18th NATIONAL CONGRESS OF
National Congress Of The Society for Thorasic, Cardiovascular Anesthesia and Intensive Care
12-15 APRIL 2012
Hilton Türkbükü Resort & Spa - BODRUM / TURKEY

Pediatric Post-operative Pain and Sedation

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Disclosures: Research grants and honoraria from Hospira and Masimo

“RESTING THE BRAIN”

Don’t worry. Be asleep.
Trust me.
I will take you into dream
and wake you up.

The New 2012 Clinical Practice Guidelines for the Management of Pain Agitation and Delirium in *Adult* ICU Patients

Slides adapted from Doug Coursin's Presentation at SCCM Houston February 2012 – with Permission

Society of Critical Care Medicine

The Intensive Care Professionals

Apologies to Apple Inc.

ICU Pain Agitation Delirium (IPAD) Guidelines

Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit

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Sponsoring Organizations: American College of Critical Care Medicine (ACCM), Society of Critical Care Medicine (SCCM), American Society of Health-System Pharmacists (ASHP), and in alliance with the American College of Chest Physicians and the American Association of Critical-Care Nurses

Financial Support: ACCM, SCCM, University of Cincinnati (Charles P. Kishman, Jr., MSLS, Information Services Librarian)

Guidelines Group

21 multi-professional, multi-institutional, clinically active, intensive care physicians, nurses, pharmacists with expertise in assessing and managing pain, agitation and delirium in critically ill patients

Taskforce divided into 4 subcommittees

1. ***ICU pain & analgesia***
2. ***ICU agitation & sedation***
3. ***ICU delirium***
4. ***Related clinical outcomes***

- Developed keywords & key questions for search
- Questions
  - Descriptive & actionable
  - Structuring actionable clinical management questions using:
    - *Population Intervention Comparison*

      Outcomes

      (PICO) format

PICO

Basis for lit search & backbone of CPGs

In adult mechanically ventilated ICU patients, does sustained use of BZs vs. non-BZ-based sedation impact outcomes such as duration of mechanical ventilation, ICU LOS, & ICU related complications (VAP, delirium, self-extubation with re-intubation within 48 hours) & cost of ICU care?

- P = adult mechanically ventilated pts
- I = BZ-based sedation
- C = nonBZ-based sedation
- O = ventilator time (or ventilator-free time), ICU LOS, self-extubation, delirium, & cost of ICU care

What's new? – Methodology

- Replaced Cochrane type method with
  - Grades of Recommendation, Assessment, Development & Evaluation (GRADE) system
    - www.gradeworkinggroup.org
  - Structured system to rate quality of evidence & grade strength of recs in clinical practice
- Reviewed, evaluated, & summarized literature
- Developed clinical statements (*descriptive*) & recommendations (*actionable*) using the nominal group method

Quality of evidence for each statement & recommendation was determined to be:

- High (A)
- Moderate (B)
- Low/very low (C)

Strength of Recommendations

- Strong (1)
- Weak (2)
  - Either favor (+) or against intervention (-)
- NO recommendation (0)
  - Due to lack of evidence or a lack of consensus
  - ≥ 50% voting in *favor* & ≤ 20% voting *against*

What's new & different?

1) More *patient-centered* (i.e., focus on symptoms of Pain, Agitation, Delirium PAD) rather than medication-centered

2) More comprehensive approach to prevent & treat PAD

3) Systematic approach to searching relevant clinical databases aided by a professional librarian

- Charles Kishman, Univ of Cincinnati

4) Created electronic web-based database (Refworks®) simultaneously accessible to all taskforce members

5) Modified Delphi method with anonymous electronic voting scheme to achieve group consensus for all statements & recommendations

6) Systematic comparison of various pain, sedation, & delirium scales based on psychometric properties (i.e., reliability & validity), & feasibility in critically ill adults

Limitations on Disclosure of Guidelines

- Approved by Boards of Regents of SCCM, ASHP, ACCP and ACCN
- Under review by the editorial board of *Critical Care Medicine*
- **Therefore only allowed to discuss 10,000 meter overview.**

What I Can Tell You the Guidelines say

- Patient is going to have pain at rest and with movement
- **Excess pain is bad**
- **Monitoring for pain important**
  - Assess, treat as needed, reassess regularly
  - Self report of pain better than behavioral scales
  - Vital Signs not reliable indicators for pain or pain control, but can guide to assess/reassess pain & pain treatment

Therapies

- **Multimodal**
  - **Pharmacological & non-pharmacological** (music, massage, sleep)
  - **Opioids** – 1st line for non-neuropathic pain
    - All available IV opioids titrated to similar pain intensity endpoints equally effective
    - Use **non-opioids** to limit side effects of opioids
    - NSAIDs acetominophen, ibuprofen – renal/liver function, risk bleed???
    - Dexmedetomidine reduce need for opioids
- **Consider regional** – LA +/- opioids
  - Check coagulation
  - Clear neuraxial spine
  - Monitor volume status carefully

Guidelines say

- **Monitor for depth of sedation**
  - Use protocols for monitoring, reassess regularly
  - **Richmond agitation sedation scale (RASS)** & **Sedation-Agitation Scale (SAS)** most valid & reliable scales for assessing quality & Depth of Sedation: **(Ramsay Sedation Scale** most simple and most used)
  - Recommend objective measures of brain function (**BIS, Sedline (PSI), SE, AEP, & NI**) as 1° method to monitor Depth of Sedation in comatose and/or paralyzed patients. Monitor EEG for non-convulsive seizure activity

Ramsay Sedation Scale

1 Anxious and agitated or restless or both

2 Cooperative, oriented, and tranquil

3 Responding to commands only

4 Asleep, brisk response to stimuli*

5 Asleep, sluggish response to stimuli*

6 Asleep, no response to stimuli*

* light glabellar tap

Ramsay, et al. *Brit Med J.* 1974;2(920):656-659.

SEDline™

Sedation

- The animated ICU
- Controlled **lighter sedation** better than deeper sedation
- Maintain **cognitive function**
  - Shorter length mechanical ventilation, LOS in ICU and hospital

Delirium associated with:

- Increased mortality
- Increased ICU LOS
- Development of post-ICU cognitive dysfunction

Guidelines Recommend

- Routinely monitor for delirium
- **Confusion Assessment Method in the ICU (CAM-ICU)**
- **Intensive Care Delirium Screening Checklist (ICDSC) most valid & reliable delirium monitoring tools**
  - **Quick & reliable**

DELIRIUM – Prevention & Treatment

- Early mobilization as able
- No clear cut pharmacological agent or protocol appears to prevent delirium
  - Haloperidol, atypical antipsychotics, DO NOT appear to prevent delirium
  - Dexmedetomidine may shorten the duration of delirium
  - No evidence of efficacy for haloperidol
- BZ use may be a risk factor for delirium
- Conflicting data on risk of various opioids
- Unclear role of propofol – await NIH study

