioids are relatively ineffective and cause nausea, vomiting, and dizziness after tourniquet deflation, but several NSAIDs have been shown to be beneficial, dexmedetomidine improves block quality and postoperative analgesia.

KEY WORD: Dexmedetomidine, lidocaine, IVRA

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INTRODUCTION

Intravenous regional anesthesia, also called a Bier's block, can provide surgical anesthesia for short surgical procedures (45–60 min) [1].

CHOICE OF THE ANESTHETIC DRUG

Prilocaine is the preferred local anesthetic because of its high therapeutic index. Lidocaine has also been used for many years and appears to be a safe alternative. Ropivacaine has also been extensively evaluated for IVRA [2-6].

A variety of adjuvants have been used in IVRA to decrease tourniquet pain, improve block quality, and prolong analgesia after cuff deflation.[7] Opioids are relatively ineffective and cause nausea, vomiting, and dizziness after tourniquet deflation, but several NSAIDs have been shown to be beneficial [3].

Motor and sensory block occurs within 5–10 min. For prolonged surgery, the cannula is left in situ. The cuff may be deflated after 60–90 min for 5 min, the arm re-emptied of blood and the tourniquet re-inflated. Half the initial dose is then injected. Thus, safe tourniquet time is not exceeded [2].

MECHANISM OF ACTION

Mechanism of action is unclear, but may include:

- Drug action on nerve trunks.
- Drug action on nerve endings [8-10].

Adverse effects:

- Tourniquet discomfort [11]
- Rapid return of sensation after tourniquet release, resulting in subsequent pain [11]
- Failure of the anesthesia (occurs in 11%) [3]
- Toxic reactions from malfunctioning tourniquets or deflating the tourniquet prior to 20-25 minutes [11].
- The technique is used carefully in patients with severe arteriosclerosis and hypertension, since the tourniquet may not completely compress the arteries. Similar special care has been suggested in patients with obesity [2].

DEXMEDETOMIDINE

The first α_2 -adrenoceptor agonist was synthesized in the early 1960s to be used as a nasal decongestant. Early application of the new substance, now known as clonidine, showed unexpected side effects, with sedation for 24 hours and symptoms of severe cardiovascular depression.

[12-14]. It has recently become evident that complete anesthesia is possible by employing new, more potent α_2 agonists, such as medetomidine and its stereoisomer, Dexmedetomidine [14].

MECHANISM OF ACTION

α_2 -AR agonists manifest clinical effects after binding to G-Protein-coupled α_2 -AR, existing in three subtypes (α_2A , α_2B , and α_2C) with each having different physiological functions and pharmacological activities. These receptor subtypes are found ubiquitously in the central, peripheral, and autonomic nervous systems, as well as in vital organs and blood vessels [15].

Dexmedetomidine is 8 to 10 times more selective towards α_2 -AR than clonidine [16]. Neither clonidine nor dexmedetomidine is totally selective for any of the α_2 -AR subtypes, but dexmedetomidine seems to have higher α_2A -AR and α_2C -AR affinity than clonidine [17-24].

Using a dexmedetomidine as adjuvant in regional anesthesia is still not validated. Addition of 0.5 $\mu\text{g}/\text{kg}$ dexmedetomidine to lidocaine for intravenous regional anesthesia improves the quality of anesthesia and perioperative analgesia without causing side effects [25]. The effect of adding a small dose of 3 μg of intrathecal dexmedetomidine to 12 mg bupivacaine significantly prolongs sensory and motor block [25]. Dexmedetomidine confers arousable sedation with ease of orientation, anxiolysis, mild analgesia, lack of respiratory depression and hemodynamic stability at moderate doses; it also was used for sedation in difficult airway patients; during fiberoptic intubation, and for sedation of a patient with difficult airway [26]

Postoperative period: Dexmedetomidine special properties favor its use in recovery. In addition to its sympatholytic effects, analgesic effects and decreasing of shivering effect, the preservation of respiratory function allows the continuation of the dexmedetomidine infusion in the extubated, spontaneously breathing patient. The possibility of ongoing sedation and sympathetic block could be beneficial in reducing high heart rates of early postoperative ischemic events in high-risk patients undergoing noncardiac surgery [20, 25].

Dexmedetomidine is not recommended in patients with advanced heart block and ventricular dysfunction [15]. DA has classified it as a category C as a risk for pregnancy, so the drug should be used with extreme carefulness in pregnant women [18].

