Journal of Medical Sciences

ISSN 1682-4474

science alert

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Research Paper

J. Med. Sci., 8 (7): 660-664
1st November, 2008

Adding Clonidine or Dexmedetomidine to Lidocaine During Bier's Block: A Comparative Study

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This prospective randomised double- blinded study was designed to compare the effects of adding either clonidine or dexmedetomidine to lidocaine during Bier's block. Forty ASA I or II patients scheduled for elective upper limb body surface surgery under Bier's block were recruited. Bier's block was achieved using lidocaine in to which either dexmedetomidine 1 μg kg^{-1} or clonidine 1 μg kg^{-1} was added. There was no significant difference between the two groups regarding the onset or regression of both the sensory and motor blockades. Intra-operatively, there was a significant reduction in the number of patients requiring analgesia and its consumed amount in the Dexmedetomidine group (0% and 0 μg, respectively) compared to the Clonidine group (40% and 27±43 μg, respectively). Similarly, in the post-operative period there was a reduction in the number of patients requiring analgesia and its consumed amount in the Dexmedetomidine group (5% and 2.5±11 μg, respectively) compared to the Clonidine group (35% and 32±24.5 μg, respectively). The quality of anaesthesia was significantly better in the Dexmedetomidine group compared to the Clonidine group. Patients in the Dexmedetomidine group were more sedated briefly post-operatively. This study reveals that, adding dexmedetomidine to lidocaine during Bier's block is better than adding clonidine.

Key words: Regional anaesthesia, Bier's block, local intravenous regional anaesthesia, clonidine, dexmedetomidine

JMS (ISSN 1682-4474) is an International, peer-reviewed scientific journal that publishes original article in experimental & clinical medicine and related disciplines such as molecular biology, biochemistry, genetics, biophysics, bio-and medical technology. JMS is issued eight times per year on paper and in electronic format.

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INTRODUCTION

Bier's block was first described in 1908 for anaesthesia of the hand and forearm and the earliest agent injected into the isolated vascular space was procaine (Brown and Fink, 1998). The technique regained popularity in the 1960's when Holmes used lidocaine (Holmes, 1998). Lidocaine remains the standard Local Anaesthetic (LA) agent for surgical procedures in many countries, especially North America (Henderson *et al*., 1997) and prilocaine is used widely in Europe (Bader *et al*., 1988).

Bier's block is simple to administer, reliable, cost-effective and is ideal for short operative procedures on the extremities performed on an ambulatory basis and avoids the hazards of general anaesthesia in patients with severe systemic diseases (Chilvers *et al*., 1997), e.g., liver impairment in whom regional anaesthesia is particularly useful provided coagulation profile is acceptable (Millwala *et al*., 2007).

Disadvantages include concerns about LA toxicity, slow onset, poor muscle relaxation, tourniquet pain and minimal postoperative pain relief. The ideal Bier's block solution should have the following features: rapid onset, reduced dose of LA, reduced tourniquet pain and prolonged post-deflation analgesia. None of the currently available local anaesthetics fulfill these qualities and hence the need for a LA adjuvant.

Several LA adjuvants have been attempted with variable degrees of success but their use was limited by side effects, e.g., mivacurium (Torrance *et al*., 1997) or limited efficacy, e.g., opioids and acetylsalicylate (Choyce and Peng, 2002; Corpataux *et al*., 1997).

Recently, α_2-adrenergic receptor (adrenoceptor) agonists have been the focus of interest for their sedative, analgesic and peri-operative sympatholytic and cardiovascular stabilizing effects in addition to their general anaesthetic sparing effect and their ability to prolong LA-induced analgesia when used in regional blocks (Murphy *et al*., 2000; Kamibayashi and Maze, 2000).

Indeed, the addition of clonidine to lidocaine during Bier's block was shown to improve tourniquet pain tolerance but did not influence the speed or quality of Bier's block (Gentili *et al*., 1999). Its effect on prolonging post-operative analgesia is controversial (Gentili *et al*., 1999; Kleinschmidt *et al*., 1997; Reuben *et al*., 1999). Reported side-effects include post-cuff deflation hypotension and sedation (Kleinschmidt *et al*., 1997; Gentili *et al*., 1999; Choyce and Peng, 2002).

