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# A PROSPECTIVE STUDY TO ASSESS THE OPTIMUM LOADING DOSE OF DEXMEDETOMIDINE TO FULFILL CRITERIA OF ANAESTHESIOLOGIST, SURGEON AND PATIENT SATISFACTION IN MONITORED ANAESTHESIA CARE UNDER LOCAL INFILTRATION

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**ABSTRACT**

**Background and aim :** Dexmedetomidine , an alpha-2 agonist , a safe sedoanalgesic agent is being used for more than two decades in intensive care and operation theatres . We utilized it's sedoanalgesic properties for day care surgeries and tried to find out the minimum loading dose that satisfies anaesthesiologist , surgeon and the patient.

**Methods :** 18-50 years , 80 patients, ASA I and II, scheduled for surface surgeries under local infiltration were given dexmedetomidine in incremental doses of 0.2mcg/kg starting from 0.3 mcg/kg with maintenance infusion of 0.2 mcg/kg/hr. Bolus doses of 0.1 mcg/kg were given as and when required but not excceeding the loading dose(LD). We observed patient's PR, MAP, Ramsay sedation score (RSS) and post operative analgesia duration. Anaesthesiologist's (ASS), surgeon's (SSS) and patient's (PSS) satisfaction scores were evaluated .

**Results:** There was an insignificant but definite fall in MAP and PR with all loading doses. To achieve RSS of 3, maximum bolus doses were required with 0.5mcg/kg whereas no bolus dose was needed in 0.9 and 1.1mcg/kg dose. Maximum ASS, PSS and SSS were achieved at 0.9mcg/kg LD.

**conclusion :** we conclude that 0.9 mcg/kg was the minimum LD required to achieve a sedation score of 3 with ASS,PSS and SSS $\geq$ 85% and maximum postoperative analgesia duration.

**KEYWORDS :** Dexmedetomidine, monitored anaesthesia care, sedoanalgesia, satisfaction scores

## Introduction

Loads of surgeries on day care basis are increasing with an intense necessity to provide good and safe anaesthesia under monitored anaesthesia care.There are many elective surgeries which can be performed under local infilteration . However surgery under local anaesthesia only and being awake all the time during the procedure gives lots of horrifying thoughts , discomforts and unnecessory stress to the patient, producing undesirable haemodynamic changes and non co-operation during and after the procedure. To overcome this many drugs like opioids, benzodiazepines, dexmedetomidine and propofol are used. For the above mentioned cause and use the doses given can sometimes satisfy patient and surgeon but anaesthesiologist's concern is to protect the patients from any adverse effect of the dose given. Dexmedetomidine is highly selective and potent α-2 adrenergic recepter agonist with sympatholytic , analgesic , sedative and amnestic properties producing a unique state of conscious sedation in which patient is sedated but arousable with mild vocal or tactile stimulus. It causes no respiratory depression and was approved by FDA for procedural sedation in non intubated patients in October 2008[1]. We used this drug as sole agent utilizing its analgesic and arousable sedation properties in day care surface surgeries under local infilteration anaesthesia lasting for upto one hour. Moreover the drug has short elimination half life of 2 to 2.5 hours so is best suited for day care surgeries[2].

Haemodynamically it shows dose and rate of infusion dependant initial increase in blood pressure and reflex bradycardia[3] as a consequence of initial peripheral vasoconstrictive action of alpha receptors [4] thereafter the central sympatholytic action becomes predominant showing gradual fall in blood pressure.

**Aim of study:** To find out the optimum loading dose (LD) of dexmedetomidine as a sole sedo analgesic agent within the permitted clinical range in monitored anaesthesia care fulfilling the criteria for anaesthesiologist's, patient and surgeon satisfaction without adding any other sedative or analgesic.This optimum dose would provide arousable sedation, no pain, maximum comfort, minimum stress and best of physiological and psychological state to patients without any significant alterations in haemodynamics, respiration and oxygenation in intraoperative and postoperative phase.