Sedation scoring systems: Ramsay scale: described in 1974. Score ranges from 1 (awake) to 6 (no response).

Motor Activity Assessment Scale (MAAS): developed for patients undergoing surgery in 1999. Score ranges from 0 (unresponsive) to 6 (dangerously agitated and uncooperative).

Richmond Agitation Sedation Score (RASS): developed in 2002. Score ranges from 5 (unrousable) to +4 (combative, dangerous) [25-32].

THE AIM

To compare the different doses of dexmedetomidine as adjuvant to lidocaine in intravenous regional anesthesia.

MATERIALS AND METHODS

After the study proposal was approved by the Iraqi scientific council of anesthetic committee, simple randomized double blinded prospective clinical trial study was carried out in 90 patients that gave informed consent to participate in this study. Patients were picked in al-Yarmook teaching hospital in the period of January 1st 2016 till July 1st 2016.

INCLUSION CRITERIA

- Patients were of ASA I and ASA II type
- Aged 18-60 years old
- Weighting 65 – 100 kg

EXCLUSION CRITERIA

- Patient refusal
- Any contraindication to any drugs used in the study
- In whom using of tourniquet was either impossible or contraindicated.
- Patient with severe peripheral vascular disease and neurological disease
- Patient with hemolytic disease, especially sickle cell anemia, epilepsy, hypertension, myocardial infarction, cardiac arrhythmias, heart block, psychiatric disorders.
- Potential procedures to last for more than 60 min were also not considered.
- Therapy with adrenergic receptor antagonist, calcium channel blocker and angiotensin converting enzyme inhibitors.

All patients were prepared for intravenous regional anesthesia by putting intravenous cannula in both limbs, 22g cannula at the site to operate, monitoring of pulse rate, noninvasive blood pressure measuring, checking conscious level and ECG, double pneumatic tourniquet location in the arm proximal to the operative site, exsanguination of the operative limb done and inflation of proximal tourniquet to a value equal to twice the systolic blood pressure. Then injection of the desired solution of 40 ml (not more than 3 mg / kg of lidocaine (toxic dose)) was done.

Patients were divided randomly in to 3 groups.

Group 1: got solution 40 ml of 0.5% lidocaine diluted with normal saline.

Group 2: got 39 ml 0.5% lidocaine with dexmedetomidine 0.5 $\mu\text{g}/\text{kg}$ in 1.0 ml to make final volume to 40ml.

Group3: received 39 ml 0.5% lidocaine with dexmedetomidine 1 $\mu\text{g}/\text{kg}$ in 1.0 ml to make final volume to 40 ml.

The time when the patients were unable to feel the pinprick after the injection of drug was considered as the time of onset of sensory loss and the time when the patients were unable to flex or move fingers and appearance of the wrist drop after the injection of drug was considered as the time of onset of motor loss. Assessment of onset of sensory block

Table I. Age distribution among the study groups

Age	Mean	SD	Range
Group 1	41.766	13.260	20 – 60
Group 2	42.266	12.616	21 - 60
Group 3	42.833	13.513	21 – 60
All groups	42.288	12.994	20 - 60

Table II. Distribution of the study groups according to sex

Sex	Male	Percentage	Female	Percentage
Group 1	20	66.6%	10	33.4%
Group 2	19	63.3%	11	36.6%
Group 3	19	63.3%	11	36.6%
All groups	58	64.4%	32	35.5%

Table III. Demographic data analysis

Dependent variable	Groups	Means	Std. Error	P value	
Age	1	2	42.260	3.342	0.998
		3	42.830	3.457	0.986
	2	1	41.760	3.342	0.998
		3	42.830	3.375	0.998
Weight	1	2	82.267	2.408	0.915
		3	81.900	2.535	0.968
	2	1	80.867	2.408	0.915
		3	81.900	2.090	0.997
Height	1	2	165.133	2.468	0.874
		3	164.667	2.600	0.955
	2	1	163.467	2.468	0.874
		3	164.667	2.129	0.995
Gender	1	2	M 19 / f 11	0.125	0.991
		3	M 20 / f 10	0.125	0.991
	2	1	M 20 / f 10	0.125	0.991
		3	M 20 / f 10	0.127	1.000

was evaluated by pinprick of the skin in the thenar eminence (median nerve), hypothenar eminence (ulnar nerve) and first web space (radial nerve) with further record.

