SciMedCentral

International Journal of Clinical Anesthesiology

Review Article

Intravenous Dexmedetomidine on Quality of Spinal Block and Duration of Postoperative Analgesia - A Systemic Review and Update

Surjya Prasad Upadhyay*, Ulka Samanth, Sudhakar Tellicherry and PiyushMallick

Department of Anesthesiology; NMC Hospital, Dubai

***Corresponding author**

Surjya Prasad Upadhyay, Department of Anesthesiology; NMC Hospital, Dubai; PO box-7832, Phone no-00971-554078445; Email: run77in@yahoo.com

Submitted: 09 April 2015

Accepted: 18 July 2015

Published: 20 July 2015

ISSN: 2333-6641

Keywords

- Intravenous dexmedetomidine
- Spinal anaesthesia
- Quality of spinal block
- Postoperative analgesia
- sedation
- Shivering

Abstract

Intravenous dexmedetomidine is been increasingly used in perioperative setting including as an adjunct to local anaesthetic in various regional techniques with an intent to either improve the block quality, increase the duration of block or to provide sedation and patient comfort during the periblock period. Intravenous dexmedetomidine when used just before or after spinal anaesthesia has many desirable effects such as adequate sedation and patient comfort, longer sensory-motor blockade, prolonged postoperative analgesia and reduced post-anaesthesia shivering. The optimal dose or method of administration of intravenous dexmedetomidine under spinal anaesthesia has not been defined yet. Current literatures suggest a ceiling effect on prolonging post-spinal analgesia after 0.5mcg/kg boluses. With increasing the dose beyond 0.5 mcg/kg resulted in unwanted side effects notably bradycardia and excessive sedation. Further study with diverse population is needed to define the optimal dose of intravenous dexmedetomidine.

INTRODUCTION

Although spinal anaesthesia has been established as simple and safe anaesthesia technique for short to intermediate duration of infra umbilical surgeries, it may not be very comfortable for all, specially those with high level of anxiety, prolonged surgeries with uncomfortable positions and inadequate level of spinal block. These patients at times may need supplementation with sedative-analgesic or conversion to general anaesthesia, with potential risk of respiratory depression and consequent hypoxemia. Dexmedetomidine being a sedative with analgesic without respiratory depressant property provides, intraoperative sedation, alleviates position related discomfort and to an extend can cover up inadequate block height along with prolonging the postoperative analgesia. Adequate sedation after spinal anaesthesia reduces patient anxiety level, physiological and psychological stress, and increases the patient and surgeon satisfactions [1,2].

Though dexmedetomidine was initially approved by FDA for short term sedation in critical care, its unique pharmacodynamic profile has render it suitable for perioperative care during general or regional anaesthesia. It is increasingly used as an adjunct to various regional techniques [3-8].

The different potential role of intravenous dexmedetomidine in neuraxial anaesthesia has not been evaluated fully, few studies have shown that it prolong the sensory-motor blockade and provide better intraoperative and postoperative analgesia [8-10]. Apart from prolonging analgesia, it has been used for prevention and treatment of shivering [11-20].

A systemic review is done after thorough search of literatures using pub-med, medline plus, google scholar using key words intravenous dexmedetomidine and spinal anaesthesia to evaluate and provide update on the use of intravenous dexmedetomidine on spinal anaesthesia block quality, duration of postoperative analgesia, intraoperative sedation following spinal anaesthesia and also to highlight its potential advantages and risk associated with its use.

Pharmacodynamic of dexmedetomidine

Dexmedetomidine is an imidazole compound, dextroisomer of medetomidine and is 7-8 times selective alpha 2 agonist

than clonidine. Alpha 2 agonist inhibits adenyl cyclage activity, reduces brainstem vasomotor center-mediated CNS activation producing sympatholysis, anxiolysis, sedation and possess some analgesic properties [12,13].

Alpha 2 receptor have been found in the peripheral and central nervous system, platelets, liver, pancreas, kidney and eyes [13,14]. The physiological responses regulated by alpha 2 receptor vary depending on their location. Brain and spinal alpha 2 receptor activation inhibit neuronal firing, which leads to hypotension, bradycardia, sedation and analgesia. Apart from action in nervous system, extra neuronal alpha 2 activation leads to decrease in salivation and secretions, decrease gastric motility, inhibit renin release, increased glomerular filtration rate; decreased intraocular pressure and decrease insulin secretion from the pancreas [15,16]. There are various sub classification of alpha 2 receptor, alpha 2 A, B and C [16]. Analgesic effects is manly mediated by alpha 2 C and alpha 2 A receptors present on the neurons of superficial dorsal horn in lamina II, when activated, it inhibits the release of pro-nociceptive transmitters namely substance P and glutamate and hyperpolarize spinal interneurons inhabiting signal transmission [17,18] whereas the sedative action of dexmedetomidine has been postulated as hyper polarization in locus ceruleus neurons on the pons and lower brainstem [alpha 2A]resulting in inhibition of noradrenaline release and inhabiting activity in descending medullospinal noradrenergic pathways [19,20]. Alpha 2 B-agonism suppresses shivering centrally, promote analgesia spinally and induces vasoconstriction in peripheral arteries. The alpha 2C receptor is also associated with sensory processing, mood and stimulant induced locomotor activity, modulation of cognition and regulation of adrenaline outflow from the adrenal medulla [17,21].