**Material and methods:** After obtaining Institutional ethical clearance this prospective interventional study was conducted during the period from December 2016 to September 2017 in Mayo Institute of Medical Sciences, Barabanki on 80 patients who attended surgical OPD and were selected, being otherwise in good health for day care surface surgeries in local infilteration anaesthesia under monitored anaesthesia care lasting for upto 45-60 min.

**Inclusion criteria :** Patients of either sex ,18-50yrs, having BMI between 18-25kg/m2 under ASA grade l and ll were included in study.

**Exclusion criteria :** Patients with cardiac, respiratory, renal, hepatic, endocrinal, and neurological diseases, comorbidities, pregnancy, hypersensitivity to local anaesthetic (lignocaine), under any drug treatment or drug absuse were excluded from the study.

**Protocol:**All patients included in study underwent preanaesthetic evaluation and routine investigations which included : complete blood count , random blood sugar , viral markers , bleeding and clotting time .

They were asked to fast for 8hrs the night before the planned procedure.

**Procedure:**After getting informed written consent for participation in the study, baseline parameters pulse, noninvasive blood pressure,re spiratory rate,Sp02 and ECG were recorded. A running IV line was secured with 20 gauge canula and 10ml/kg of Ringer's lactate(RL) infused before starting the procedure . Sensitivity test for lignocaine 2% was done thereafter. Premedication with Inj.Ranitidine 50mg, Inj. Ondensetron 4mg and antibiotics were given intravenously.

Drug preparation and delivery : Dexmedetomidine 1ml ampoule of 100mcg/ml was dissolved in 99ml of normal saline(NS) to make it 1mcg/ml and was to be given in incremental doses of 0.2 mcg, starting from 0.3 mcg/ kg. Calculated dose of dexmedetomidine was given to patients by infusion pump over a period of 10 minutes.

After completion of LD infusion, surgeon was notified to give local infiltration of lignocaine 2% without adrenaline at planned site of surgery according to need but not exceeding the maximum dose limit of 4.4mg/kg and wait for 5 minutes[5]. At this point of time we expect maximum local anaesthetic effect of lignocaine and sedoanalgesic effect of dexmedetomidine. Pulse rate (PR), mean arterial pressure (MAP) , respiratory rate(RR), Spo2 ,ECG, level of sedation and any complaints or undesirable effects of drug were observed and recorded every 5minutes starting from incision till end of surgery. Supplementary O2 with air @4lit/min was started by face mask and surgeon allowed to start the surgery after testing for the proper analgesic effect of infiltrated lignocaine. Maintenance dose of dexmedetomidine 0.2mcg/kg/hr was given till removal of surgical drapes . Supplementary bolus doses of 0.1mcg/kg were given at any

time if required[6]. Post emergence monitoring was done at 15min interval for first 30 min and every 30 minutes for next 2hrs .

Postoperative analgesia duration was defined as the time between LD and the first demand for rescue analgesia. Inj. Diclofenac 75mg diluted in 10ml of NS was given IV slowly for rescue analgesia on demand by the patient.

MAP ≤ 60mm of Hg continuing for 60 seconds was considered significant and treated by fast infusion of RL or NS[7]. Bradycardia: Heart rate ≤ 55beats/min, continuing for 30 secconds was treated by giving Inj atropine 0.6mg diluted in 3ml of distilled water intravenously. Respiratory change: Bradypnoea and desaturation was considered If respiratory rate was ≤ 9/min and Spo2 <95% respectively. Both were treated with 100% oxygenation. Tachypnoea was considered if respiratory rate was >25/min.

Inadequate sedoanalgesic effect of drug dose was considered when patient showed vocal resistance or physical movements, increase in PR , MAP and RR 20% above base line , indicating that targeted level of sedation RSS≤ 3 was not achieved by loading dose. This was treated by single or repeated bolus doses of 0.1mcg/kg of dexmedetomidine for rescue but not exceeding the loading dose . Patients who required bolus dose greater than loading dose were managed by TIVA with inj ketamine/propofol or general anaesthesia and were excluded from the study.