Assessment of onset of motor block was evaluated by asking the patients to move fingers and the effect than was recorded.

The distal tourniquet inflated 10 min after drug administration followed by deflation of the proximal one.

The tourniquet was deflated after the operation done not less than in 30 min, by deflation for 10 sec and reinflated for 1 min 3 times in a row.

Sedation of the patient was noted during the operation (according to RASS) and till 15 min after deflation.

The need for analgesia at any time during the operation was recorded and treated by giving the patients fentanyl 1 mg / kg intra-operatively and paracetamol 1 g through intravenous infusion postoperatively.

Statistical analysis was done by IBM SPSS program version 20 and Microsoft excel version 2010 , the means were compared by ANOVA methods and Dunnett t3, significance between groups were recorded if p value less than 0.05.

RESULTS

The patients mean age in the study groups was 42.288 years old ranging from 20 to 60 years , and the distribution of the study groups according to the age is shown in table I.

The male was the most common 58 (64.44%) and the female number equaled 32 (35.55%) giving a male to female ratio of 1.8:1 , the distribution of the study groups according to sex is mentioned in table II.

The patient mean weight in all groups was 81.67 kg, and the patient mean height in all groups – 164.42 cm, the

Table IV. Comparison of onset of sensory block among the groups

Groups	Means	Std. Error	P value	
1	2	3.267	0.134	< 0.001
	3	1.283	0.154	< 0.001
2	1	4.550	0.134	< 0.001
	3	1.283	0.158	< 0.001

Table V. Comparison in onset of motor block among the groups

Groups	Means	Std. Error	P value	
1	2	138.367	2.621	< 0.001
	3	201.400	4.394	< 0.001
2	1	67.267	2.621	< 0.001
	3	201.400	4.930	< 0.001

Table VI. Comparison in sensory recovery among the groups

Groups	Means	Std. Error	P value	
1	2	7.533	0.249	< 0.001
	3	5.200	0.218	< 0.001
2	1	9.917	0.249	< 0.001
	3	7.533	0.247	< 0.001

Table VII. Comparison in motor recovery among the groups

Groups	Means	Std. Error	P Value	
1	2	5.93	0.341	0.002
	3	7.57	0.263	< 0.001
2	1	4.72	0.263	0.002
	3	7.57	0.263	< 0.001

Table VIII. Comparison in sedation among the groups

Groups	Means	Std. Error	P value	
1	2	7.42	0.343	< 0.001
	3	7.73	0.259	< 0.001
2	1	4.67	0.259	< 0.001
	3	7.73	0.259	0.737

Table IX. Comparison in analgesia duration among the groups

Groups	Means	Std. Error	P value	
1	2	0.000	0.104	0.496
	3	-0.167	0.125	0.060
2	1	0.133	0.104	0.496
	3	-0.167	0.136	0.533

distribution of the patients according to their weight and height is shown in table III.

Regarding the demographic data there were no statistical significant difference between the groups regarding the age, sex, height and weight as p value were more than 0.05 between the groups as shown in table III.

But there is a significant difference between the groups in sensory onset as the group 3 showed a statistically sig-

nificant faster result than both groups 1 and 2 (p value less than 0.05) as shown in table IV.

There was also significant difference between the groups regarding the motor block onset as group 3 was the fastest in it and the group 1 was the slowest (p value more less than 0.05) as shown in table V.

There was significant differences among the groups regarding the sensory recovery time as group 3 took more time as compared with other groups for sensory recovery as shown in table VI.

There was also a significant difference among the groups regarding the motor recovery as the group 1 was the fastest one to regain the motor function and the group 3 was the least as shown in table VII.

The sedation score showed that there was no difference between the groups as the p value between the groups regarding the sedation score after the tourniquet deflation was more than 0.05 as shown in table VIII.

The duration of the analgesia differ between the groups: the group 3 was the longest in providing analgesia, followed by group 2 and then group 1; this difference was statistically significant as p value was less than 0.05 as shown in table IX.