Pharmacokinetics

Dexmedetomidine undergo first pass metabolism, so has very poor bio-availability if administered orally. Intravenous dexmedetomidine in the dose range of 0.2-0.7 mcg/kg/hr exhibits linear pharmacokinetics. Being lipophilic it is distributed widely, crosses blood brain barrier, volume of distribution 118 L, it is 94% protein bound and as such does not displace most protein bound drug commonly used in anaesthesia and intensive care. After I V administration, dexmedetomidine has a rapid distribution phase with a half-life of 6 min and the elimination half-life of 2 hrs with a clearance rate of 39l/hr. Context-sensitive-half-life varies from 4 min for 10 min infusion to 250 min for 8 hr infusion. Dexmedetomidine undergoes complete biotransformation by glucoronidation and by cytochrome P-450 mediated aliphatic hydroxylation to inactive water soluble metabolites, 95% of which is excreted in urine and the remaining in faeces. The dose need to be adjusted in patients with hepatic failure owing to lower rate of metabolism [22-24].

Intravenous dexmedetomidine and spinal anaesthesia

Intravenous dexmedetomidine before or just after spinal block is not a new concept. The intent of using intravenous dexmedetomidine is either to increase the quality and duration of sensory-motor block, prolonging the postoperative analgesia, providing sedation during surgery and or for anti-shivering prophylaxis. The timing and dosing method of intravenous dexmedetomidine in spinal anaesthesia varies in different studies. Commonly used method of intravenous dexmedetomidine is either as loading dose just before or after spinal anaesthesia [9,25-29], loading dose followed by continuous infusion [8, 30-33]. Most commonly used loading dose is 0.5 mcg/kg to 1mcg/kg over 10 min and infusion dose range from 0.2mcg/kg/hr to 1mcg/kg/hr [22,23].

Intravenous dexmedetomidine on Quality of sensory-motor blockade

Several clinical studies have been published on the effect of intravenous dexmedetomidine on spinal anaesthesia. Most of these studies and meta-analysis has shown that intravenous dexmedetomidine given just before or after spinal anaesthesia improved the quality and duration of spinal block [9,24-30]. There are many variation in the dosing and method of administration, so it challenging to reliably translate the result into clinical practice. Spinal anaesthesia might shorten the onset of sensory-motor blocked due to alpha-2 receptor activation induced inhibition of nociceptive impulse transmission [8] dexmedetomidine has been reported to potentiate the effects of intrathecal local anaesthetics. The mechanism of synergistic action of dexmedetomidine on spinal local anaesthesia is still not clear. However, supra-spinal, spinal or direct analgesia and or vasocostriction activities are involved [34]. More-over, dexmedetomidine produces a greater degree of differential blockade by preferentially blocking the myelinated A-alpha-fibers involved in motor conduction [24].

Block Characteristics

Onset of sensory/ motor blockade: Few studies have evaluated the onset time of sensory block after spinal anaesthesia, Reddy et al have compared intravenous dexmedetomidine with clonidine reported that dexmedetomidine shortened onset of sensory-motor block [35] but other studies are not supporting the faster onset of sensory/motor block [9,10,24-27]. Few study have reported intravenous dexmedetomidine shortened the onset time by 30-60 sec, which might be clinically significant but it was insignificant statistically [8,30,32].

Block Height: There are limited studies on effect of intravenous dexmedetomidine on sensory-motor block height. Some studies have reported higher level of sensory-motor blockade of hyperbaric bupivacaine by the use intravenous dexmedetomidine [27, 30,32, 35, 36]. Lee et al using two different dose of dexmedetomidine [0.5mcg/kg Vs 1 mcg/kg] reported higher level of sensory block in both group of dexmedetomidine in comparison to placebo [9]. Abdallah et al did quantitative analysis in a meta-analysis after collecting data from the studies showing higher sensory block, but they failed to see any statistically significant increase in height of block by use of dexmedetomidine [24].

Duration of block: Most of the studies on intravenous dexmedetomidine were to assess the duration of sensory/motor blockade. Sensory block duration -though there are many variation in the dosing method and timing of intravenous dexmedetomidine, - but most of the studies have reported significantly increased duration of sensory blockade by use of

intravenous dexmedetomidine [8-10, 25-32, 34-36,]. Only one study did not find any difference in block quality with the use of low dose dexmedetomidine infusion that was used solely for the purpose of intraoperative sedation [33]. Few studies have observed differences in sensory and motor blockade, compared with the prolongation of sensory block, the duration of motor block was not affected by use of intravenous dexmedetomidine [27,32,35]. In a recent meta-analysis on use of intravenous dexmedetomidine on the duration of spinal anesthesia, 7 moderate to high quality studies were analysed by Abdallah et al. [24] Sensory block duration was prolonged by at least 34% [CI limit, Point estimate 38%] and motor blockade by at least 17% [CI limit, point estimate 21%). Another meta-analysis on the effects of intravenous and intrathecal dexmedetomidine in spinal anaesthesia found that whatever route of administration, dexmedetomidine could prolong the sensory and motor blockade, although there was significant heterogeneity in the duration of sensory and motor in intravenous route, such results were not consistently in intrathecal route [37]. Lee at al using two different dosing of dexmedeteomidine 0.5 mcg/kg and 1mck/kg bolus observed similar prolongation in sensory-motor block in comparison to placebo, however, there was no difference in block quality between the two different dosing of dexmedetomidine, [9] which also match with the observation by Jaakola et al [38] where there is ceiling effect on analgesia at 0.5mcg/kg.