**ANAESTHESIOLOGIST'S OBSERVATION AND ASSESM ENT REGARDING SEDATION**

Sedation is an essential part of surgical procedure in this study to minimize pain, anxiety and discomfort to patients. The six levels of Ramsay sedation scale(8) (RSS) allow clinical assessment of sedation by anaesthesiologist therefore was used to quantify patients sedation level as follow.

1 Patient is anxious and agitated or restless, or both.
2 Patient is cooperative, oriented and tranquil.
3 Patient responds to commands only.
4 Patient exhibits brisk response to light glabellar tap or loud auditory stimulus.
5 Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus.
6 Patient exhibits no response.

In our study the targeted level of patients sedation at Ramsay sedation scale(RSS) was ≤3 until a need for deeper level of sedation was felt. However utmost vigilance was observed to avoid respiratory depression and tackle airway related complications.

Assesment of satisfaction scores: Minimum targeted percentage of satisfaction score for anaesthesiologist(ASS), patient(PSS) and surgeon(SSS) was ≥ 85

Assesment of patient satisfaction was based on a friendly interrogation just before their discharge regarding their experiences with sedation and analgesia during the surgical procedure by asking following questions and requesting them to answer in affirmative or negative.

(1)Did you feel any pain during surgery?
(2)Did you feel relaxed through out the procedure?
(3)Did you feel you are in safe hands?
(4) Would you prefer to undergo surgery by same anaesthetic technique in future if needed?
(5)Would you recommend same anaesthetic technique and care for similar surgical procedure to your near and dear ones?.

Analysis of answers:The affirmative answer to first question confirms adequacy of local infiltration which was primary prerequisite to asses optimum loading dose.The answer,yes I was relaxed and felt to be in safe hands along with recommending the same technique on self and near and dear ones, reflects patient's satisfaction.

Assesment of surgeon's satisfaction: At the end of surgery the surgeon was requested to give his unbiased opinion regarding his experience in performing surgery under above mentioned anaesthesia technique considering following points and give reasons for his opinion.

(1)Immobility of patients
(2)Analgesia
(3)Quality of surgical field in terms of bleeding .

Assesment of anaesthesiologist's satisfaction was based on following points.

(1) Maintenance of desired level of sedation on RSS
(2) Haemodynamic and respiratory stability during intraoperative and post operative period.
(3) Number of bolus doses required.
(4) Duration of surgery well within expected limits of time.
(5) Occurrence of complication in perioperative period like shivering, nausea or vomiting.
(6) Duration at which first demand for rescue analgesia came.

**Analysis:**Mantinence of level of sedation ≤3 on RSS, haemodynamic stability, occurrence of nil to minimal complication, no requirement of bolus dose, sustained maintenance of Spo2 between 100%- 95% during intra and post operative period and delayed call for first rescue analgesia satisfied us. However prolongation of surgery or due to any other reason, conversion of technique to TIVA or GA caused disatisfaction.

**TABLE 1 : DEMOGRAPHIC DISTRIBUTION OF PATIENTS ACCOR DING TO AGE AND SEX**

| S.No | Age group | Male Patients (M) | Female patients(F) | Total (M+F) |
|---|---|---|---|---|
| 1 | 18-25 | 8 | 7 | 15 |
| 2 | 26-33 | 13 | 16 | 29 |
| 3 | 34-41 | 11 | 9 | 20 |
| 4 | 42-50 | 7 | 9 | 16 |
| Total | | 39 | 41 | 80 |

**TABLE 2 :DISTRIBUTION OF PATIENTS ACCORDING TO TYPE AND MEAN DURATION OF SURGERY**

| S.No. | Type of surgery | Total | Mean duration ( in minutes) |
|---|---|---|---|
| 1. | Tympanoplasty | 15 | 45±5 |
| 2. | Resuturing of abdominal wound | 1 | 50 |
| 3. | Lipoma | 5 | 35.7±8 |
| 4. | Unilateral hydrocele | 32 | 45.2±3 |
| 5 | Fibroadenoma breast | 27 | 40±5 |
| TOTAL | | 80 | |