Dexmedetomidine, a potent α_2 adrenoceptor agonist, is approximately 8 times more selective toward the α_2 adrenoceptors than clonidine (Khan *et al*., 1999). Dexmedetomidine-lidocaine mixture has been used recently to provide Bier's block and was shown to improve the quality of anaesthesia, tourniquet pain and reduce post-operative analgesic requirement (Memis *et al*., 2004; Esmaoglu *et al*., 2005). Its effect on the speed of onset of Bier's block is controversial (Memis *et al*., 2004; Esmaoglu *et al*., 2005). These reports suggest that it would be a better adjuvant to lidocaine in providing Bier's block in comparison to clonidine. However, there is no direct comparison between these two agents to enable clinicians to favour one α_2 agonist over the other. Therefore, this study was designed to compare the effects of adding either clonidine or dexmedetomidine to lidocaine during Bier's block.

MATERIALS AND METHODS

Forty adult American Society of Anaesthesiologists (ASA) Class I or II patients scheduled for elective upper limb body surface surgery at the Theodor Bilharz Research Institute were recruited during the period from April, 2006 to September, 2007. A written informed consent to participate in this prospective randomised double-blind study was obtained after the study has been approved by the Local Institutional Ethics Committee. Patients with Raynaud's disease, sickle cell anaemia or a history of allergy to any drug used were excluded from the study. Sedative premedication was omitted. Standard monitors including electrocardiography, non-invasive Blood Pressure (BP) measurement and pulse oximeter were used (Dragger Infinity Kappa Monitor Version VF-5W, Germany). Patients were allocated randomly into two groups according to a sealed envelope technique.

Two intravenous (IV) cannulae were inserted, one (22G) in the hand of the side to be operated on and the other (20G) in the contra lateral hand for crystalloid infusion and drug administration. A double tourniquet (Tourniquet 2800 ELC, UMB; Medizintecknik, GmbH, Germany) was positioned on the upper operative arm. The operative extremity was exsanguinated by elevation and wrapping it with a 10 cm Esmarch bandage. The proximal tourniquet was inflated to 100 mmHg more than systolic BP to a minimum of 250 mmHg and the Esmarch bandage was removed. Circulatory isolation of the operative arm was confirmed by inspection of the hand and by the absence of the radial pulse.

The Bier's block was achieved using 3 mg kg^{-1} lidocaine diluted with saline to a total volume of 40 mL to which either clonidine (Catapresan 150 μg kg^{-1}, Boehringer Ingelheim, Ingelheim, Germany) 1 μg kg^{-1} (Clon Group) or dexmedetomidine (Precedex 100 μg mL^{-1})

Abbott, Illinois, USA) 1 μg kg^{-1}(Dex Group) was added. The Bier's block solutions were administered slowly via the cannula over 1 min in the operated limb. An assistant not participating in the study prepared the Bier's block solution while the attending anaesthetist was not aware of the composition of the used Bier's block solution.

Sensory block was assessed at 30 sec intervals using a 25-G short bevelled needle. Sites used for sensory testing included the thenar eminence (median nerve), hypothenar eminence (ulnar nerve) and first web space (radial nerve). In addition, sensory regression was assessed at these same nerve sites at 30 sec intervals after tourniquet deflation. Motor function was assessed by asking the patient to flex and extend his/her wrist and complete motor block was noted when no voluntary movement was possible. After sensory and motor blocks were achieved, the distal tourniquet was inflated to 250 mmHg, the proximal tourniquet was released and surgery started.

Mean Arterial Pressure (MAP) and Heart Rate (HR) were recorded every 5 min. A 20% decrease of mean arterial pressure compared to the preoperative values was regarded as hypotension and ephedrine 6 mg IV increments every 3 min was then injected until BP returned to within the accepted 20% of baseline value. HR lowers than 50 beats min^{-1} was regarded as bradycardia and atropine 0.3 mg IV every 3 min was given until HR exceeded 50 beats min^{-1}.

Pain (tourniquet or post-operative) was assessed using a 10 cm visual analogue scale (VAS) where 0 equals no pain at all while 10 equals the worst pain imaginable. An IV bolus of fentanyl 25 μg was administered if supplemental analgesia was required (pain VAS score>3) either intra- or post-operatively. Intra-operative and post-operative fentanyl consumption was recorded.

At the end of the operation, the quality of anaesthesia was assessed according to the following numeric scale: excellent (4): no complaint from patient; good (3): minor complaint with no need for supplemental analgesics; moderate (2): complaint which required supplemental analgesics; unsuccessful (1): patient was given general anaesthesia. After bandaging the wound, tourniquet deflation was performed by the cyclic deflation-inflation technique. Sensory and motor blocks were then tested every 30 sec as during induction of Bier's block and the regression times were noted.

