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Research Article

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Application of Dexemedetomidine as Monitored Anesthesia Care for Surgical Procedural Sedation

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Abstract

Background: *Anesthesia for short procedures or ambulatory surgery as (awake fiber-optic bronchoscopy, ophthalmic procedures, back injections, awake craniotomy and other minor procedures) has several challenges to an anesthetist. Use of Dexemedetomidine (Precedex) medication for procedural sedation in non-intubated patients could be used prior to or during surgical procedures. Dexemedetomidine has some characters of ideal anesthetic for perioperative use as rapid start of action and termination with low lipid solubility, easy to give by infusion, achieve a well balanced sedation, can maintain airway reflexes, and less effect on respiration.*

Methodology: *41 patients of either sex, aged 18 to 60 yrs of ASA grade I and II were used as a sample; all adults over 18 years (most surgical patents coming at that time). All pediatrics, patients with multiple co morbidities, patient's refusing; known or admitted alcohol or drug abusers, allergic to the drugs involved in the study and prisoners were excluded. Patients were randomized to receive a Loading dose of 0.5 to 1 mcg/kg IV over 10 minutes then maintenance IV infusion in dosage regimen of 0.2 to 0.4 mcg/kg/hour IV, titrate to effect.*

Results: *41 cases observed for vital signs, depth of sedation, patient response, and arousal effect. Results showed 30 cases got good smooth deep sedation without complications. 11 cases got low blood pressures with low heart rates needed stopping infusion, pressor support medications.*

Conclusion: *Precedex dosing should be individualized and titrated to desired clinical response. It should be administered using a controlled infusion device with full monitoring devices and oxygen supplement.*

Keywords

- **Dexemedetomidine (DEX)**: Precedex®; Hospira, Lake Forest, IL, USA; and Dexdor; Orion Corporation, Espoo, Finland.
- Procedural Sedation
- Operation Theatre
- Surgical Procedures
- Controlled Infusion
- Clonidine
- α- alpha receptors - α2-agonist
- Awake Intubation
- Fiber-optic Intubation

Data Availability

The authors confirm that all data underlying the findings are fully available without restriction. All relevant data are within the paper and their supporting information files.

Introduction

Anesthesia for short procedures or ambulatory surgery as (awake fiber-optic bronchoscopy, ophthalmic procedures, back injections, awake craniotomy and other minor procedures) has several challenges to an anesthetist. The patient must be sedated to a state where patient can tolerate the surgical procedure, alert responding and co-operative like in awake craniotomy for neurocognitive testing [1].

Adequate anesthesia and analgesia have to be achieved to level that patient is alert, comfortable, responding without pain. The depth of sedation, anxiolysis should be titrated to avoid adverse events as obtunded airway, affection of respiration, high carbon dioxide, coughing, low blood pressure and other hemodynamic abnormalities [2, 3].

Dexemedetomidine has some characters of ideal anesthetic for perioperative use as rapid start of action and termination with low lipid solubility, easy to give by infusion, achieve a well balanced sedation, can maintain airway reflexes, and less effect on respiration [4].

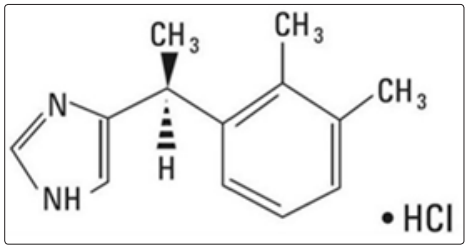
Now, it has been found that Dexemedetomidine without any known active or toxic metabolites therefore; it is USA Food and Drug

Administration (FDA) approved for sedation via IV bolus and continuous administration up to 24 h on intubated patients and for procedural anxiolysis in locations outside the critical care unit (ICU) and operation theatre [5].

Structure-Organic Chemistry

Precedex (Dexemedetomidine hydrochloride) in 0 .9% Sodium Chloride Injection is a clear solution tolerable for intravenous injection after dilution. Dexemedetomidine HCL is the S-isomer of medetomidine and is chemically characterized as (+)-4-(S)-[1-(2,3-dimethylphenyl)ethyl]-1H-imidazole monohydrochloride [6].