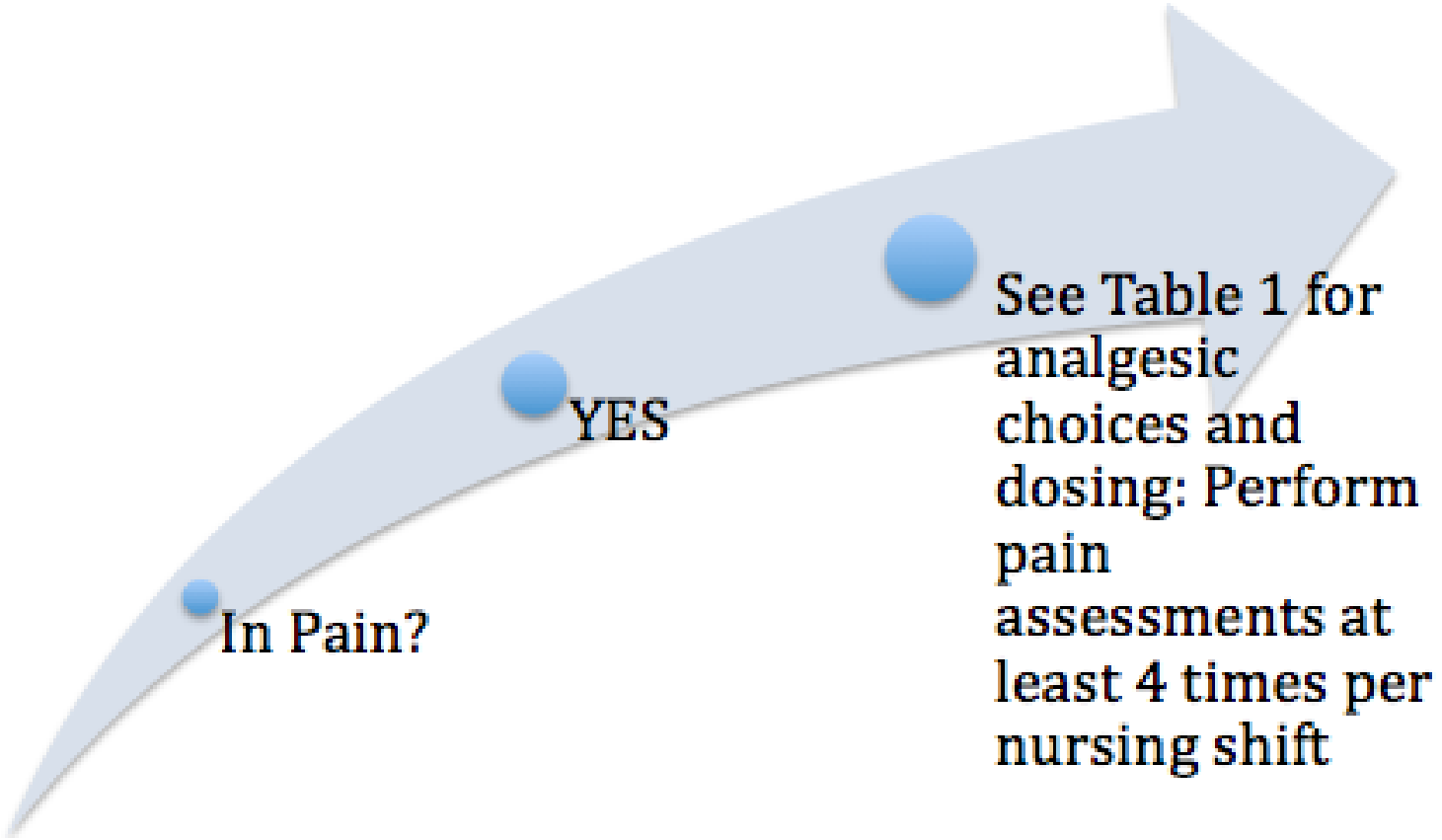
Final Recommendation

A multidisciplinary ICU team approach

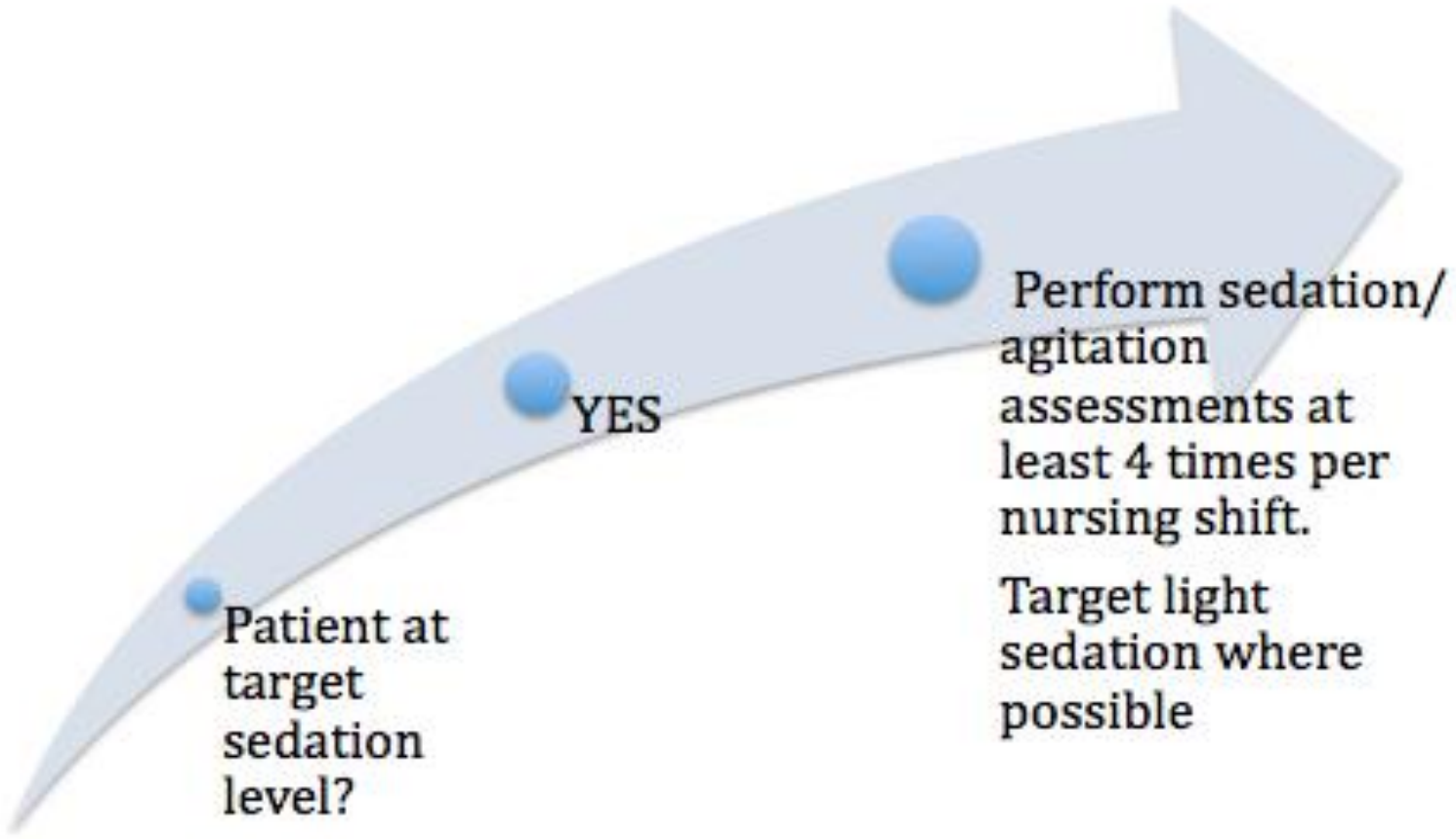
- That includes provider education
- Pre-printed and/or computerized protocols & order forms, &
- A quality ICU rounds checklist

Be used to facilitate PAIN, AGITATION & DELIRIUM management guidelines or protocols in adult ICUs

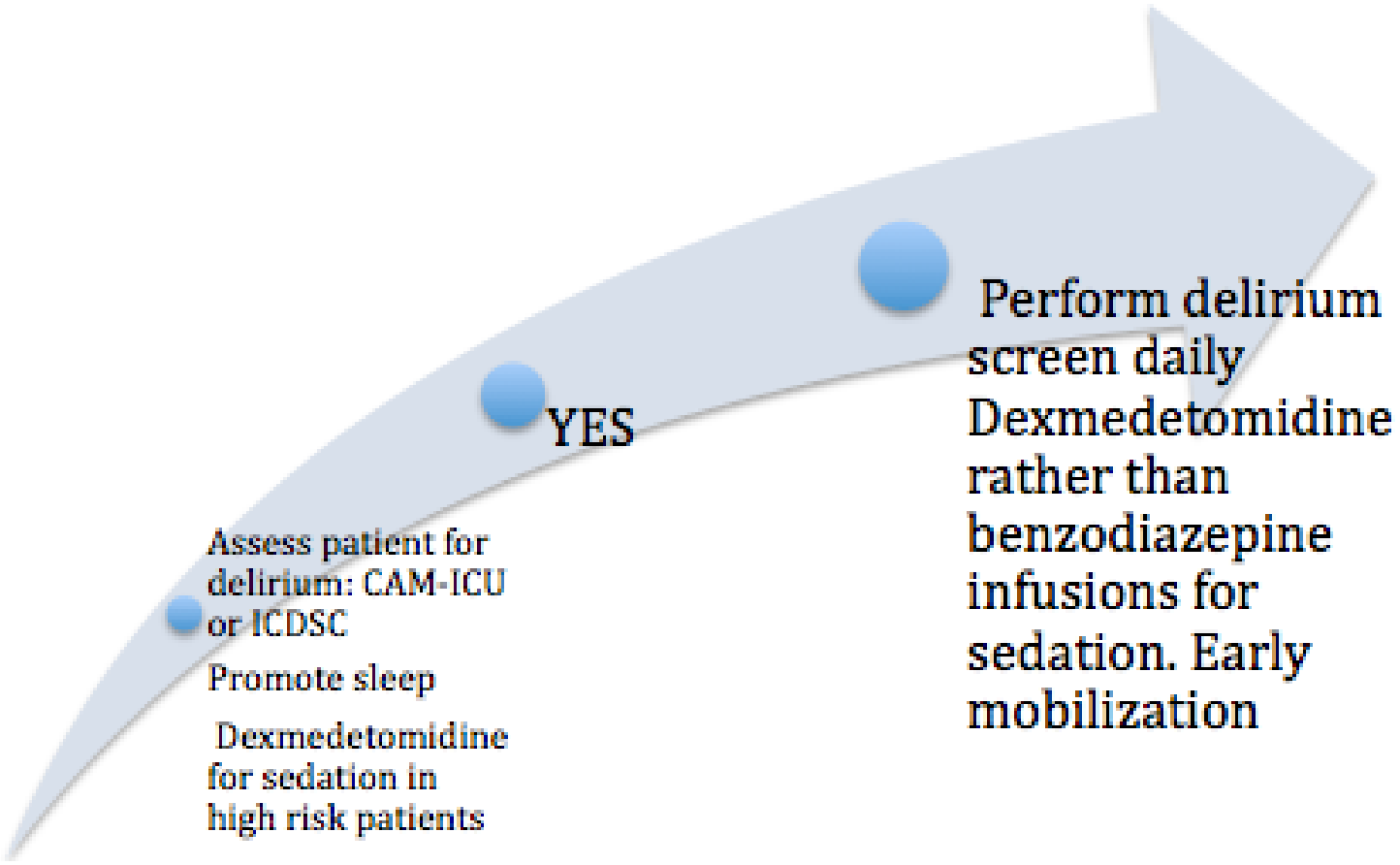
1. Pain


In Pain?
YES
See Table 1 for analgesic choices and dosing: Perform pain assessments at least 4 times per nursing shift

Agitation/Sedation



Delirium


Assess patient for delirium: CAM-ICU or ICDSC
Promote sleep
Dexmedetomidine for sedation in high risk patients
YES
Perform delirium screen daily
Dexmedetomidine rather than benzodiazepine infusions for sedation. Early mobilization

Pediatric Sedation and Analgesia

- 3 Drugs to discuss:

- **1 Propofol**
- **2. Ketamine**
- **3. Dexmedetomidine**

Complex Pediatric Heart Disease

- Single ventricle physiology
- Balanced circulation physiology
- Cardiomyopathy
- Aortic stenosis
- Requires understanding of underlying lesion and type of circulation: Are changes in SVR/PVR going to be important? What oxygen saturations are to be expected?

Propofol

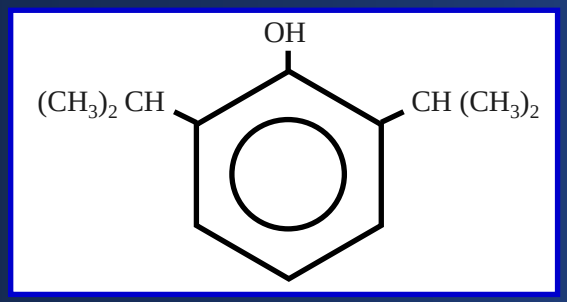
Propofol

Clinical Effects

- Sedation[1]
- Hypnosis[1]
- Anxiolysis[1]
- Muscle relaxation[1]
- ↓ ICP[1]
- ↓ Cerebral metabolic rate[1]
- Antiemetic[2]

Adverse Effects

- Respiratory depression (exacerbated by opioids)[1]
- Hypotension[1]
- Decreased myocardial contractility[3]
- Preservative issues[4]
- Potential for infection[4]
- Tolerance[5]
- Propofol infusion syndrome[6]
- ↑ Serum triglycerides[4]



[1]Harvey MA. *Am J Crit Care*.1996;5:7-16.
[2]Apfel CC, et al. *Anaesthesist*. 2005;54:201-9.
[3]Lerch C, et al. *Br Med Bull*. 1999;55:76-95.
[4]Diprivan [package insert]. AstraZeneca Pharmaceuticals; 2004.
[5]Zapantis A, et al. *Crit Care Nurs Clin N Am*. 2005;17:211-223.
[6]Riker RR, et al. *Pharmacotherapy*. 2005;25(5 Pt 2):8S-18S.