A recent double blind study with intrathecal [3 mcg] and intravenous [0.5 mcg/Kg] dexmedetomidine against placebo [saline] reported prolonged duration of sensory-motor block in comparison to placebo. When Intrathecal and intravenous dexmedetomidine group were compared, the duration was longer in intrathecal group. There was no effect on the block onset or maximum block height [38].

Postoperative analgesia

Most of the studies have reported prolongation of postoperative analgesia by use of intravenous dexmedetomidine. But there were many variation in the methodology or study design, lot of different methods or techniques were used to evaluate the postoperative analgesia, in some studies it was evaluated as pain score or time for first analgesic request, whereas in other studies it was used as additional opioid requirement or opioid sparing effect. In a meta-analysis by Abdullah et al revealed that use of intravenous dexmedetomidine resulted in 61% reduction in pain score at 6 hrs and 53% prolongation of the time of first analgesic request [24]. Annamalai et al has used 1mcg/kg dexmedetomidine as slow bolus over 10 min, either 10 min before or 30 min after the spinal anaesthesia with bupivacaine and reported reduced pain score and longer duration of postoperative analgesia by dexmedetomidine. The timing of dexmedetomidine injection did not make any difference in the postoperative analgesia or other block characteristics [27].

Recent double blind study by Dinesh et al reported prolongation of first analgesic request and significant reduction in 24 hrs mean analgesic requirement by use of intravenous dexmedetomidine in compared to placebo [30]. Reddy et al compared intravenous dexmedetomidine[0.5 mcg/kg] with clonidine [1 mcg/kg]as premedication before giving the spinal anaesthesia with bupivacaine, observed significantly longer interval for the first analgesic request in dexmedetomidine group [35].

Sedation under spinal anaesthesia

Though regional anaesthesia confer many benefits and patient satisfaction in terms of staying awake during the procedure, early family contact and early food intake, [39] from anaesthesiologist point of view, rapid postoperative recovery and preservation of protective airway reflexes are the most important advantages of regional anaesthesia. But many patients don't like to be awake to remember or recall the intraoperative procedure [40] and frequently request for some form of sedation. The aim of sedation in regional anaesthesia technique includes general patient comfort, freedom from specific discomfort and some amnesia for entire procedure [41]. Proper sedation has shown to improve the patient satisfaction during regional anaesthesia [42, 43] and may be considered as a means to increase the patient acceptance for regional anaesthesia technique. Sedation not only increases the patient acceptance for regional anaesthesia, it may sometime cover up for inadequate or insufficient block and can help to reduce the requirement of opioid analgesic and indirectly contribute to reduction in postoperative nausea and vomiting [44-46].

The sedative action of dexmedetomidine differs from other agents [benzodiazepine and propofol which act through GABA receptor and produces clouding of consciousness and at times patient co-opertion may be lost, [47] the sedation produced by dexmedetomidine is like that of natural sleep as it act on the locus ceruleus of the brain, which induces sedation resembling natural sleep by means of sleep modulation and maintaining respiratory control [48-50]. Moreover dexmedetomidine has no or minimal effect on respiratory rate and tidal volume [51]. Most of the studies on intravenous dexmedetomidine have used either a loading dose or loading dose followed by infusion and sedation was a secondary outcome measure. Few studies have been done on intravenous dexmedetomidine where sedation was the primary measure [1,52,53] . Adequate sedation has been reported with lower dose of dexmedetomidine [0.5mcg/kg with or without infusion) [1,8,9,52] excessive sedation has been reported when intravenous dexmedetomidine [1mcg/kg]was given as bolus dose [1,9,26,27,31,34,52-54].

Ok HK et al conducted a study on intravenous dexmedetomidine to find out the optimal dose for sedation after spinal anaesthesia. After a loading dose of dexmedetomidine 1mcg/kg over 10 min, patients were divided into three group, one group to receive 0.2mc/kg/hr, another group 0.4mcg/kg/hr and third group saline as placebo [1]. All patient had good sedation till 60 min, after that the saline treated group had less sedation, whereas, 0.2mcg/kg/hr infusion group sedation was prolonged for 80 min and 0.4mcg/kg/hr infusion group by 120 min. Choi and Lee has compared two different loading dose 0.6mcg/kg and 1 mcg/kg of dexmedetomidine after spinal anaesthesia, similar sedation level were observed 5 min after the loading dose, but there was more hypotension and bradycardia incidences in 1 mcg/kg group [52].