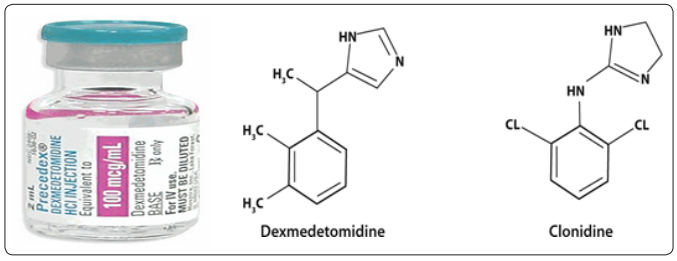
Precedex has an empirical formula is $C_{13}H_{16}N_2$ • HCl- Figure 1



Dexemedetomidine hydrochloride is a white or almost white powder that is freely soluble in water and has a PKa of 7.1. Its partition coefficient in-octanol: water at pH 7.4 is 2.89.

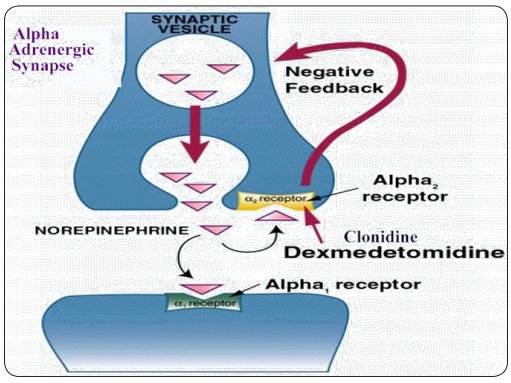
Precedex Injection is supplied as a clear, colorless, isotonic solution with a pH of 4.5 to 7.0. Each mL contains 118 mcg of Dexemedetomidine hydrochloride equivalent to 100 mcg (0.1mg) of Dexemedetomidine and 9 mg of sodium chloride in water and is to be used after dilution. The solution is preservative-free and contains no additives or chemical stabilizers [7, 8].

It is related chemically to clonidine, but it is more attar-actability for α2 over α1-receptors (with ratio of 1,600:1, compared to 200:1 for clonidine) - (Figure: 2) [9].



Mechanism of Action (Figure 3)

Dexemedetomidine is a selective alpha2-adrenergic receptor drug agonist. It is active at a variety of sites throughout the central neuronal system. The sedative and anxiolytic effects of Dexemedetomidine result primarily from its action on the locus ceruleus of the brainstem. Stimulation of α2-adrenergic receptors at this location inhibits central sympathetic output, leading to more firing of inhibitory neurons. The action of Dexemedetomidine at α2-adrenergic receptors in the dorsal horn of the spinal cord modifies release of substance P and produces its painless effects [9, 10].



Pharmacokinetics

With intravenous (IV) injection, Dexemedetomidine has a rapid distribution, with a 50% distribution time of approximately 6 minutes in adults [11, 12]. It is extensively distributed, with a volume of distribution of 118 L and protein binding of 94%. Dexemedetomidine exhibits linear kinetics over the recommended dosage range of 0.2 to 0.7mcg/kg/hr. It is extensively metabolized through both the cytochrome P450 enzyme system, by aliphatic hydroxylation via CYP2A6, and direct glucuronidation. N-glucuronidation produces inactive metabolites, while aliphatic hydroxylation produces active 3-hydroxy-dexmedetomidine, which then undergoes glucuronidation, and 3-carboxy-dexmedetomidine. N-methylation produces active 3-hydroxy-N-methyl-dexmedetomidine, 3-carboxy-N-methyl-dexmedetomidine, and Dexemedetomidine-N-methyl-O-glucuronide. These metabolites are excreted in urine (95%) and feces (4%). Dexemedetomidine has a terminal elimination half-life of approximately 2 hours and a clearance of 39 L/hr in adults. Dose reduction is needed for patients with hepatic impairment [12].

Indications

Dexemedetomidine can be used for anxiolysis, relief of pain and stress intraoperative for many as following: [13, 14, 15, 16].