KETAMINE - What's Old is New Again

PHARMACODYNAMICS

- Dosing:
  - Sedation/Analgesia
    - IV: 0.5 – 1.0 mg/kg
    - IM/ rectal: 2.5 – 5.0 mg/kg
    - PO: 5 – 6 mg/kg
  - Induction
    - IV: 1.0 – 2.5 mg/kg
    - IM/ rectal: 5 – 10 mg/kg
  - Infusion
    - 15-80 mcg/kg/min
      - Augment with diazepam IV 2 -5 mg or midazolam IV 1 -2 mg
  - Epidural/ Caudal
    - 0.5 mg/kg
      - Dilute in saline or local anesthetic (1 mL/kg)

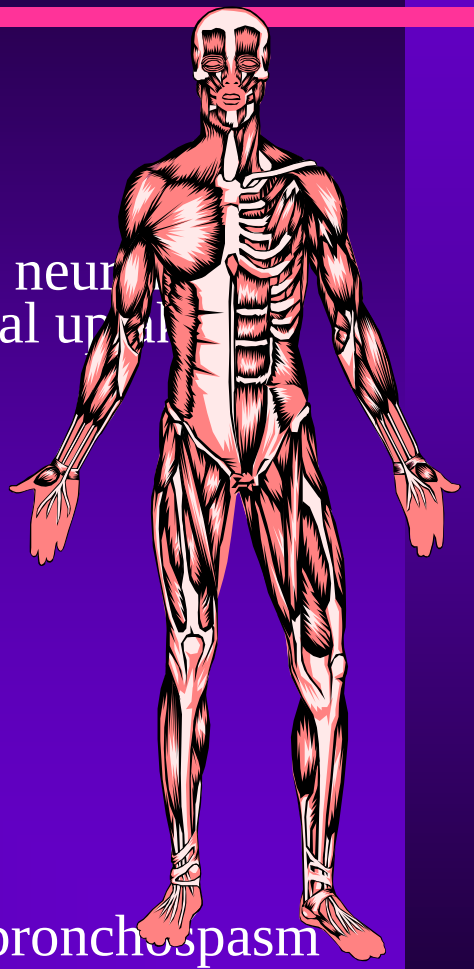
PHARMACOKINETICS

- Onset of action:
  - IV <30 seconds
  - IM/ rectal 3 – 4 minutes
- Peak effects:
  - IV 1minute
  - IM/ rectal 5 – 20 minutes
  - PO 30 minutes
- Duration of action:
  - IV 5 - 15minute
  - IM/ rectal 12 – 25 minutes
  - Epidural 4 hours
- Metabolism:
  - Demethylation & hydroxylation by hepatic CYP
  - One of the produced metabolites is active
    - Norketamine (Metabolite I)
    - Has a potency of 30% of the parent drug & longer half-life

Ketamine

- Cardiovascular system:
  - Direct myocardial depressant
    - Overriden by the central sympathetic stimulation, neur[illegible] release of catecholamines, & inhibition of neuronal up[illegible] catecholamines.
  - Increase in systemic arterial pressure
  - Increase in heart rate
  - Increase in cardiac output

- Pulmonary system:
  - Bronchial smooth muscle relaxant
    - As effective as inhalational agents in preventing bronchospasm
  - Increase in pulmonary arterial pressure
  - Increases salivary & tracheobronchial secretions



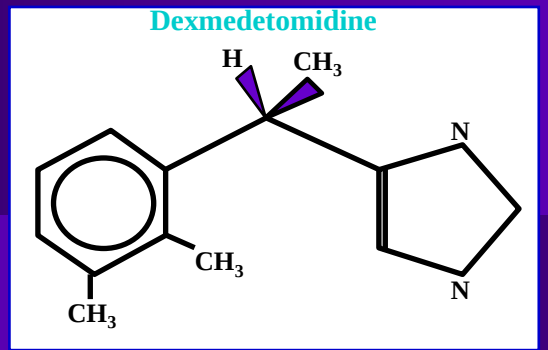
α_2 Agonists: Dexmedetomidine

Clinical Effects

- Antihypertensive[1,2]
- Sedative[1,2]
- Analgesic[1,2]
- ↓ Shivering[3]
- Anxiolytic effects[4]
- Patient rousability[4]
- Potentiates effects of opioids, sedatives, and anesthetics[2]
- Decreased sympathetic activity[5]

Adverse Effects

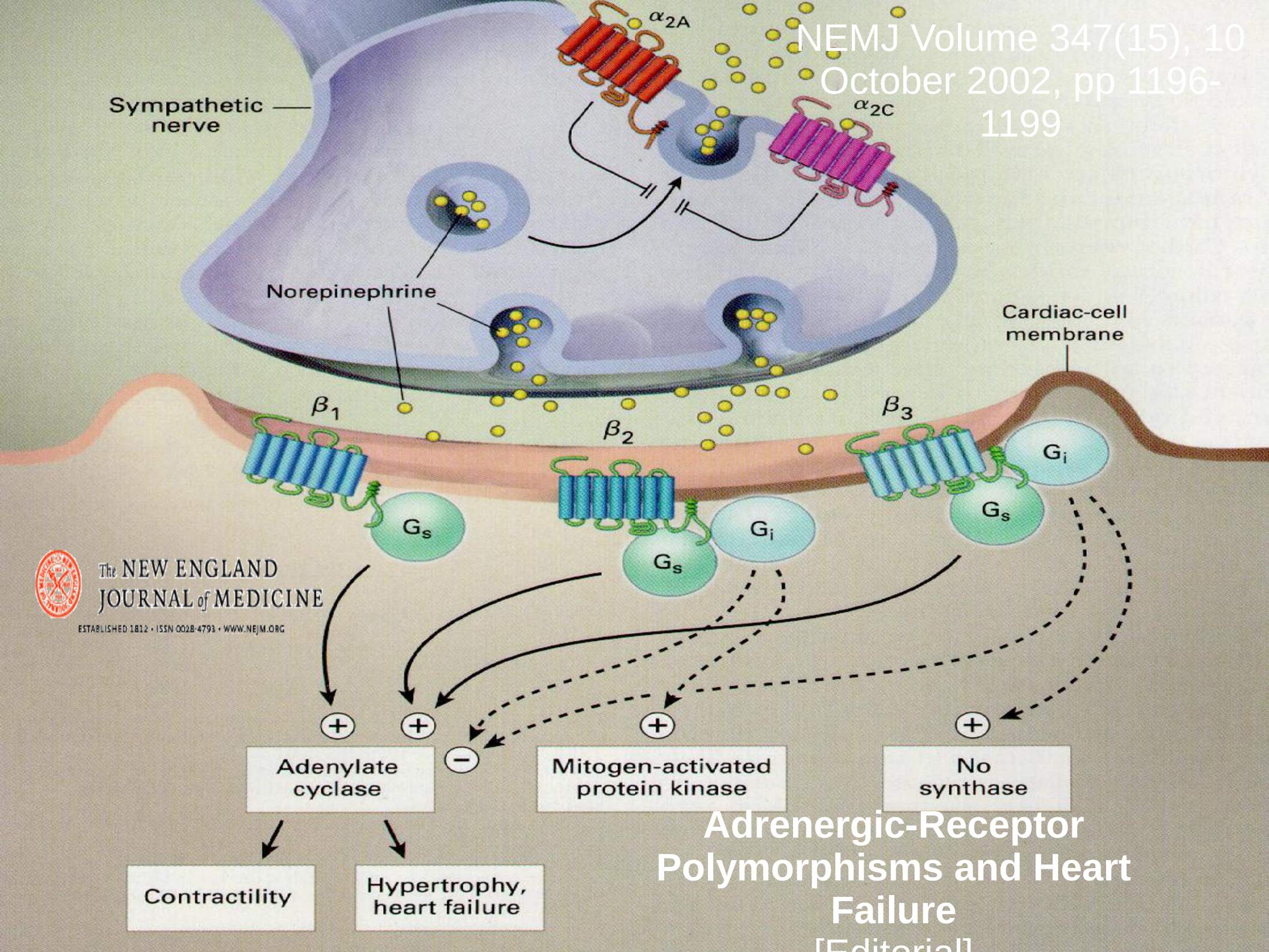
- Bradycardia[6]
- Hypotension[6]
- Dry mouth[2]
- Vasoconstriction with rapid infusion or at high doses[2]
- Nausea[2]



[1]Kamibayashi T, et al. *Anesthesiology*. 2000;93:1345-1349.
[2]Precedex [package insert]. Lake Forest, IL: Hospira Inc; 2004.
[3]Doufas AG, et al. *Stroke*. 2003;34:1218-1223.
[4]Riker RR, et al. *Pharmacotherapy*. 2005;25(5 Pt 2):8S-18S.
[5]Venn RA, et al. *Brit J Anaesthesia*. 2001;87:684-690.
[6]Shehabi Y, et al. *Intensive Care Med*. 2004;30:2188-2196.

METABOLISM

- Almost 100% biotransformation
  - Glucuronidation
  - Cytochrome P450 mediated
  - Metabolites all inactive – urinary elimination
- Significant ↑ $t_{1/2}$ in hepatic failure (7.5 hr)
- <1% excreted as unchanged
- No significant effect of renal impairment



NEMJ Volume 347(15), 10 October 2002, pp 1196-1199

Adrenergic-Receptor Polymorphisms and Heart Failure

[Editorial]

Clinical Characteristics of Dexmedetomidine

- Cooperative sedation[1]
- Analgesia[2,3]
- **NO RESPIRATORY DEPRESSION**
- Organ protection (ie, neural, renal, cardiac)[1]
- Anxiolysis[2,3]
- Controls hyperadrenergic response to stress[1-3]
- Reduces shivering[3]
- Diuretic action[4]
- Mimics natural sleep[1,5]

[1]Aantaa R, et al. *Drugs of the Future*. 1993;18:49-56.
[2]Kamibayashi T, et al. *Anesthesiology*. 2000;93:1345-1349.
[3]Wagner BKJ, et al. *Clin Pharmacokinet*. 1997;33:426-453.
[4]Goodman LS, et al. *The Pharmacological Basis of Therapeutics*. New York, NY: McGraw-Hill;2004:232-235.
[5]Huupponen E, et al. *Acta Anaesthesiol Scand*. 2008;52:289-294.