A comparative study between dexmedetomidine and remifentanil infusion as sedation technique for arthoscopic

knee surgery under spinal anaesthesia by Kirman et al observed higher sedation in dexmedetomidine [1mcg/kg bolus followed by 0.2mcg/kg/hr infusion]group than remifentanil [0.5mcg/kg bolus followed by 3 mcg/kg/hr). Although dexmedetomidine treated group exhibited deeper sedation, there was no haemodynamic or respiratory depression. Whereas remifentanil treated group had lighter sedation with short recovery time but exhibited higher incidences of respiratory depression [53].

Dexmedetomidine has linear pharmacokinetics and dose dependent sedative action, when a loading dose of dexmedetomidine 1 mcg/kg administered over 10 min, the average peak concentration was reached in 17 min with terminal half-life of 2 hr 10 min [55]. So a single bolus dose might be sufficient for procedure lasting less than 60 min whereas continuous infusion is needed for longer procedure. The recommended dose of dexmedetomidine for sedation is 1 mcg/kg bolus followed by 0.2-0.7 mcg/kg/hr for conscious sedation or procedural sedation, [22] however the optimal sedative dose of after spinal anaesthesia has not been defined, spinal anaesthesia as such have some sedative action because of blockade of ascending somatosensory transmission that depress the excitability of reticulo-thalamo-cortical arousal mechanism, [56] because of this patients under spinal anaesthesia require much lower dose of any sedative drug.

Dexmedetomidine and shivering

Incidences of shivering under spinal anaesthesia has been reported as high as 40-60% [57,58]. Shivering not only cause discomfort to the patient, it increases the oxygen consumption, increases catecholamine level subjecting the patient to a higher risk of cardiovascular complications [57-59].The Alpha-2 receptor agonists are known to possess antishivering property by lowering shivering and vasoconstriction threshold without increasing respiratory depression, nausea-vomiting unlike the other antishivering drugs like meperidine [60,61]. In addition, it has central hypothalamic thermoregulatory effects [62].

Intravenous Dexmedetomidine in dose range of 0.5 to 1 mcg/kg has been used successfully used either for prevention [11,63-65] or treatment [66,67] of shivering after general or regional anaesthesia. Intravenous dexmedetomidine 0.5mcg/kg as loading dose was found 100% effective in treatment of post anaesthesia shivering following general anaesthesia in children [66]. Gupta et al using tramadol *Vs* demedetomidine, observed that dexmedetomidine was equally effective, but was associated with favorable outcome such as shorter time for complete cessation of shivering and less incidences of nausea-vomiting [67].

Intravenous dexmedetomidine and adverse outcome

Most commonly reported adverse effects after intravenous dexmedetomidine are Bradycardia requiring atropine and hypotension. Hypotension and bradycardia are common physiological response to spinal anaesthesia due to blockade of sympathetic system. The primary physiologic alteration are decrease preload and cardiac volume, which combine with bradycardia to reduce arterial blood pressure and cardiac output.

Hypotension

As we all know, hypotension occurs easily with spinal anaesthesia and it can be treated with either fluid loading, ephedrine or phenylephrine [68,69]. The incidence of hypotension requiring intervention after spinal anaesthesia remained same despite use of intravenous demedetomidine. None of the studies so far has shown that dexmedetomidine increases the hypotension after spinal anaesthesia [24,70].

Bradycardia

Haemodynamic response in the form of transient hypertension and reflex bradycardia followed by hypotension and bradycardia has been described with the use of higher dose and rapid infusion of dexmedetomidine [71,72]. Most studies on intravenous dexmedetomidine with dose of 1mcg/kg loading dose over 5-10 min had bradycardia as one of the prominent side effect with incident up to 30-40% [26, 29-31,34,73].

Meta-analysis on the intravenous dexmedetomidine and spinal anaesthesia by Abdullah et al has found that there was 3.7 fold increase in bradycardia incidence and it was more significant where dexmedetomidine initial loading dose was infused over a shorter period such as over 5 to 10 min, compared with those studies where initial loading dose was administered over 20 min [24]. Similarly Niu et al in a meta-analysis found that use of dexmedetomidine either intravenously or intrathecally resulted higher incidence of bradycardia requiring atropine [37].

Other adverse events

There are no reports of increase incidences of any adverse effects directly or indirectly attributed by use of intravenous dexmedetomidine.

Dexmedetomidine and organ protection

Dexmedetomidine come into debate after some recent work on dexmedetomidine in experimental animal model has shown that it might have some organ protective effects [74], particularly by modulation of cytokine and inflammatory mediators in variety of ischemia and ischemic-reperfusion injury [75-80]. However, there is no report of such study in human being. One study has demonstrated that use of dexmedetomidine in post-bypass period in coronary bypass surgery had lower incidence of acute kidney injury [81-83]. The ability to protect against organ dysfunction, notably myocardial, renal and neuronal, may yet to be the defining characteristic of this class of drug. Further clinical and preclinical studies are required to inform us about the diversity of therapeutic application of dexmedetomidine.