- Airway procedures as Rigid bronchoscopy, awake fiber-optic bronchoscopy .
- Difficult intubation algorithm.
- Anesthetic adjuvant in Bariatric surgery and sleep apnea patients.
- Arthroscopic knee surgery.
- Neurosurgical procedures as awake craniotomy.
- Posterior spine fusions; DEX Lowers requirements for propofol and inhalation agents
- Cardiac surgery induction
- Painful procedures as Extracorporeal shock-wave lithotripsy
- Burn dressing change
- Lumbar puncture
- Bone marrow biopsy
- Central venous line placement
- Chest tube insertion
- Dental procedures
- Monitored Anesthesia Care as gynecological, urological, burns patients, trauma patients, ophthalmic procedures, back injections, awake craniotomy, drug-induced sleep endoscopy, magnetic resonance imaging (MRI) and Anterior mediastinal mass biopsy [15, 16].

Methodology

The study was approved by the appropriate Institutional Review Board (IRB), and written informed consent was obtained from all adult subjects participating in the study.

The study done by authors; Drs. Ali Saad, Aamil Haameem (registration not applicable)

41 patients of either sex, aged 18 to 60yrs of ASA grade I and II were used as a sample; all adults over 18 years (most surgical patents coming at that time).

All pediatrics, patients with multiple comorbidities, Patient's refusing; known or admitted alcohol or drug abusers, allergic to the drugs involved in the study and prisoners were excluded.

41 Patients were randomized to receive a Loading dose of 0.5 to 1 mcg/kg IV over 10 minutes then maintenance IV infusion in dosage regimen of 0.2 to 0.4 mcg/kg/hour IV, titrate to effect.

Start loading dosage of 0.5-1 mcg/kg IV over 10 minutes then Maintenance 0.2-0.4 mcg/kg/hour IV titrate to effect.

35 patients did not need any midazolam adjuvant as sedative during procedure. Other 6 patients needed only 2mg IV boluses.

Results

Our Research study is a prospective, clinical case study

Study was done on adults (target population) with total 41 cases in number. All patients were ASAI, II without multiple co-morbidities.

Dexemedetomidine injection is available in 200 mcg/2ml clear glass vials (100mcg/ml); for single use only.

11 patients of total 41 cases in the study had marked bradycardia with slow heart rate reached 30 to 40 beats per min and lower blood pressure (systolic blood pressure dropped to 80 to 90 mmHg) on monitor. Other 30 cases got good smooth deep sedation without complications.

It was found that giving rapid bolus over short time can cause rapid affection on heart rate and blood pressure; that's why tapered IV infusion was preferred mode of Dexemedetomidine administration with good monitoring of vital signs and giving IV fluids with standby pressor agents beside patient.

Most of patients responded well to IV fluids, pressor agents as ephedrine or phenylephrine with oxygen therapy during procedure.

Discussion

Precedex administration for sedation of non-intubated patients prior to and/or during surgical and other procedures under monitored anesthesia care was evaluated in randomized clinical trial including safety and efficacy. Precedex in patients undergoing awake fiber-optic intubation prior to a surgical or diagnostic procedure also was included in the study.

Dexemedetomidine may be used as a total intravenous anesthetic agent in certain patients if doses are increased to a high tolerable level [15, 16].

Previous studies on assessing Dexemedetomidine as a general anesthetic found that supplementary agents were necessary, but the doses of Dexemedetomidine had not reached the high levels of administration reported here [16].

Dosage Regimens

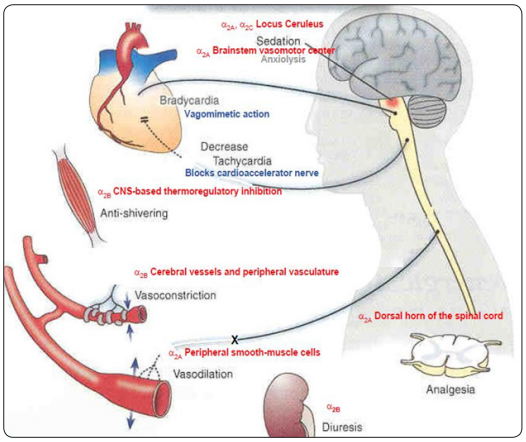
Initiation of Procedural Sedation

- For adults: a loading infusion of one mcg/kg over 10 **minutes**. For less invasive procedures such as ophthalmic surgery, a loading infusion of 0.5 mcg/kg given over 10 **minutes**.
- **For awake fiber optic intubation in adult patients:** a loading infusion of one mcg/kg over 10 **minutes**.
- **For patients over 65 years of age:** a loading infusion of 0.5 mcg/kg over 10 minutes.
- **For adult patients with impaired hepatic function:** a dose reduction should be done [17].