**TABLE 3 : SHOWING MEAN ARTERIAL PRESSURE AND PULSE RATE IN INTRAOPERATIVE AND POST OPERATIVE PHASE**

| Time (in minutes) | 0.5 mcg | | 0.7 mcg | | 0.9 mcg | | 1.1 mcg | |
|---|---|---|---|---|---|---|---|---|
| | MAP | PR | MAP | PR | MAP | PR | MAP | PR |
| **Baseline(0)** | 85±5 | 74.2±4 | 84.2±2 | 72.3±2 | 84.5±5 | 78.5±0 | 86.8±2 | 76.6±4 |
| **15 min** | 82.2±3 | 71.1±3 | 78.2±3 | 69.0±3 | 75.1±2 | 67.0±2 | 74.4±4 | 67.5±3 |
| **20** | 83.4±1 | 69.6±2 | 77.7±5 | 68.6±4 | 74.4±3 | 66.8±1 | 74.6±3 | 66.4±2 |
| **25** | 90.2±4 | 72.6±4 | 78.3±4 | 69.5±4 | 75.1±1 | 67.9±1 | 76.3±3 | 66.6±5 |
| **30** | 103.3±2 | 90.5±3 | 84±5 | 78.4±4 | 76.8±6 | 66.7±2 | 75.5±5 | 67.1±3 |
| **35** | 92.1±3 | 82.3±3 | 97.3±3 | 96.3±3 | 80.1±3 | 68.9±3 | 75.3±4 | 64.3±5 |
| **40** | 102.2±6 | 92.3±2 | 85.5±2 | 80.2±2 | 79.9±5 | 71.0±3 | 78.6±5 | 65.1±6 |
| **45** | 87.6±2 | 79.2±4 | 83.3±1 | 77.7±4 | 82.3±3 | 72.2±3 | 78.3±4 | 67.2±1 |
| **End of Surgery** | 100.4±4 | 91.1±2 | 84.1±2 | 76.0±1 | 83.1±1 | 75.5±4 | 80.6±6 | 71.1±1 |
| **Post op** | | | | | | | | |
| **15** | 86.2±5 | 81.1±2 | 86.1±5 | 74.4±2 | 86.1±2 | 78.6±4 | 84.1±2 | 72.0±1 |
| **30** | 86.3±5 | 78.8±6 | 86.5±3 | 73.7±1 | 88.0±1 | 80.2±4 | 82.2±3 | 73.5±3 |
| **60** | 99±2 | 90.6±5 | 98.7±2 | 97.8±3 | 89.2±2 | 84.4±3 | 84.8±3 | 84.3±2 |
| **90** | | | | | 92.2±4 | 88.7±4 | 93.1±2 | 90.0±1 |
| **120** | | | | | 102.2±3 | 93.1±3 | 100.1±1 | 92.2±2 |

· Sx : surgery

**TABLE 4: SEDATION SCORE AND BOLUS DOSE**

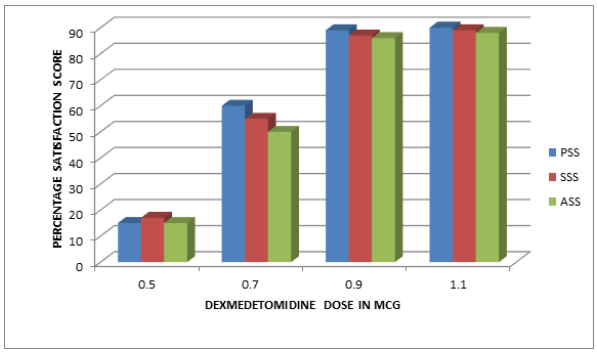
| Time (in minutes) | 0.5 Mcg | Bolus dose | 0.7 Mcg | Bolus dose | 0.9 Mcg | Bolus Dose | 1.1 Mcg | Bolus Dose |
|---|---|---|---|---|---|---|---|---|
| Baseline | Normal ,awake | | Normal ,awake | | Normal , awake | | Normal , awake | |
| 15 (at incision) | 2 | | 2 | | 2 | | 2 | |
| 20 | 2 | | 2 | | 2 | | 3 | |
| 25 | 2 | | 2 | | 3 | | 3 | |
| 30 | 1 | + | 2 | | 3 | | 3 | |
| 35 | 2 | | 1 | + | 3 | | 3 | |
| 40 | 1 | + | 2 | | 3 | | 3 | |
| 45 | 2 | | 2 | | 2 | | 3 | |
| End of surgery | 1 | + | 2 | | 2 | | 2 | |
| Post op | | | | | | | | |
| 15 | 2 | | 2 | | 2 | | 2 | |
| 30 | 2 | | 2 | | 2 | | 2 | |
| 60 | 1 | | 1 | | 2 | | 2 | |
| 90 | | | | | 2 | | 2 | |
| 120 | | | | | 1 | | 1 | |