SUMMARY

Intravenous dexmedetomidine when administered in patients undergoing surgery under spinal anaesthesia has a definite role in providing adequate intraoperative sedation, good quality of block, prolonging the postoperative analgesia and reduces incidence of shivering. It definitely prolongs the duration of sensory block as shown by various studies, the duration of motor block has inconsistent results and hence it is inconclusive till this moment. Similarly the onset of block, height of block has conflicting results in different study and there

is no strong evidence till this time to prove that intravenous dexmedetomidine shorten the block onset time or increase the block height. The timing of dexmedetomidine injection did not make any difference in the postoperative analgesia or other block characteristics. Increasing the loading dose beyond 0.5 mcg/kg, there is proportionate increase in side effects notably bradycardia requiring atropine and excessive sedation. More adverse effects were also reported when loading dose of 1 mcg/kg was infused over short period (5-10 min).

Optimal dosing of intravenous dexmedetomidine has not been defined yet. Similar postoperative analgesia has been achieved without using the loading infusion also. No loading or low loading dose of 0.25 to 0.5mcg/kg or loading over longer period [more than15min]followed by infusion might be more safer and appropriate to provide the adequate intraoperative sedation, good quality of block with prolonged postoperative analgesia. Future studies using different dosing regimen such as isolated bolus followed by infusion or isolated infusion alone might clear our knowledge and understanding of the proper dosing of intravenous dexmedetomidine in patients under spinal anaesthesia.

CONCLUSION

Intravenous dexmedetomidine provides adequate intraoperative sedation, increases patient comfort, improves spinal block quality, prolong the postoperative analgesia and also reduces post-anaesthesia shivering. More incidences of bradycardia and excessive sedation is warranted with higher dose approaching 1mcg/kg. Further studies are required to define the optimum dose of intravenous dexmedetomidine in spinal anaesthesia for its various pharmodynamic effects.

REFERENCES

1. Ok HG, Baek SH, Baik SW, Kim HK, Shin SW, Kim KH. Optimal dose of dexmedetomidine for sedation during spinal anesthesia. Korean J Anesthesiol. 2013; 64: 426-431.
2. De Andrés J, Valía JC, Gil A, Bolinches R. Predictors of patient satisfaction with regional anesthesia. Reg Anesth. 1995; 20: 498-505.
3. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg. 2000; 90: 699-705.
4. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: a novel sedative-analgesic agent. Proc (Bayl Univ Med Cent). 2001; 14: 13-21.
5. Bajwa S, Kulshrestha A. Dexmedetomidine: an adjuvant making large inroads into clinical practice. Ann Med Health Sci Res. 2013; 3: 475-483.
6. Afonso J, Reis F. Dexmedetomidine: current role in anesthesia and intensive care. Rev Bras Anestesiol. 2012; 62: 118-133.
7. Sudheesh K, Harsoor S. Dexmedetomidine in anaesthesia practice: A wonder drug? Indian J Anaesth. 2011; 55: 323-324.
8. Harsoor S, Rani DD, Yalamuru B, Sudheesh K, Nethra S. Effect of supplementation of low dose intravenous dexmedetomidine on characteristics of spinal anaesthesia with hyperbaric bupivacaine. Indian J Anaesth. 2013; 57: 265-269.
9. Lee MH, Ko JH, Kim EM, Cheung MH, Choi YR, Choi EM. The effects of intravenous dexmedetomidine on spinal anesthesia: comparision of different dose of dexmedetomidine. Korean J Anesthesiol. 2014; 67: 252-257.
10. Gupta K, Tiwari V, Gupta PK, Pandey MN, Agarwal S, Arora A. Prolongation of subarachnoid block by intravenous dexmedetomidine for sub umbilical surgical procedures: A prospective control study. Anesth Essays Res 2014; 18: 8: 175-178.
11. Usta B, Gozdemir M, Demircioglu RI, Muslu B, Sert H, Yaldiz A. Dexmedetomidine for the prevention of shivering during spinal anesthesia. Clinics (Sao Paulo). 2011; 66: 1187-1191.
12. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs. 2000; 59: 263-268.
13. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg. 2000; 90: 699-705.
14. Hoffman BB. Adrenoreceptor activing and other sympathomimetic drugs.In: Katzung B. Basic and Clinical Pharmacology. 9Th ed. New york, NY: McGraw-Hill. 2003; 9:134-139.
15. Afsani N. Clinical Application of dexmedetomidines. S Afr J Anaesthesiol Analg 2010; 16: 50-56.
16. Fairbanks CA, Stone LS, Wilcox GL. Pharmacological profiles of alpha 2 adrenergic receptor agonist identified using genetically altered mice and isobolographic analysis. Pharmacol Ther 2009; 123:224-38.
17. Philipp M, Brede M, Hein L. Physiological significance of alpha (2)-adrenergic receptor subtype diversity: one receptor is not enough. Am J Physiol Regul Integr Comp Physiol. 2002; 283: R287-295.
18. Ishii H, Kohno T, Yamakura T, Ikoma M, Baba H. Action of dexmedetomidine on the substantia gelatinosa neurons of the rat spinal cord. Eur J Neurosci. 2008; 27: 3182-3190.
19. Guo TZ, Jiang JY, Buttermann AE, Maze M. Dexmedetomidine injection into the locus ceruleus produces antinociception. Anesthesiology. 1996; 84: 873-881.
20. Carollo DS, Nossaman BD, Ramadhyani U. Dexmedetomidine: a review of clinical applications. Curr Opin Anaesthesiol. 2008; 21: 457-461.
21. Afonso J, Reis F. Dexmedetomidine: current role in anesthesia and intensive care. Rev Bras Anestesiol. 2012; 62: 118-133.
22. Precedex® prescribing information. Hospira, Inc. 2004.
23. Dexmedetomidine. Drug Facts and Comparisons. Effects. 2005.
24. Abdallah FW, Abrishami A, Brull R. The facilitatory effects of intravenous dexmedetomidine on the duration of spinal anesthesia: a systematic review and meta-analysis. Anesth Analg. 2013; 117: 271-278.
25. Jung SH, Lee SK, Lim KJ, Park EY, Kang MH, Lee JM, et al. The effects of single-dose intravenous dexmedetomidine on hyperbaric bupivacaine spinal anesthesia. J Anesth. 2013; 27: 380-384.
26. Hong JY, Kim WO, Yoon Y, Choi Y, Kim SH, Kil HK. Effects of intravenous dexmedetomidine on low-dose bupivacaine spinal anaesthesia in elderly patients. Acta Anaesthesiol Scand. 2012; 56: 382-387.
27. Annamalai A, Singh S, Mahrous DE. Can Intravenous Dexmedetomidine prolong Bupivacaine intrathecal Spinal Anaesthesia. J Anesth Clin Res 2013; 4: 12: 372-377.
28. Reddy VS, Shaik NA, Donthu B, Sannala VK, Jangam V. Intravenous dexmedetomidine versus clonidine for prolongation of bupivacaine spinal anesthesia and analgesia: A randomized double-blind study. J Anaesthesiol Clin Pharmacol 2013; 29: 342-347.
29. Elcicek K, Tekin M, Kati I. The effects of intravenous dexmedetomidine on spinal hyperbaric ropivacaine anesthesia. J Anesth. 2010; 24: 544-548.