Maintenance of Procedural Sedation

- For adult patients: Maintenance infusion is started at 0.6 mcg/kg/hour and titrated according to best level of sedation, dose adjustment needed in renal patients.
- For intubation: a maintenance infusion of 0.7 mcg/kg/hour is preferred till the endotracheal tube is secured.
- For patients over 65 years of age: doses range from 0.2 to 1 mcg/kg/hour. [17, 18].

Clinical Effects: Shown in Figure: 4



Cardiovascular

Dexemedetomidine has a biphasic blood pressure effect in form of a short high blood pressure phase with following lower. The two staged effect is mediated by two different α2-receptors subtypes' receptors: α-2B receptors which mediates initial high blood pressure stage and later lower blood pressure is mediated by the α2A-receptors. In young age with high levels of parasympathetic tone; low heart rate and sometimes cardiac arrest have been reported but they were well treated with anti-parasympathetic agents as atropine, glycopyrrolate [19].

Centrally

Dexemedetomidine lowers cerebral blood flow and cerebral metabolic oxygen consumption with limited effect on intracranial pressure (ICP). Dexemedetomidine modulates cognitive performance with sedative, analgesic, and anxiolytic effects. Studies found that DEX has some neuroprotective effects through lowering circulating and brain catecholamines levels [20, 21].

Respiratory

Dexemedetomidine can affect respiration as deep sleep state does without depression. It doesn't affect respiration rate or ventilation in spontaneously breathing critical care patients postoperative. It can facilitate weaning and removal of endotracheal tube (recovery) in trauma/ surgical critical care unit patients with stable hemodynamics and preserved respiration [22, 23, 24].

Others

Dexemedetomidine enhances peripheral pre-synaptic α2-adrenergic receptors which inhibit the firing catecholamines leading to diminished sympathetic response to surgery. Some studies concluded that Dexemedetomidine can cause more excretion of water and salt in urine (more urine output). It was found that Dexemedetomidine doesn't inhibit production of steroids if used as intravenous infusion for short time; although it is imidazole form (unlike etomidate) [25, 26].

Adverse effects

Dexemedetomidine may cause unwanted systemic effects as low or high blood pressure, slow heart rate, dry oral cavity, sense of vomiting or gastric discomfort, high temperature, rigors, cyanosis and weak muscles. It was also reported that Dexemedetomidine can cause cardiac abnormalities, heart block or even cardiac arrest, inverted T-wave, rapid heart rate, myocardial ischemia, syncopal attacks and rare heart failure. It may cause airway obstruction, inadequate respiration, tingling nerve sensation or slight paralysis and high blood levels of potassium, glucose or lactic acid [26-28].

Conclusion

Dexemedetomidine is a very useful medication enlisted in the family of drugs used in anesthesia. It can be utilized in a wide range of applications as discussed before at the same time requiring caution during its use. High cost is its limiting factor.

Decreases in heart rate and blood pressure were modest, predictable and well treated. Some patients were arousable, responding to calls. DEX produced good sedation with anxiolysis and lowered need for other sedatives.

Dexemedetomidine should be used with caution in patients with low circulatory volume, shock or accompanied with hypnotics and analgesics.

Dexemedetomidine dosage should be individualized and titrated to desired clinical response.

Dexemedetomidine is not indicated for infusions longer than 24 hours. Precedex should be administered using a controlled infusion device.

Arterial Blood pressure, Heart rate, Respiratory rate and Oxygen saturation levels should be monitored during and after the infusion as clinically applicable.

Besides, patients should be instructed to report symptoms occurring within 48 hours after Dexemedetomidine injection as weakness, disorientation, more sweating, weight loss, abdominal pain, diarrhea, constipation, affected level of consciousness.

Dexemedetomidine has become a part of ambulatory anesthesia, offers anesthetic sparing and maintains hemodynamics.

As pharmacological effects of Dexemedetomidine can be reversed by α2-AR antagonist atipamezole, addition of Dexemedetomidine with atipamezole can provide titratable form of sedation in the future.

Conflict of Interests

The authors declare no competing financial interests.

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