Sedation was assessed on a 1-5 numeric scale where, (1) completely awake, (2) awake but drowsy, (3) asleep but responsive to verbal commands, (4) asleep but responsive to tactile stimuli and (5) asleep and not responsive to any stimulus. The VAS for pain and the sedation score were measured during surgery (0, 5, 10, 15, 20 and 40 min after the injection of anaesthetics) and after tourniquet deflation (at 0, 15, 30, 60 and 120 min).

All measurements were recorded by a blinded colleague anaesthetist not participating to the study who was unaware of the drug allocation. Any local or systemic complications were recorded during the study period.

Statistical analysis: Patient's characteristics data, duration of surgery, tourniquet times, sensory and motor blocks onset and regression time, and analgesic consumption were analysed using t-test. Gender distribution was analysed with Chi square-test. The Quality of anaesthesia, pain and sedation scores were analysed using the Mann-Whitney U-test. A $p<0.05$ was considered as statistically significant.

RESULTS

There was no significant difference in the demographic data, duration of surgery or the tourniquet time between the two groups (Table 1). There was no significant difference between the two groups regarding the onset or regression of both the sensory and motor blockades (Table 1).

There was a statistically significant reduction in the visual analogue score for both the tourniquet pain and the early post-operative pain in the dexmedetomidine group compared to the clonidine group throughout the operative period (Table 2). During both the intra-operative and early post-operative periods, there was a statistically significant reduction in the number of patients requiring rescue analgesia, as well as, in the amount of analgesia consumed in the dexmedetomidine group compared to the clonidine group (Table 3). The quality of anaesthesia was significantly better in the dexmedetomidine group compared to the clonidine group (Table 3). Post-operatively, there was a statistically significant increase in the sedation score at 15, 30 and 60 min after tourniquet release in the Dex group compared to the clon. group (Table 4). None of the patients developed

Table 1: Demographic data, duration of surgery and tourniquet and block characteristics

Measured parameters	Clonidine group	Dexmedetomidine group
Age (years)	39.0±17	43.0±7.0
Weight (kg)	71.0±19	73.0±11.0
Gender (F/M)	10/5	9/6
Duration of surgery (min)	40.0±17	37.0±12.0
Tourniquet time (min)	48.0±11	46.0±14.0
Sensory block onset (min)	4.1±3.2	5.3±2.8
Motor block onset (min)	10.2±4.1	11.2±2.4
Sensory block recovery (min)	6.1±2.3	7.1±1.9
Motor block recovery (min)	6.2±1.5	5.8±3.1

Data are presented as Mean±SD unless otherwise indicated

Table 2: The Visual Analogue Scale (VAS) during the operative period (Tourniquet pain) and early post-operative period

	Timing (min)										
	After tourniquet application						After tourniquet deflation				
Groups	0	5	10	15	20	40	0	15	30	60	120
Clon.	0	2	3	3	3	5	0	2	2.5	3	3
group	(0-0)	(1-3)	(1-6)	(2-5)	(2-6)	(3-7)	(0-4)	(0-6)	(0-7)	(0-7)	(0-7)
Dex.	0	0	0	0	1	3	0	0	0	0	0
group	(0-0)	(0-0)*	(0-1)*	(0-1)*	(0-1)*	(0-5)*	(0-3)	(0-1)*	(0-2)*	(0-3)*	(0-5)*

Clon. group: Clonidine group. Dex. group: Dexmedetomidine group. Data are presented as median (range). *p<0.05 compared to the clonidine group

Table 3: The quality of anaesthesia and the peri-operative analgesia consumption

Measured parameters	Clon. group	Dex. group
Quality of anaesthesia score	2 (2-4)	3 (3-4)*
No. patients receiving intra-operative fentanyl (%)	8 (40%)	0*
Intra-operative fentanyl consumption (μg)	27 (43)	0*
No. of patients receiving fentanyl in the recovery room (%)	7 (35%)	1 (5%)*
Fentanyl consumption in the recovery room (μg)	32 (24.5)	2.5 (11)*

Clon. group: Clonidine group. Dex. group: Dexmedetomidine group. Quality of anaesthesia data are presented as median (range). Fentanyl consumption data are presented as Mean±SD. No. of patients data are presented as number (%.) *p<0.05 compared to the clonidine group

Table 4: The post-operative sedation score

	Time (min)				
Groups	0	15	30	60	120
Clonidine group	1 (1-2)	2 (1-3)	1 (1-2)	1 (1-2)	1 (1-2)
Dexmedetomidine group	1 (1-2)	3 (1-3)*	2 (2-3)*	1(1-3)*1	1 (1-2)

Data are presented as median (range). *p<0.05 compared to the clonidine group

significant bradycardia or hypotension requiring rescue medications or other side effects apart from the fore-mentioned sedation.

