Dosing Guidelines for Precedex®

Nonintubated Procedural Sedation

and

ICU Sedation

Precedex® Overview

- Precedex is indicated for sedation of initially intubated and mechanically ventilated patients during treatment in an intensive care setting and for sedation of nonintubated patients prior to and/or during surgical and other procedures.[1]
- Precedex should be administered by continuous infusion not to exceed 24 hours.
- Precedex should be administered only by persons skilled in the management of patients in the intensive care or operating room setting.[1]
- Due to the known pharmacologic effects of Precedex, patients should be continuously monitored.[1]
- The most common adverse reactions with Precedex (incidence >2%) are hypotension, bradycardia and dry mouth.[1]
- Due to the increased incidence of bradycardia and hypotension in the elderly, and the potential for reduced clearance in patients with impaired hepatic or renal function, dose reductions should be considered in these patient types.[1]

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What to Expect

Cardiovascular Effects

- Clinically significant episodes of brad
arrest have been associated with Pre
in young, healthy volunteers with high
different routes of administration, suc
infusion or bolus administration.[1]
- Moderate heart rate and blood press
be anticipated with Precedex.[2]
- If medical intervention is required for
hypotension or bradycardia, treatmen
  - Decreasing or stopping the infusion
  - Increasing the rate of IV fluid admin
  - Elevation of lower extremities
  - Use of pressor agents, such as glyc
  atropine or ephedrine
- Because Precedex decreases sympa
activity, hypotension and/or bradycar
to be more pronounced in hypovolem
patients with diabetes mellitus or chr
as well as in the elderly.[1]
- Because Precedex has the potential
induced by vagal stimuli, clinicians sh
to intervene with anticholinergic agen
glycopyrrolate or ephedrine) to modif
- Caution should be exercised when a
to patients with advanced heart block
ventricular dysfunction.[1]
- Use with caution when coadministeri
vasodilators or negative chronotropic
pharmacodynamic effects.[1]
- Transient hypertension has been obs
the loading dose in association with
vasoconstrictive effects of Precedex.

General

ICU Sedation

- In two pivotal Phase III clinical trials of ICU patients treated with Precedex®, the largest mean decrease in heart rate was approximately 7% and the largest mean decreases in systolic and diastolic blood pressures were 10% and 11%, respectively.[2]

Procedural Sedation

- Precedex has been studied in two pivotal Phase III clinical trials of nonintubated patients receiving monitored anesthesia care (MAC) sedation for a variety of surgical procedures as well as patients undergoing awake fiberoptic intubation.[1]
- The table on page 5 shows the frequency at which Precedex-sedated patients undergoing MAC sedation may experience hypotension or bradycardia and the frequency at which certain types of interventions may be needed to manage these adverse events.

Incidence and Interventions for Hypot
in Patients Undergoing Procedural Se

	Hypotension (n=318)
Overall Incidence	173 (54%)
Intervention	(n=173)
No Intervention Required	113 (65%)
Intervention Required	60 (35%)
Type of Intervention When Required‡	(n=173)
Ephedrine or Phenylephrine	55 (32%)
Glycopyrrolate	-
Atropine	-
Calcium Chloride	2 (1%)
Dopamine	1 (<1%)
IV Fluid Administration	16 (9%)
Precedex Dose Reduced	9 (5%)
Precedex Discontinued	1 (<1%)

*Hypotension was defined in pivotal trial protocols in a as SBP <80 mm Hg, DBP <50 mm Hg or >30% decre infusion values.