- **+ : bolus dose**

**TABLE 5 : TIME OF RESCUE ANALGESIA**

| DOSE (in mcg) | TIME OF RESCUE ANALGESIA (in minutes) |
|---|---|
| 0.5 | 55.2± 3 |
| 0.7 | 64.5±4 |
| 0.9 | 116.6±6 |
| 1.1 | 124.5±4 |

**FIGURE 1 : SATISFACTION SCORES**




- PSS – PATIENT'S SATISFACTION SCORE
- SSS- SURGEON'S SATISFACTION SCORE
- ASS- ANAESTHESIOLOGIST'S SATISFACTION SCORE

**RESULTS:** In our study percentage of male and female patients was 48.75(n=39) and 51.25(n=41),with a maximum of 16.25%(n=13) and 20%(n=16) in age group of 26-33yrs. According to type of surgery 40%(n=32)cases of unilateral Hydrocele , 33.75% (n=27) Fibroadenoma breast,18.75%(n=15) Tympano plasty,6.2 5%(n=5 )Lipoma and one case of abdominal resuturing were done. Duration of surgery performed varied from minimum of 35.7+8 minutes to a maximum of 50 minutes.

As shown in table 3 & 4 there was an insignificant but definite fall in mean MAP and PR with all loading doses between 15-20 minutes. Patients receiving 0.5mcg/kg loading dose showed gradual rise in mean MAP and PR at 20 min , with a maximum rise at 30 minutes indicating need for bolus doses at 30 mins, 40mins and almost at end of surgery .They were in RSS score 2 except at 30 and 40 mins,and towards end of surgery when RSS score was 1. In post operative phase they remained in RSS 2 and demanded rescue analgesia at 55.2±3 mins. Patients receiving loading dose of dexmedetomidine 0.7mcg/kg showed rise in mean MAP and PR reaching a peak at 35mins and required single bolus dose at 35mins. However there was again a rise at one hour with a fall in RSS to 1 with demand for rescue analgesia at 64.5±4 min . Patients receiving loading dose of 0.9mcg/kg &1.1mcg/kg did not show sudden rise in MAP and PR in intraoperative and post operative period and remained in RSS 3 during 25 to 40 mins and 20 to 45mins respectively. Demand for rescue analgesia was at 116.6±6 to 124.5±4 mins respectively . There was no significant change in respiratory rate, oxygenation and ECG with all the loading doses in intraoperative and post operative period. As regards complications only 1patient having abdominal resuturing had shivering who received loading dose 1.1mcg/kg. No other compli cations in form of nausea or vomiting was there with any loading dose.

Patients, Anaesthesiologist's and Surgeon's Satisfaction scores at different loading doses of dexmedetomidine.

After analyzing the observations with different LD we found that at 0.5 LD patients, anaesthesiologist's and surgeon's satisfaction scores were very poor ranging between 15%,15% and 17% respectively. However with 0.7 LD patient's satisfaction score(PSS) improved to 60% whereas surgeon's (SSS) and anaesthesiologist's satisfaction scores(ASS) were 55% and 50% only.There was a rise in PSS to 89%,SSS to 87% and ASS to 86% by increasing LD from 0.7 to 0.9mcg/kg with an increase in duration of first call for rescue analgesia by 52.1±2mins which was highly significant ( $p<0.05$). Further increasing LD by an increment of o.2mcg/kg to make it 1.1mcg/kg showed ASS 88%, SSS 89% and PSS 90% with a minor increase in duration of demand for rescue analgesia by 7.9 mins which was not significant ( $p> 0.05$) .