DISCUSSION

The results of this study reveals that the onset and regression times for both the sensory and motor block of Bier's block using either clonidine-lidocaine or dexmedetomidine-lidocaine mixtures, at the doses used in this study, are similar. However, the dexmedetomidine-lidocaine mixture provided better quality of anaesthesia and tourniquet tolerance, provided longer post-deflation analgesia with reduction of operative and early post-operative analgesic consumption. In the meantime, these improvements were associated with more post-operative sedation that is short-lived.

Although both lidocaine-clonidine and lidocaine-dexmedetomidine mixtures have similar sensory and motor onset and recovery times. The latter mixture however, provides better anaesthetic conditions as evidenced by the better quality of anaesthesia, better tourniquet tolerance leading to fewer patients requiring operative rescue analgesia and less analgesic consumption in those who actually required it.

The analgesic sparing effect of dexmedetomidine were not limited to the operative period but extended to the early post-operative period much more than clonidine as evidenced by the lower pain VAS scores, reduction in the percentage of patients requiring rescue analgesia in addition to reduction of analgesic consumption in those who had significant pain scores (VAS>3) in the dexmedetomidine group. The limited post-operative analgesic sparing effects of clonidine observed in this study confirm the findings of other investigators (Gentili *et al*., 1999; Kleinschmidt *et al*., 1997). The post-operative analgesic sparing effect of dexmedetomidine during Bier's block observed in the present study confirm the findings of other investigators (Memis *et al*., 2004; Esmaoglu *et al*., 2005).

The mechanism by which α_2-adrenergic receptor agonists produce analgesia and sedation is not fully understood but is likely to be multi-factorial. Peripherally, α_2-agonists produce analgesia by reducing release of nor-epinephrine (Sato and Perl, 1991) and/or causing α_2-receptor independent inhibitory effect on nerve-fibre action potentials (Gaumann *et al*., 1992).

Centrally, α_2-agonists produce analgesia and sedation by inhibition of substance P release in the nociceptive pathway at the level of the dorsal root neuron and by activation of α_2-adrenoceptors in the locus coeruleus. α_2-adrenoceptors are coupled via a pertussis toxin-sensitive G protein to potassium ion channel. Stimulation of α_2-adrenergic receptor results in an increase in the potassium ion channel conductance (Kamibayashi and Maze, 2000). It is therefore, hardly surprising that dexmedetomidine, that has 8 times the affinity of clonidine for α_2-Adrenergic receptors, caused more post-cuff deflation sedation compared to clonidine in the present study (Kamibayashi and Maze, 2000; Khan *et al*., 1999). This latter finding confirm the finding of Esmaoglu *et al*. (2005), who reported significant post-deflation sedation using the same dose of dexmedetomidine used in the present study (Esmaoglu *et al*., 2005). To the contrary, other investigators using half the dose used in this study did not observe increased post-deflation sedation (Memis *et al*., 2004).

Originally, the 24 h analgesic consumption was planned to be carried out by phone survey since all of

these cases were performed on a day-case basis. However, adequate number of useful data could not be obtained from patients in that way and therefore; this parameter was not included in the statistical analysis.

CONCLUSION

The results of this study reveals that the onset and regression times for both the sensory and motor block of Bier's block using either clonidine-lidocaine or dexmedetomidine-lidocaine mixtures, at the doses used in this study, are similar.

However, the dexmedetomidine-lidocaine mixture provided better quality of anaesthesia, tourniquet tolerance and operative and early post-operative analgesia at the expense of short- lived increased post-deflation sedation. Overall, the results of this study favours the addition of dexmedetomidine compared to clonidine to lidocaine for the performance of Bier's block. Further studies are needed to determine the optimum dose of dexmedetomidine for use with lidocaine for Bier's block.

ACKNOWLEDGMENT

The author would like to thank Prof. F. Abou-Rabia for her invaluable assistance.

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