30. Dinesh CN, Sai Tej NA, Yatish B, Pujari VS, Mohan Kumar RM, Mohan CV. Effects of intravenous dexmedetomidine on hyperbaric bupivacaine spinal anesthesia: A randomized study. Saudi J Anaesth. 2014; 8: 202-208.

31. Al- Mustafa MM, Badran IZ, Abu-Ali HM, Al-Barazangi BA, Massad IM, Al-Ghanem SM. Intravenous dexmedetomidine prolongs bupivacaine spinal analgesia. Middle East J Anesthesiol 2009; 20: 225-231.

32. Kaya FN, Yavascaoglu B, Turker G, Yildirim A, Gurbet A, Mogol EB, et al. Intravenous dexmedetomidine, but not midazolam, prolongs bupivacaine spinal anesthesia. Can J Anaesth. 2010; 57: 39-45.

33. Edno Magalhães, Luís Cláudio de Araújo Ladeira, Cátia Sousa Govêia, Beatriz Vieira Espíndola. Intravenous dexmedetomidine for sedation does not interfere with sensory and motor block duration during spinal anesthesia. Rev. Bras. Anestesiol. 2006; 56: 01-07.

34. Saadawy I, Boker A, Elshahawy MA, Almazrooa A, Melibary S, Abdellatif AA, et al. Effect of dexmedetomidine on the characteristics of bupivacaine in a caudal block in pediatrics. Acta Anaesthesiol Scand. 2009; 53: 251-256.

35. Reddy VS, Shaik NA, Donthu B, Reddy Sannala VK, Jangam V. Intravenous dexmedetomidine versus clonidine for prolongation of bupivacaine spinal anesthesia and analgesia: A randomized double-blind study. J Anaesthesiol Clin Pharmacol. 2013; 29: 342-347.

36. Swati Bisht, Sudha Prasad. Intravenous Dexmedetomidine Prolongs Bupivacaine Spinal Anesthesia. Journal of Evolution of Medical and Dental Sciences. 2014; 3: 1745-1752.

37. Niu XY, Ding XB, Guo T, Chen MH, Fu SK, Li Q. Effects of intravenous and intrathecal dexmedetomidine in spinal anesthesia: a meta-analysis. CNS Neurosci Ther. 2013; 19: 897-904.

38. Hamed AM, Talaat SM. Effect of intravenous versus intrathecal low-dose dexmedetomidine on spinal block in lower limb orthopedic surgery. Ain-Shams J Anaesthesiol 2014; 7: 205-210.

39. De Andrés J, Valía JC, Gil A, Bolinches R. Predictors of patient satisfaction with regional anesthesia. Reg Anesth. 1995; 20: 498-505.

40. Macario A, Weinger M, Carney S, Kim A. Which clinical anaesthesia outcomes are important to avoid? The perspective of patients. Anesth Analg 1999; 89: 652-658.