†Bradycardia was defined in pivotal trial protocols as < or >30% decrease from prestudy drug infusion values

‡Other possible interventions included elevation of low Patients may have received multiple forms of interven

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Treatment Options for Drug-induced Bradycardia or Hypotension

In Precedex® clinical trials, atropine, glycopyrrolate and ephedrine were effective in the treatment of most episodes of Precedex-induced bradycardia. However, in some patients with significant cardiovascular dysfunction, more advanced resuscitative measures were required.[1,3]

Glycopyrrolate Dosing for Drug-induced Bradycardia or Hypotension

Glycopyrrolate Injection may be used during surgery to counteract drug-induced or vagal reflexes and their associated arrhythmias (e.g., bradycardia). It should be administered intravenously as single doses of 0.1 mg (0.5 mL) and repeated, as needed, at intervals of 2 to 3 minutes.[4]

Atropine Dosing for Drug-induced Bradycardia or Hypotension

Initial single doses in adults vary from around 0.5 mg to 1 mg (5-10 mL of a 0.1 mg/mL solution). Administration of less than 0.5 mg can produce a paradoxical bradycardia because of the central or peripheral parasympathomimetic effects of low doses in adults.[5]

When the recurrent use of atropine is essential in patients with coronary artery disease, the total dose should be restricted to 2 to 3 mg (maximum 0.03 to 0.04 mg/kg) to avoid the detrimental effects of atropine-induced tachycardia on myocardial oxygen demand. For patients with bradyasystolic
dose of atropine is administered intraven
every 3 to 5 minutes if asystole persists.
(0.04 mg/kg) given IV is a fully vagolytic
The administration of this dose of atropin
for patients with bradyasystolic cardiac a
administration of atropine can be used in
IV access. The recommended adult dose
endotracheal administration is 1 to 2 mg
not to exceed 10 mL of sterile water or n

Ephedrine Dosing for Dru Bradycardia or Hypotensi

Ephedrine is indicated to counteract the
of spinal or other types of nontopical con
Depending on the clinical circumstances
Injection may be given subcutaneously, i
intravenously. Usual adult dose: 25 to 50
50 mg) injected subcutaneously or intran
to 0.2 to 1 mL of 5% solution) is usually a
minimize hypotension secondary to spina
doses should be governed by blood pres
Absorption (onset of action) by the intran
rapid (within 10 to 20 minutes) than by su
The intravenous route may be used if an
is desired.[6]

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Titrate Precedex® and Concomitant Medications to Effect

Coadministration of Precedex with anesthetics, sedatives, hypnotics and opioids can enhance the pharmacodynamic effects of these agents. Specific studies have confirmed these effects with sevoflurane, isoflurane, propofol, alfentanil and midazolam. A decrease in the dosage of Precedex or the concomitant agent may be required.[1]

These effects have been demonstrated in pharmacodynamic studies of healthy subjects and in patients undergoing sedation while taking the medications listed below.

Anesthetic Gases	
• Sevoflurane[a,7]	• Isoflurane[b,c,8,9]
IV Sedatives or Anxiolytics	
• Midazolam[d,8]	• Propofol[e,10]
Opioid-based Analgesics	
• Morphine[f,11]	• Alfentanil[g,8]

These clinical trials are of different designs in a variety of patient populations. Because clinical trials are conducted under widely varying conditions, rates observed may not be directly compared to other trials and may not always reflect the rates observed in practice.

[a]Sevoflurane. Dexmedetomidine 0.7 ng/m
of sevoflurane by 17% in patients under

[b]Isoflurane. Low- and high-dose infusions
decreased the end-tidal isoflurane conc
respectively, necessary to elicit the desi
50% of healthy subjects.[8]

[c]Isoflurane. Dexmedetomidine decreased
by 47% in patients who also received th
as induction agents.[9]

[d]Midazolam. In healthy subjects, the effe
combination with dexmedetomidine on s
with greater degrees of synergy occurrin
sedation. At higher degrees of sedation,
effect of dexmedetomidine on midazolam

[e]Propofol. In healthy subjects, dexmedeto
propofol concentrations required for sed
of motor response by approximately one
required for sedation and induction of an
reduced in the presence of dexmedetom

[f]Morphine. A single IV dose of 1 mcg/kg
10 minutes before induction reduced pos
consumption by 28% at identical pain sc
control.[11]

[g]Alfentanil. In the presence of dexmedeto
is needed to produce the same degree
impact on respiratory function can be le
alfentanil when coadministered with Pre

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