**Discussion:**

There are many studies in literature where dexmedetomidine is combined with other drugs like midazolam, butorphanol, fentanyl ketamine or nalbuphine to achieve better sedation score by utilising combined effect of two or more drugs.[9,10,11] Since safety and early discharge is main concern in monitored anaesthesia care we used dexmedetomidine alone. In our study we emphasised that adequate infilteration of local anaesthetic agent is the essential part of assessing optimum loading dose of dexmedetomidine for procedural sedation. We tried to keep noise free atmosphere in OT which in turn caused less disturbance to patient and reduced anxiety and hence lessened dose requirement . In a study conducted by Mahmoud Hasan Mohammad et al[9] to reduce dose of dexmedetomidine an additional dose of local anaesthetic agent was given whenever patient complained of pain. To prolong the effect of lignocaine most of the times adrenaline is used but our study design did not allow use of adrenaline to observe uninfluenced haemodynamic effects of different LD of dexmede tomidine.

In a study by using dexmedetomidine in doses of 1mcg/kg they found definite but upto 10 to 15% reduction in MAP and PR which is consistant to findings in our study.[12] In another study a loading dose of 0.5mcg/kg and 1.0mcg/kg with a maintenance dose 0f 0.2mcg/kg/hr was given with similar haemodynamic changes as were found in our study[13].

The drug is metabolized in the liver through glucoronide conjugation and biotransformation by cytochrome P450 enzyme system. There are no active or toxic metabolites therefore it has minimal residual or toxic effects so is best suited for day care surgeries.

So far respiratory effect of dexmedetomidine is concerned it is very safe even if dose exceeds upto the limit that plasma level reaches 15 times of that achieved with usual dose because arousal of patient due to hypercapnonic apnoea can occur[1]. The hypnotic effect is mediated by hyperpolarisation of noradrenergic neurons in the locus ceruleus of the brainstem, which is the primary site in modulating wakefulness.[1]

In our study poor level of sedation causing anxiety, restlessness and agitation was seen in all patients receiving loading dose of dexmedetomidine 0.3mcg/kg. Repetition of bolus doses thrice could not improve level of sedation in all the cases. As according to study plan bolus doses should not exceed loading dose, they were immediately switched over to TIVA and excluded from study. Rapid IV bolus of 0.25 to 0.5mcg/kg administered over 5 sec in children having undergone heart transplant replicated excellent haemodynamic s in a study conducted by Jooste EH et al in 2010[7]. Encouraged with above mentioned study we administered bolus dose to our patients in 30 secs.

In another study a loading dose of 0.5mcg/kg and 1.0mcg/kg with a maintenance dose 0f 0.2mcg/kg/hr was given with similar haemodynamic changes as were found in our study[13].

Dexmedetomidine has been used as a sole agent by TIVA technique in high doses ranging upto 10mcg/kg/hr with ventilatory and haemodynamic stability and no need to support ventilation[14].

Consistent with previous studies in our study we observed that dexmedetomidine as sedoanalgesic is a safe drug for day care surgeries in a wide dose range .

**Difficulties encountered and limitations**

Selection of cases was difficult as we included ASA I and II patients only with different types of surgeries involving different surgeons which was at the same time necessary also to find out optimum LD of dexmedetomidine. Extremes of ages, ASA III and IV, patients with comorbidities, emergency and obstetric cases are yet to be evaluated. Satisfaction is a subjective feeling so quantifing its evaluation was difficult. Although satisfied with anaesthesia technique two surgeons commented that time taken in handing over patients to them for surgery was long and one surgeon was not happy for its cost. Both expressions were not relevant for determining optimum loading dose of dexmedetomidine so were ignored.

**Conclusion:** In our study we found that 0.9mcg/kg loading dose of dexmedetomidine fulfilled criteria of patients, anaesthesiologists and surgeon satisfaction score with haemodynamic stability , maintenance of oxygenation minimum perioperative complications and delayed demand for rescue analgesia. As per requirement of our study design we acheived the target of ≥85% satisfaction scores with this dose.

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