Extubation on Dexmedetomidine

- Dexmedetomidine has been continuously infused in mechanically ventilated patients
  - Prior to extubation
  - During extubation
  - And post-extubation
  - It is *not* necessary to **discontinue** prior to extubation
- Excellent sedation control before, during and after extubation
- Consider converting to dexmedetomidine for weaning protocol

The Efficacy of Dexmedetomidine in Patients with Noninvasive Ventilation: A Preliminary Study

Shinji Akada, MD, PhD

Shinhiro Takeda, MD, PhD

Yuko Yoshida, MD

Keiko Nakazato, MD

Masaki Mori, MD

Takashi Hongo, MD, PhD

Keiji Tanaka, MD, PhD

Atsuhiro Sakamoto, MD, PhD

BACKGROUND: Agitation is associated with failure of noninvasive ventilation (NIV). We investigated the effect of dexmedetomidine in patients with NIV.

METHODS: This was a prospective clinical investigation in an intensive care unit. Dexmedetomidine was infused in 10 patients in whom NIV was difficult because of agitation.

RESULTS: Ramsay and Richmond Agitation-Sedation Scale scores were maintained at 2.94 ± 0.94 and -1.23 ± 1.30, respectively. All patients were successfully weaned from NIV, and the respiratory state was not worsened.

CONCLUSION: This study shows that dexmedetomidine is an effective sedative drug for patients with NIV.

(Anesth Analg 2008;107:167-70)

α_2 – Agonists and Cognitive Function

- There is strong evidence that α_2 – agonists improve prefrontal cortical function (PFC)
- PFC shares reciprocal projections with:
  - Parietal association cortex specialized for visuospatial processing
  - Medial temporal lobe important to memory abilities
  - Anterior cingulate cortex involved in organizing complex cognitive function
  - Caudate nucleus that regulates motor behavior
- NE's beneficial action in the PFC appear to result from stimulation of α_2 (A) – receptors postjunctional to NE terminals

Arnstein et el. Arch Gen Psychiatry 1996

Acta Anaesthesiol Scand 2010; **54**: 710–716

ACTA ANAESTHESIOLOGICA SCANDINAVICA
doi: 10.1111/j.1399-6576.2009.02177.x

Dexmedetomidine provides cortical neuroprotection: impact on anaesthetic-induced neuroapoptosis in the rat developing brain

R. D. SANDERS[1], P. SUN[1], S. PATEL[1], M. LI[2], M. MAZE[1] and D. MA[1]
[1]*Magill Department of Anaesthetics, Pain Medicine and Intensive Care, Imperial College London, Chelsea and Westminster Hospital, London UK and* [2]*Department of Anesthesiology, Peking University Third Hospital, Beijing, China*

Neuroprotective effects of Dexmedetomidine

- Inhibition of ischemia induced NE release may be associated with neuroprotection
- Dex prevents delayed neuronal death after focal ischemia
- Dex decreased total ischemic volume by 40% compared to placebo

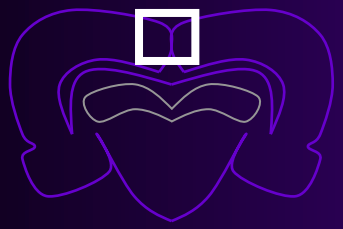
  Jolkkonen J et al. Euro J Pharm 1999

  Hoffman WE et al Anesthesiology 1991

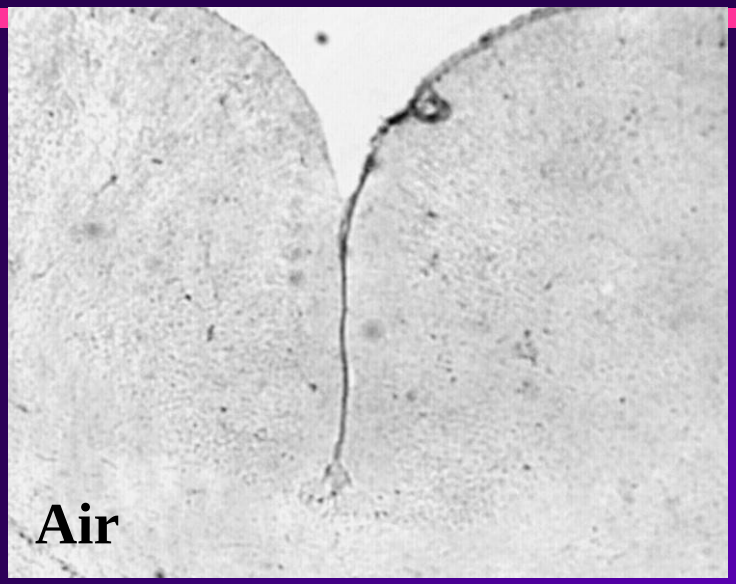
- Dex enhances glutamine disposal by oxydative metabolism in astrocytes

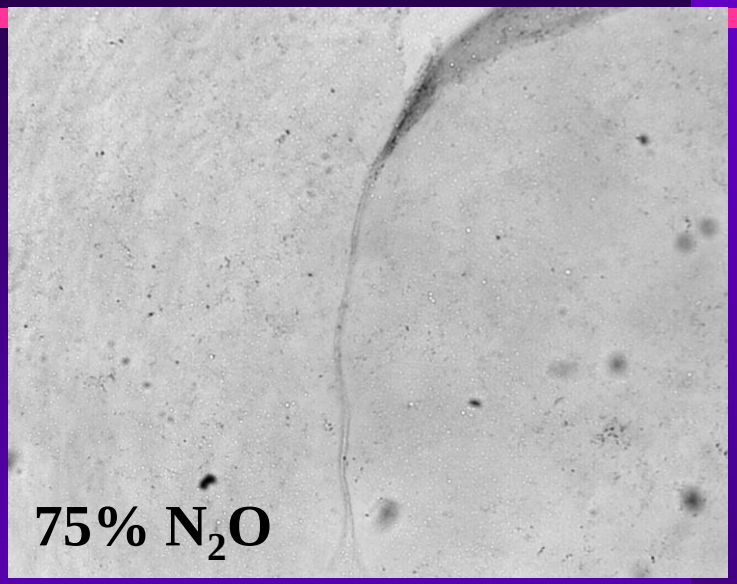
  Huang R et al. J Cereb Blood Metab 2000

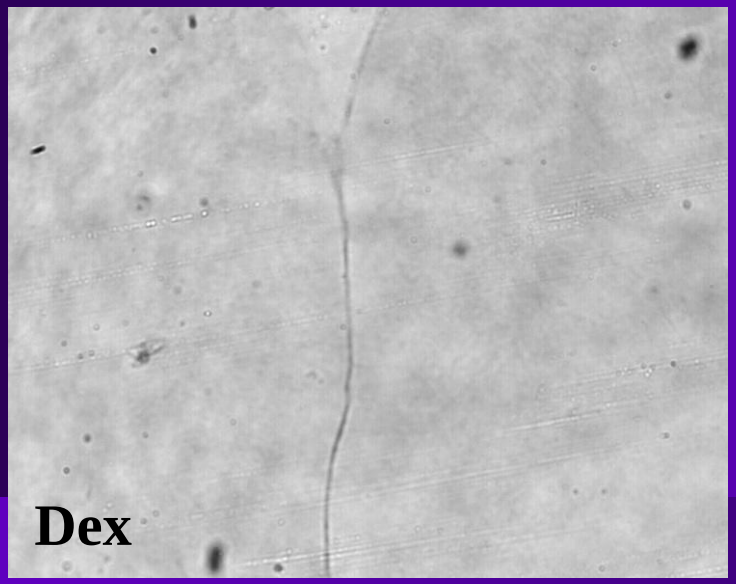
Apoptotic Neurodegenerative Effects of Anesthetics in Neonates

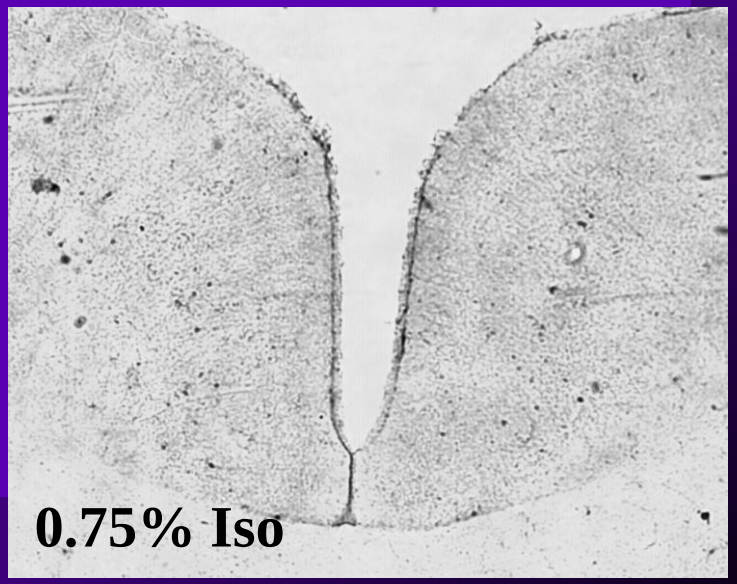


Apoptosis induced by anesthetics as measured with caspase-3 immunostaining in the cortex