41. Höhener D, Blumenthal S, Borgeat A. Sedation and regional anaesthesia in the adult patient. Br J Anaesth. 2008; 100: 8-16.

42. Wu CL, Naqibuddin M, Fleisher LA. Measurement of patient satisfaction as an outcome of regional anesthesia and analgesia: a systematic review. Reg Anesth Pain Med. 2001; 26: 196-208.

43. Villeret I, Laffon M, Ferrandière M, Delerue D, Fusciardi J. Which propofol target concentration for ASA III elderly patients for conscious sedation combined with regional anaesthesia. Ann Fr Anesth Reanim. 2003; 22: 196-201.

44. Avramov MN, White PF. Use of alfentanil and propofol for outpatient monitored anesthesia care: determining the optimal dosing regimen. Anesth Analg. 1997; 85: 566-572.

45. Pavlin DJ, Coda B, Shen DD, Tschanz J, Nguyen Q, Schaffer R, et al. Effects of combining propofol and alfentanil on ventilation, analgesia, sedation, and emesis in human volunteers. Anesthesiology. 1996; 84: 23-37.

46. Wresch KP. Analgesia and sedation to supplement incomplete regional anesthesia. Anaesthesist. 1995; 44 Suppl 3: S580-587.

47. Aho M, Erkola O, Kallio A, Scheinin H, Korttila K. Comparison of dexmedetomidine and midazolam sedation and antagonism of dexmedetomidine with atipamezole. J Clin Anesth. 1993; 5: 194-203.

48. Ust Y, GÃ M, ErdoA Yan O, Benlidayi ME. Dexmedetomidine versus midazolam in outpatient third molar surgery. J Oral Maxillofac Surg. 2006; 64: 1353-1358.

49. Guo TZ, Jiang JY, Buttermann AE, Maze M. Dexmedetomidine injection into the locus ceruleus produces antinociception. Anesthesiology. 1996; 84: 873-881.

50. Huupponen E, Maksimow A, Lapinlampi P, Sarkela M, Saastamoinen A, Snapir A, et al. Electroencephalogram spindle activity during dexmedetomidine sedation and physiological sleep. Acta Anaesthesiol Scand 2008; 52: 289-294.

51. Hsu YW, Cortinez LI, Robertson KM, Keifer JC, Sum-Ping ST, Moretti EW, et al. Dexmedetomidine pharmacodynamics: Part I: crossover comparison of the respiratory effects of dexmedetomidine and remifentanil in healthy volunteers. Anesthesiology 2004; 101: 1066-1076.

52. Choi JR, Lee JS. Comparison of two loading doses of dexmedetomidine for sedation during spinal anesthesia. European Journal of Anesthesiology. 2014; 31: 132-133.

53. Kirman N, Kucukebe OB, Abdullayev R, Aksoy E, Gogus N. Dexmedetomidine and Remifentanil as adjunct to Regional Anaesthesia, a Randomized clinical Trial. Glo Adv Res J Med Sci. 2014; 9: 233-239.

54. Tekin M, Kati I, Tomak Y, Kisli E. Effect of Dexmedetomidine IV on the Duration of Spinal Anesthesia with Prilocaine: A Double-Blind, Prospective Study in Adult Surgical Patients. Curr Ther Res Clin Exp. 2007; 68: 313-324.

55. Lee S, Kim BH, Lim K, Stalker D, Wisemandle W, Shin SG, et al. Pharmacokinetics and pharmacodynamics of intravenous dexmedetomidine in healthy Korean subjects. J Clin Pharm Ther. 2012; 37: 698-703.

56. Antognini JF, Jinks SL, Atherly R, Clayton C, Carsten E. Spinal anaesthesia indirectly depresses cortical activity associated with electrical stimulation of the reticular formation. Br J Anaesth. 2003; 9: 233-238.

57. De Witte J, Sessler DI. Perioperative shivering: physiology and pharmacology. Anesthesiology. 2002; 96: 467-484.

58. Bhattacharya P, Bhattacharya L. Post anaesthesia shivering (PAS): A review. Indian J Anaesth 2003; 47: 88-93.

59. Buggy DJ, crossley AW. Thermoregulation, mild perioperative hypothermia and postanaesthetic shivering. Br. J Anaesth 2000; 84: 615-628.

60. Talke P, Tayefeh F, Sessler DI, Jeffrey R, Noursalehi M, Richardson C. Dexmedetomidine does not alter the sweating threshold, but comparably and linearly decreases the vasoconstriction and shivering thresholds. Anesthesiology. 1997; 87: 835-841.

61. Kurz A, Ikeda T, Sessler DI, Larson M, Bjorksten AR, Dechert M, et al. Meperidine decreases the shivering threshold twice as much as the vasoconstriction threshold. Anesthesiology 1997;86:1046-1054

62. Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S, et al. Dexmedetomidine and clonidine in epidural anaesthesia: A comparative evaluation. Indian J Anaesth. 2011; 55:116-121.

63. Karaman S, Gunusen I, Ceylan A, Karaman Y, Cetin EN, Derbent A, et al. Dexmedetomidine infusion prevents postoperative shivering in patients undergoing gynaecologic laparoscopic surgery. Turk J Med Sci. 2013; 43: 232-237.