DISCUSSION

A variety of adjuvants have been used in IVRA to decrease tourniquet pain, improve block quality, and prolong analgesia after cuff deflation [7]. As it was shown in the study, dexmedetomidine improves block quality and postoperative analgesia.[3]

The sensory block onset among the groups was fast in group 3 (1.2 min) and it was statistically significant (the fastest among the groups with p value between group 1 and 3 and group 2 and 3 was less than 0.001). The group 2 (mean sensory block onset equaled 3.2min) was faster than group 1 (mean time – 4.5 min) with a p value less than 0.001 and this was compatible with Gupta et al[35] as they show that the sensory block onset was faster in 1 µg/kg dexmedetomidine than the 0.5 µg/kg dexmedetomidine and faster than lidocaine only and this was compatible with our study.

In Rayan et al. [33-36], Memis et al. [8], Nitin et al. [37] and Nasr et al. [39]the dexmedetomidine group was significantly faster to perform sensory block than lidocaine group and this was compatible with our study.

The motor block onset time was faster in group 3 compared with group 1 and group 2 (p value less than 0.001 in both), and group 2 was significantly faster than group 1 (p value less than 0.001).

Gupta et al. show that the motor block onset was faster in 1 µg/kg dexmedetomidine group compared to 0.5 µg/kg dexmedetomidine group and lidocaine group, and this was compatible with our study.

In Rayan et al. [36], Memis et al. [8], Nitin et al. [37] and Nasr et al. [39] the dexmedetomidine group was significantly faster in motor block onset than lidocaine group and compatible with our study.

The sensory recovery time for the group 1 was 4.7 min, group 2 – 5.9 min and for group 3 – 7.5 min; for the group

3 it took significantly more time to return the sensitivity than for group 1 (p value < 0.001) and group 2 (p value = 0.002), while for the group 2 took more time than group 1 (p value was 0.002).

In other studies, like Rayan et al. [36], Memis et al. [8] and Nasr et al. [39] it is shown that the IVRA dexmedetomidine groups took significantly more time than lidocaine ones to return the sensitivity, and this makes them compatible with our study.

The motor recovery time in group 1 was 4.67 min, group 2 – 7.4 min and group 3 – 7.7 mi; the group 1 was the fastest one to return the motor skills function as compared with group 2 and group 3 (p value less than 0.001); there was no significant difference between group 2 and 3 (p value = 0.737).

Rayan et al. [36], Memis et al. [8] and Nasr et al. [39] indicate that the IVRA dexmedetomidine groups took significantly more time than groups that received only lidocaine to return the motor skills, and this agrees with our study.

The sedation score in the groups shows the group 3 was the most sedated group after tourniquet deflation, but this was not statistically significant compared with group 1 and group 2.

This was compatible with Gupta et al [35] that notes there was no significant differences between two groups. In the study by Memis et al [8], no sedation was detected while using of 0.5 µg/kg dexmedetomidine for IVRA during intra-operative or postoperative period as in our study.

In Nasr et al [39] sedation score was significantly higher after tourniquet deflation in dexmedetomidine group and lasted for 30 min and this is incompatible with our study.

In analgesia requirement time after the operation, the group 3 needed analgesia after 201 min, group 2 – after 138 min and group 1 needed it after 67 min. Group 3 had the maximum time to call for analgesia than group 1 and 2 (p value less than 0.001) and group 2 needed it more than group 1 (p value less than 0.001).

In Gupta et al. [35] the 1 µg/kg dexmedetomidine group has the longest time to have analgesia after the operation as compared with 0.5 µg/kg dexmedetomidine group as in our study.

In Rayan et al. [36], Memis et al. [8], Nitin et al. [37], and Nasr et al. [39] the IVRA dexmedetomidine group had longer time for analgesia than the lidocaine group as in our study.

CONCLUSIONS

- Dexmedetomidine appeared to be effective in decreasing the sensory block onset time and motor block onset time than lidocaine with no significant hemodynamic change.
- Dexmedetomidine is effective in prolonging the motor recovery and sensory recovery than dose of the lidocaine alone.
- The analgesic requirement takes more time when using Dexmedetomidine with lidocaine in IVRA.
- Dexmedetomidine in dose of 1 µg/kg was more effective than the 0.5 µg/kg dexmedetomidine in the indexes of

sensory onset time, motor recovery time, sensory recovery time and analgesic requirement.

RECOMMENDATION

We recommend using Dexmedetomidine with lidocaine as adjuvant in the IVRA, at dose 1 µg/kg.

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Conflict of interest:

The Authors declare no conflict of interest.

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A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article