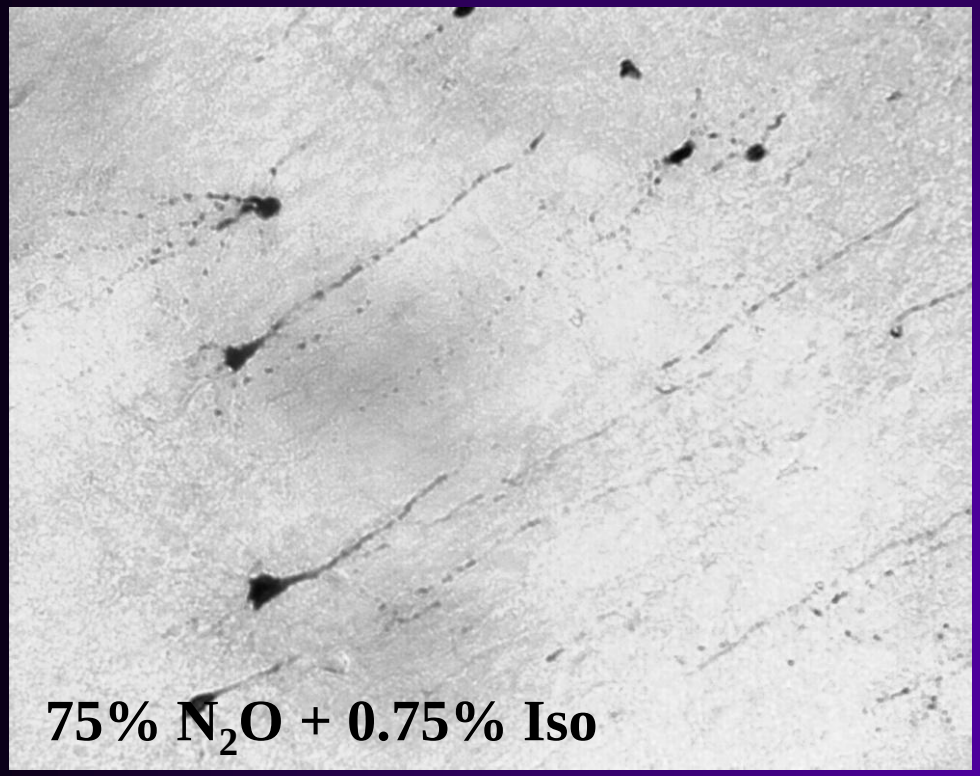


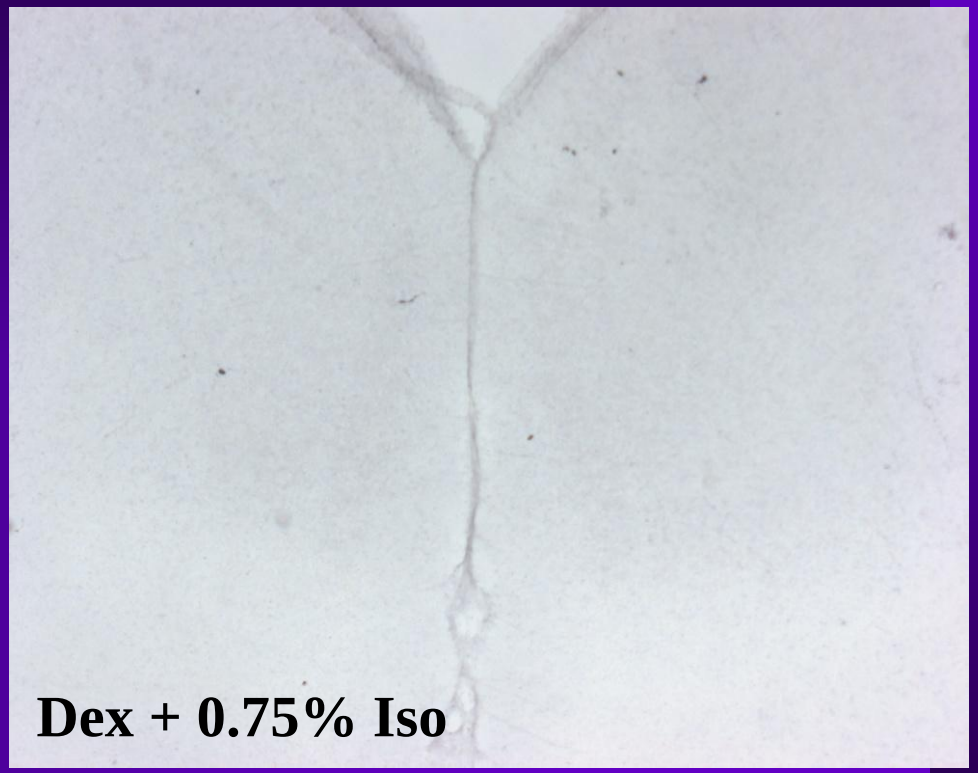






Apoptotic Neurodegenerative Effects of Anesthetic Combinations





Apoptosis induced by combinations of anesthetics as measured with caspase-3 immunostaining in the cortex

Gross Morphologic changes induced by 90 min H-I

Published in final edited form as:
J Neurosurg Anesthesiol. 2009 October ; 21(4): 286–291. doi:10.1097/ANA.0b013e3181a71f11.

A retrospective cohort study of the association of anesthesia and hernia repair surgery with behavioral and developmental disorders in young children

Charles DiMaggio, PhD, MPH, PA-C[*], Lena S. Sun, MD[†], Athina Kakavouli, MD[‡], Mary W. Byrne, PhD, MPH, FAAN[§], and Guohua Li, MD, DrPH[**]

[*] Assistant Professor of Clinical Epidemiology (in Anesthesiology), Mailman School of Public Health, College of Physicians and Surgeons, Columbia University, New York, NY

95% CI 1.3, 4.1). Our findings add to recent evidence of the potential association of surgery and its concurrent exposure to anesthetic agents with neurotoxicity and underscore the need for more rigorous clinical research on the long-term effects of surgery and anesthesia in children.

A786
October 18, 2010
8:00:00 AM - 10:00:00 AM
Room Upper 26A
Exposure to Anesthesia and Risk of Developmental and Behavioral Disorders in a Twin Cohort

** Charles DiMaggio, Ph.D., Lena S. Sun, M.D., Guohua Li, M.D., Dr.PH.
Department of Epidemiology, Columbia University Mailman School of Public Health, New York, New York; Department of Anesthesiology, Columbia University College of Physicians and Surgeons, New York, New York

Introduction: There is mounting evidence from in vitro and in vivo studies that volatile anesthetic agents may have profound neurotoxic effects on the developing brain. The clinical relevance of these findings to children undergoing anesthesia, however, remains unclear. The purpose of this study is to assess the association between exposure to anesthesia under three years of age and the risk of developmental and behavioral disorders in a large birth cohort of twins.

Methods: We constructed a retrospective cohort of 5,824 twin pairs who were born between 1999 and 2005 and who were enrolled in the New York State Medicaid program. We determined exposure status based on surgical procedures recorded for each child under three years of age, and identified developmental and behavioral outcomes by screening diagnoses coded according to the International Classification

Conclusion: The results from this large birth cohort of twins indicate that children who were exposed to anesthesia under three years of age are more likely than their peers to be subsequently diagnosed with developmental and behavioral disorders.

This excess risk cannot be fully explained by birth factors, gender, or medical utilization.

The Young: Neuroapoptosis Induced by Anesthetics and What to Do About It

Catherine E. Creeley, PhD

John W. Olney, MD

Millions of human fetuses, infants, and children are exposed to anesthetic drugs every year in the United States and throughout the world. Anesthesia administered during critical stages of neurodevelopment has been considered safe and without adverse long-term consequences. However, recent reports provide mounting evidence that exposure of the immature animal brain to anesthetics during the period of rapid synaptogenesis, also known as the brain growth spurt period, triggers widespread apoptotic neurodegeneration, inhibits neurogenesis, and causes significant long-term neurocognitive impairment. Herein, we summarize currently available evidence for anesthesia-induced pathological changes in the brain and associated long-term neurocognitive deficits and discuss promising strategies for protecting the developing brain from the potentially injurious effects of anesthetic drugs while allowing the beneficial actions of these drugs to be realized.

(Anesth Analg 2010;110:442–8)

Neuroprotection from Anesthetic Drugs

- Lithium
- Hypothermia
- Xenon
- Dexmedetomidine

Multimodal Analgesia

- Simultaneous use of multiple analgesic methods or sedation drugs.

Pediatr Cardiol 26:553–557, 2005
DOI: 10.1007/s00246-004-0707-4

Pediatric Cardiology

Propofol and Propofol–Ketamine in Pediatric Patients Undergoing Cardiac Catheterization

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[2]Department of Pediatrics, Erciyes, University School of Medicine, Kayseri, Turkey

Propofol combined with low-dose ketamine preserves mean arterial pressure better than propofol alone - without affecting the recovery and thus is a good option in pediatric patients undergoing cardiac catheterization.

Clinical Therapeutics/Volume 32, Number 4, 2010

Brief Report

Propofol/Dexmedetomidine and Propofol/Ketamine Combinations for Anesthesia in Pediatric Patients Undergoing Transcatheter Atrial Septal Defect Closure: A Prospective Randomized Study