64. Bajwa SJ, Gupta S, Kaur J, Singh A, Parmar S. Reduction in the incidence of shivering with perioperative dexmedetomidine: A randomized prospective study. J Anaesthesiol Clin Pharmacol. 2012; 28: 86-91.

65. Bozgeyik S, Mizrak A, Yendi F, Ugur BK. The effects of preemptive tramadol and dexmedetomidine on shivering during arthroscopy. Saudi J Anaesth. 2014; 8: 238-243.

66. Blaine Easley R, Brady KM, Tobias JD. Dexmedetomidine for the treatment of postanesthesia shivering in children. Paediatr Anaesth. 2007; 17: 341-346.

67. Mittal G, Gupta K, Katyal S, Kaushal S. Randomised double-blind comparative study of dexmedetomidine and tramadol for post-spinal anaesthesia shivering. Indian J Anaesth. 2014; 58: 257-262.

68. Neal JM. Hypotension and bradycardia during spinal anesthesia: Significance, prevention, and treatment. Techniques in Regional Anesthesia and Pain Management 2000; 4:148-154.

69. Lin FQ, Qiu MT, Ding XX, Fu SK, Li Q. Ephedrine versus phenylephrine for the management of hypotension during spinal anesthesia for cesarean section: an updated meta-analysis. CNS Neurosci Ther. 2012; 18: 591-597.

70. Niu XY, Ding XB, Guo T, Chen MH, Fu SK, Li Q. Effects of intravenous and intrathecal dexmedetomidine in spinal anesthesia: a meta-analysis. CNS Neurosci Ther. 2013; 19: 897-904.

71. Mason KP, Zurakowski D, Zgleszewski S, Prescilla R, Fontaine PJ, et al. Incidence and predictors of hypertension during high-dose dexmedetomidine sedation for pediatric MRI. Paediatr Anaesth. 2010; 20: 516-523.

72. Sudheesh K, Harsoor S. Dexmedetomidine in anaesthesia practice: A wonder drug? Indian J Anaesth. 2011; 55: 323-324.

73. Lugo VW, Gomez IA, Cisneros-Corral R, Martinez-Gallegos N. Intravenous dexmedetomidine versus intravenous clonidine to prolong bupivacaine spinal anaesthesia. A double blind study. Anestesia en Mexico. 2007; 19: 143–146.

74. Arora N. Prophylactic Tramadol versus Dexmedetomidine for prevention of Shivering during Spinal Anaesthesia. Int J Sci Stud 2014; 2: 7: 17-20.

75. Bahanur Cekic, Sukran Geze, Gulsum Ozkan, et al., "The Effect of Dexmedetomidine on Oxidative Stress during Pneumoperitoneum," BioMed Research International. 2014; 760323: 5.

76. Liu Xianbao, Zhan Hong, Zeng Xu, Zhang Chunfang, Chen Dunjin. "Dexmedetomidine Reduced Cytokine Release during Postpartum Bleeding-Induced Multiple Organ Dysfunction Syndrome in Rats. Mediators of Inflammation. 2013; 627831: 7.

77. J. Lempiäinen, P. Finckenberg, EE. Mervaala, M. Storvik, J. Kaivola, K. Lindstedt, et al. Dexmedetomidine preconditioning ameliorates kidney ischemia reperfusion injury, Pharma Res Per. 2014; 2: e00045.

78. Tufek A, Tokgoz O, Aliosmanoglu I, Alabalik U, Evliyaoglu O, Ciftci T, et al. The protective effects of dexmedetomidine on the liver and remote organs against hepatic ischemia reperfusion injury in rats. Intn J Surg; 11: 1:96-100.

79. Gu J, Sun P, Zhao H, Watts HR, Sanders RD, Terrando N, et al. Dexmedetomidine provides renoprotection against ischemia-reperfusion injury in mice. Crit Care. 2011; 15: R153.

80. Okada H, Kurita T, Mochizuki T, Morita K, Sato S. The cardioprotective effect of dexmedetomidine on global ischaemia in isolated rat hearts. Resuscitation. 2007; 74: 538-545.

81. Ji F, Li Z, Young JN, Yeranossian A, Liu H. Post-Bypass Dexmedetomidine Use and Postoperative Acute Kidney Injury in Patients Undergoing Cardiac Surgery with Cardiopulmonary Bypass. PLoS One. 2013; 10: e77446.

82. Jaakola ML, Salonen M, Lehtinen R, Scheinin H. The analgesic action of dexmedetomidine--a novel alpha 2-adrenoceptor agonist--in healthy volunteers. Pain. 1991; 46: 281-285.

83. Elcicek K, Tekin M, Kati I. The effects of intravenous dexmedetomidine on spinal hyperbaric ropivacaine anesthesia. J Anesth. 2010; 24: 544-548.

Cite this article

Upadhyay SP, Samanth U, Tellicherry S, Mallick P (2015) Intravenous Dexmedetomidine on Quality of Spinal Block and Duration of Postoperative Analgesia -A Systemic Review and Update. Int J Clin Anesthesiol 3(1): 1045.