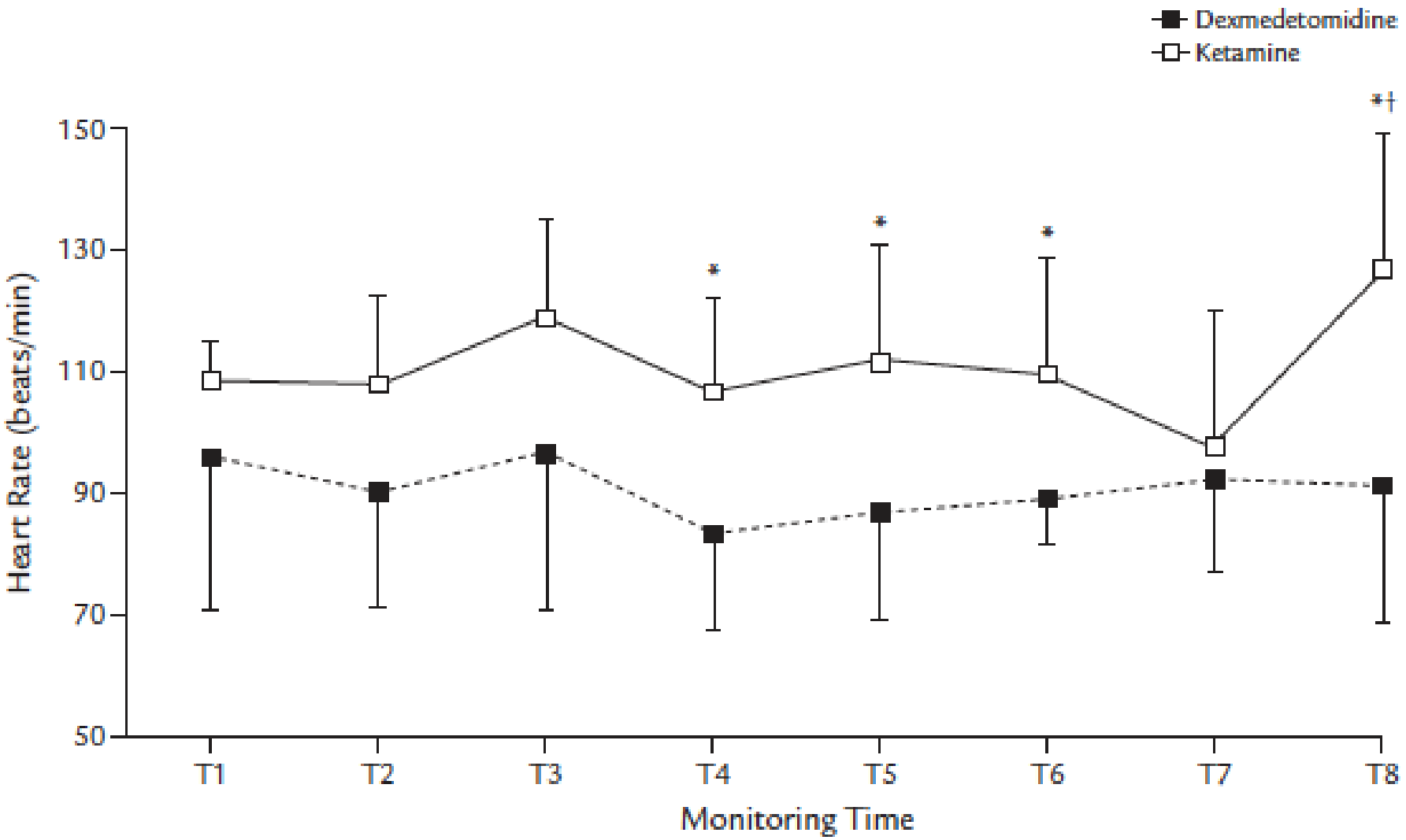
Senem Koruk, MD[1]; Ayse Mizrak, MD[1]; Berna Kaya Ugur, MD[1]; Osman Ilhan, MD[1]; Osman Baspinar, MD[2]; and Unsal Oner, MD[1]

[1]Department of Anesthesiology and Reanimation, Gaziantep University Medical School, Gaziantep, Turkey; and [2]Department of Pediatrics, Gaziantep University Medical School, Gaziantep, Turkey

Table. Demographic and clinical characteristics of the pediatric patients undergoing transcatheter atrial septal defect (ASD) closure.

Characteristic	Propofol/Dexmedetomidine Group (n = 9)	Propofol/Ketamine Group (n = 9)
Sex, male/female	5/4	3/6
Age, mean (SD), y	12.5 (10.4)	10.1 (4.5)
Weight, mean (SD), kg	40.8 (27.8)	30.0 (15.2)
ASA physical status II	9	9
Duration of ASD closure, mean (SD), min	57.0 (8.5)	48.1 (13.6)

ASA = American Society of Anesthesiologists.


Dexmedetomidine
Ketamine
Heart Rate (beats/min)
150
130
110
90
70
50
*
*
*
*†
T1
T2
T3
T4
T5
T6
T7
T8
Monitoring Time

CONCLUSIONS

This study compared propofol/dexmedetomidine and propofol/ketamine combinations in pediatric patients undergoing transcatheter ASD closure. Sufficient anesthesia was provided in both groups. Heart rate was determined to be significantly higher in the ketamine group at several time points, and the recovery period was significantly shorter with dexmedetomidine. No severe adverse effects were recorded with either combination. In this small study, both dexmedetomidine and ketamine in combination with propofol were well tolerated.

Cardiovascular Effects of Dexmedetomidine Sedation in Children

Jackson Wong, MD,* Garry M. Steil, PhD,* Michelle Curtis, PNP,† Alexandra Papas, BS,‡ David Zurakowski, PhD,§ and Keira P. Mason, MD§

BACKGROUND: Dexmedetomidine (DEX) affects heart rate (HR), mean arterial blood pressure, cardiac index (CI), stroke index (SI), and systemic vascular resistance index (SVRI) in adults. In this study we sought to determine whether similar effects occur in children undergoing DEX sedation.

METHODS: Hemodynamic changes in children were followed during IV DEX sedation for radiological procedures. One group of 8 patients (DEX-brief) received a bolus (2 mcg/kg bolus over 10 minutes) and completed the procedure within 10 minutes. The second group of 9 patients (DEX-prolong) received the bolus plus additional DEX as needed to maintain sedation for procedures lasting longer than 10 minutes (additional 1 mcg/kg/hr infusion with second bolus if needed). CI, SI, and SVRI were measured using a continuous noninvasive cardiac output monitor. Changes in hemodynamic variables at minutes 10, 20, and discharge (time at which patient achieved Aldrete Score ≥9) were compared to baseline by repeated measures ANOVA with effect sizes reported as mean [95% confidence interval].

RESULTS: Data were obtained during 8 DEX-brief and 9 DEX-prolong procedures. In DEX-brief, HR and CI decreased (18.9 [2.3 to 35.5] bpm and 0.74 [0.15 to 1.33] L/min/m^2; respectively) at T1. There was no change in any other hemodynamic variables and all hemodynamic variables returned to baseline at recovery. In DEX-prolong, both HR and CI remained decreased (24.0 [8.3 to 39.6] bpm, 1.51 [0.95 to 2.06] L/min/m^2; respectively) at recovery. In addition, SI was decreased (8.01 [1.71 to 14.31] mL/m^2) and SVRI was increased (776.0 [271.9 to 1280.4] dynes-sec/cm^5/m^2) at recovery in the DEX-prolong group. There were no significant changes in mean arterial blood pressure in either group.

CONCLUSION: DEX decreases CI in children and has a cumulative effect. For patients undergoing prolonged procedures HR and CI remained decreased at the time of discharge together with a decrease in SI and an increase in SVRI. (Anesth Analg 2012;114:193–9)

Cardiovascular Effects of Dexmedetomidine Sedation in Children

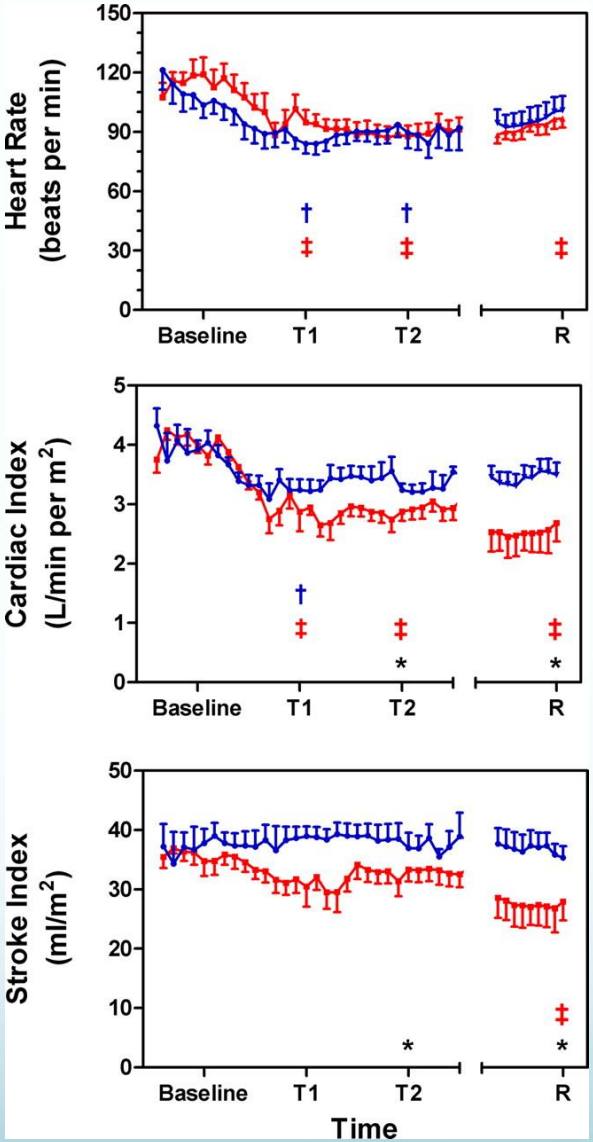
Table 2.

Demographics

	DEX-brief	DEX-prolong
Total subjects	8	9
Gender (male/female)	4/4	7/2
Age (year)	2.8 (range 0.3–6.1)	2.4 (range 1.2–4.3)
Weight (kg)	13.5 (range 6–20)	13.0 (range 11–17)
Height (cm)	92 (range 67–107)	86 (range 78–106)

- Children undergoing procedures less than 10 min in duration (dexmedetomidine [DEX]–brief) received 2 mcg/kg DEX over 10 minutes. Children with procedures longer than 10 min (DEX–prolong) received the initial 2 mcg/kg of DEX plus additional DEX as need to obtain and maintain a Ramsay Sedation Score of 4. No significant differences was found between the 2 treatment groups (P>0.05 all).

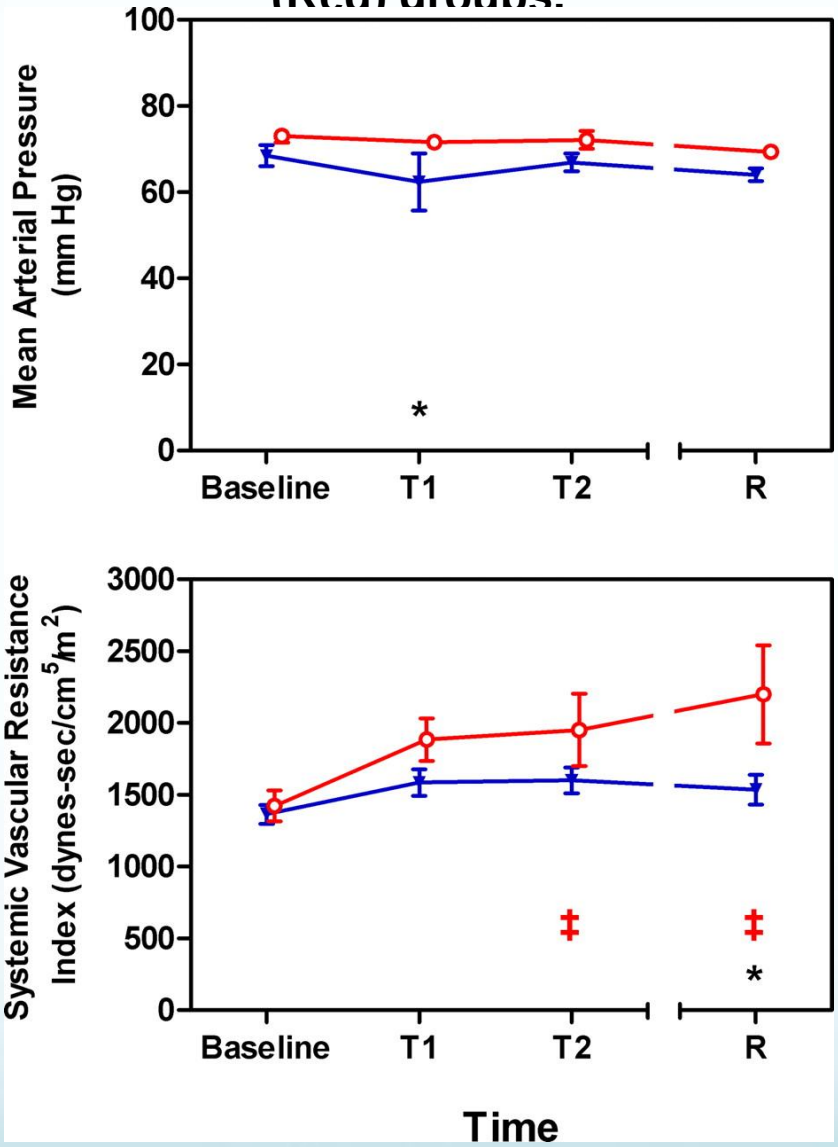
Time course of the effects of dexmedetomidine (DEX) on heart rate (HR; mean ± SEM), cardiac index (CI), and stroke index (SI) in children undergoing brief (DEX-brief; Blue; ≤10 min) and prolonged (DEX-prolong; Red, >10 min) procedures.



Wong J et al. Anesth Analg 2012;114:193-199

ANESTHESIA & ANALGESIA

Effects of dexmedetomidine (DEX) on mean arterial blood pressure (MAP; mean ± SEM) and systemic vascular resistance index (SVRI) in the DEX-brief (Blue) and DEX-prolong (Red) groups.



Wong J et al. Anesth Analg 2012;114:193-199

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In summary:

This is the first study to report the effect of DEX sedation on CI, SI, and SVRI in children without cardiac disease during radiological procedures.

We found that DEX decreases CI and SI with a concomitant increase in SVRI.

We found the effects to be dose-dependent and to persist up to 1 hour after discontinuing the sedative.

Society for Pediatric Anesthesia

Section Editor: Peter J. Davis

Acute Hemodynamic Changes After Rapid Intravenous Bolus Dosing of Dexmedetomidine in Pediatric Heart Transplant Patients Undergoing Routine Cardiac Catheterization

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BACKGROUND: Dexmedetomidine is a highly selective α_2-adrenoceptor agonist with sedative, anxiolytic, and analgesic properties that has minimal effects on respiratory drive. Its sedative and hypotensive effects are mediated via central α_{2A} and imidazoline type 1 receptors while activation of peripheral α_{2B}-adrenoceptors result in an increase in arterial blood pressure and systemic vascular resistance. In this randomized, prospective, clinical study, we attempted to quantify the short-term hemodynamic effects resulting from a rapid IV bolus administration of dexmedetomidine in pediatric cardiac transplant patients.

METHODS: Twelve patients, aged 10 years or younger, weighing ≤40 kg, presenting for routine surveillance of right and left heart cardiac catheterization after cardiac transplantation were enrolled. After an inhaled or IV induction, the tracheas were intubated and anesthesia was maintained with 1 minimum alveolar concentration of isoflurane in room air, fentanyl (1 μg/kg), and rocuronium (1 mg/kg). At the completion of the planned cardiac catheterization, 100% oxygen was administered. After recording a set of baseline values that included heart rate (HR), systolic blood pressure, diastolic blood pressure, central venous pressure, systolic pulmonary artery pressure, diastolic pulmonary artery pressure, pulmonary artery wedge pressure, and thermodilution-based cardiac output, a rapid IV dexmedetomidine bolus of either 0.25 or 0.5 μg/kg was administered over 5 seconds. The hemodynamic measurements were repeated at 1 minute and 5 minutes.

RESULTS: There were 6 patients in each group. Investigation suggested that systolic blood pressure, diastolic blood pressure, systolic pulmonary artery pressure, diastolic pulmonary artery pressure, pulmonary artery wedge pressure, and systemic vascular resistance all increased at 1 minute after rapid IV bolus for both doses and decreased significantly to near baseline for both doses by 5 minutes. The transient increase in pressures was more pronounced in the systemic system than in the pulmonary system. In the systemic system, there was a larger percent increase in the diastolic pressures than the systolic pressures. Cardiac output, central venous pressure, and pulmonary vascular resistance did not change significantly. HR decreased at 1 minute for both doses and was, within the 0.5 μg/kg group, the only hemodynamic variable still changed from baseline at the 5-minute time point.

CONCLUSION: Rapid IV bolus administration of dexmedetomidine in this small sample of children having undergone heart transplants was clinically well tolerated, although it resulted in a transient but significant increase in systemic and pulmonary pressure and a decrease in HR. In the systemic system, there is a larger percent increase in the diastolic pressures than the systolic pressures and, furthermore, these transient increases in pressures were more pronounced in the systemic system than in the pulmonary system. (Anesth Analg 2010;111:1490–6)

ANESTHESIA & ANALGESIA

Table 1. Demographic Data of All Study Patients

	0.25 μg/kg	0.5 μg/kg
Total no. of patients	6	6
Age (mo)	66 ± 30	82 ± 23
Weight (kg)	20 ± 5	22 ± 1
BSA (m^2)	0.79 ± 0.15	0.86 ± 0.10
Time posttransplant (mo)	42 ± 20	57 ± 38
Gender, male/female	3/3	4/2

Data represented as an average ± SD.

BSA = body surface area.

P = not significant for all comparisons.

Table 2. Hemodynamic Responses to Dexmedetomidine

	0.25 μg/kg			0.5 μg/kg		
	Baseline	1 min	5 min	Baseline	1 min	5 min
SBP (mm Hg)	93 ± 4	110 ± 5	89 ± 2	96 ± 7	122 ± 6	93 ± 4
DBP (mm Hg)	52 ± 3	67 ± 4	50 ± 2	56 ± 8	80 ± 9	54 ± 5
HR (beats/min)	92 ± 7	81 ± 5	86 ± 6	91 ± 5	80 ± 3	75 ± 4
sPAP (mm Hg)	20 ± 1	22 ± 1	19 ± 2	21 ± 0.3	25 ± 1	21 ± 1
dPAP (mm Hg)	11 ± 1	12 ± 2	10 ± 1	12 ± 1	13 ± 1	11 ± 1
wPAP (mm Hg)	10 ± 1.0	12 ± 0.7	10 ± 0.8	12 ± 0.8	14 ± 0.9	12 ± 0.8
CVP (mm Hg)	6 ± 0.8	6 ± 0.7	6 ± 0.7	5 ± 0.8	6 ± 1	6 ± 1
CO (L/min)	3.2 ± 0.1	3.0 ± 0.2	3.1 ± 0.2	3.3 ± 0.2	2.8 ± 0.3	3.2 ± 0.7
SVR (dynes/s/cm^5)	1528 ± 92	2186 ± 238	1531 ± 125	1703 ± 287	2624 ± 272	1643 ± 228
PVR (dynes/s/cm^5)	129 ± 8.8	141 ± 18	124±15	95 ± 19	125 ± 29	78 ± 10

Data represented as an average ± SD.

SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate; sPAP = systolic pulmonary artery pressure; dPAP = diastolic pulmonary artery pressure; wPAP = pulmonary artery wedge pressure; CVP = central venous pressure; CO = cardiac output; SVR = systemic vascular resistance; PVR = pulmonary vascular resistance.

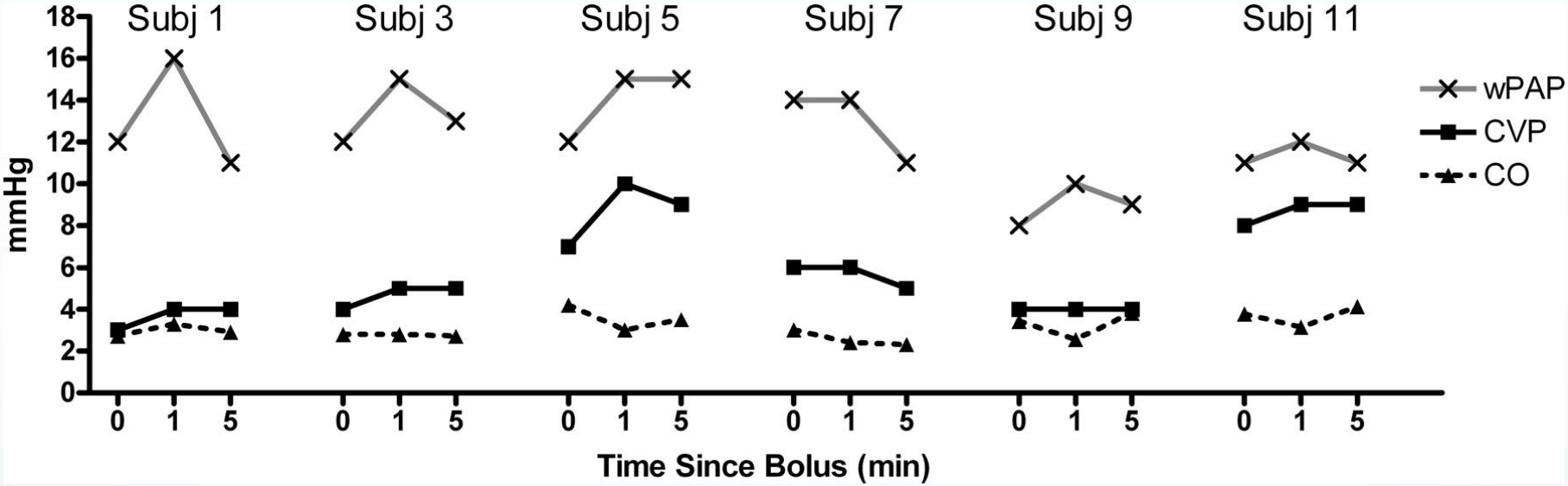
Table 3. Hemodynamic Changes Represented by the Percent Change from Baseline at 1 Minute and 5 Minutes for the 2 Concentrations of Dexmedetomidine Administered

	1 min		5 min	
	0.25 μg/kg	0.5 μg/kg	0.25 μg/kg	0.5 μg/kg
SBP (%)	19 ± 13	29 ± 9	−4 ± 9	−2 ± 12
DBP (%)	32 ± 24	51 ± 28	−3 ± 9	0 ± 16
HR (%)	−12 ± 4	−12 ± 7	−6 ± 7	−17 ± 7
sPAP (%)	14 ± 15	17 ± 13	−3 ± 7	−1 ± 11
dPAP (%)	14 ± 11	10 ± 7	−10 ± 12	−4 ± 15
wPAP (%)	22 ± 19	19 ± 12	−2 ± 10	2 ± 16
CVP (%)	1 ± 14	18 ± 18	0 ± 18	13 ± 19
CO (%)	−8 ± 12	−11 ± 19	−3 ± 9	−3 ± 14
SVR (%)	42 ± 26	69 ± 46	0 ± 14	0 ± 14
PVR (%)	9 ± 24	41 ± 61	−4 ± 25	−4 ± 44

Data represented as an average ± SD.

SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate; sPAP = systolic pulmonary artery pressure; dPAP = diastolic pulmonary artery pressure; wPAP = pulmonary artery wedge pressure; CVP = central venous pressure; CO = cardiac output; SVR = systemic vascular resistance; PVR = pulmonary vascular resistance.

Central venous pressure (CVP), cardiac output (CO), and pulmonary artery wedge pressure (wPAP) changes over time for dexmedetomidine dosed at 0.5 μg/kg.



Jooste E H et al. Anesth Analg 2010;111:1490-1496

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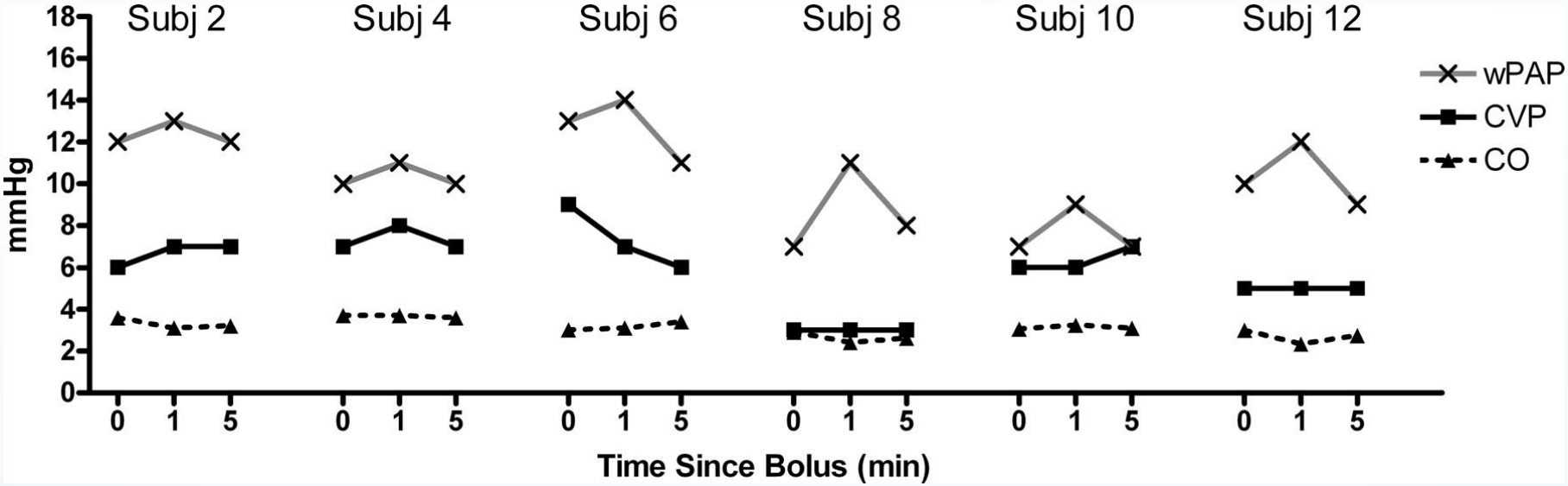
Central venous pressure (CVP), cardiac output (CO), and pulmonary artery wedge pressure (wPAP) changes over time for dexmedetomidine dosed at 0.25 µg/kg.



Jooste E H et al. Anesth Analg 2010;111:1490-1496

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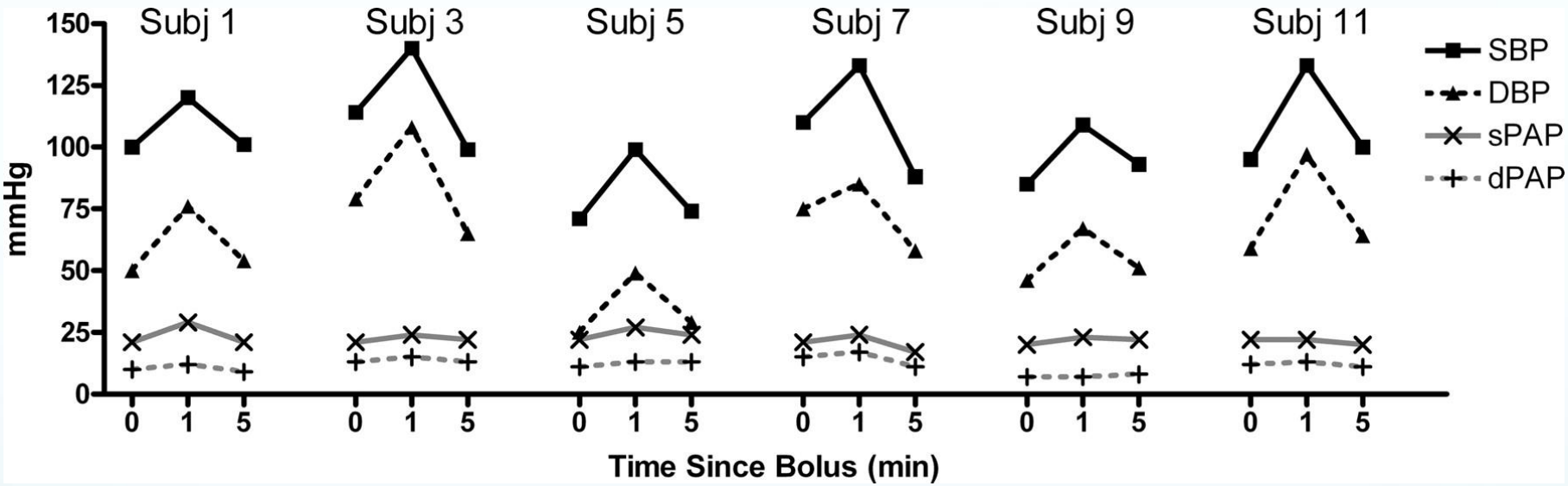
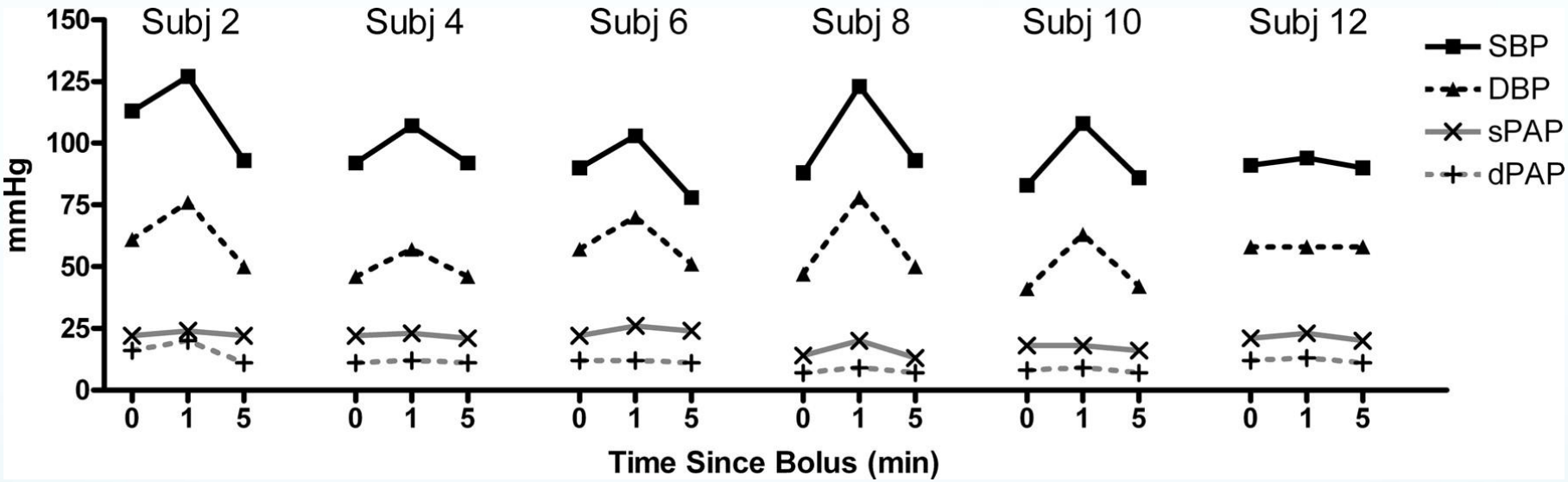
Systemic pressures and pulmonary pressures over time for dexmedetomidine dosed at 0.5 μg/kg, again showing substantial changes at 1 minute that seem to dissipate at the 5-minute time point.



Jooste E H et al. Anesth Analg 2010;111:1490-1496

Systemic pressures and pulmonary pressures over time for dexmedetomidine dosed at 0.25 µg/kg, showing substantial changes at 1 minute that seem to dissipate at the 5-minute time point.



Jooste E H et al. Anesth Analg 2010;111:1490-1496

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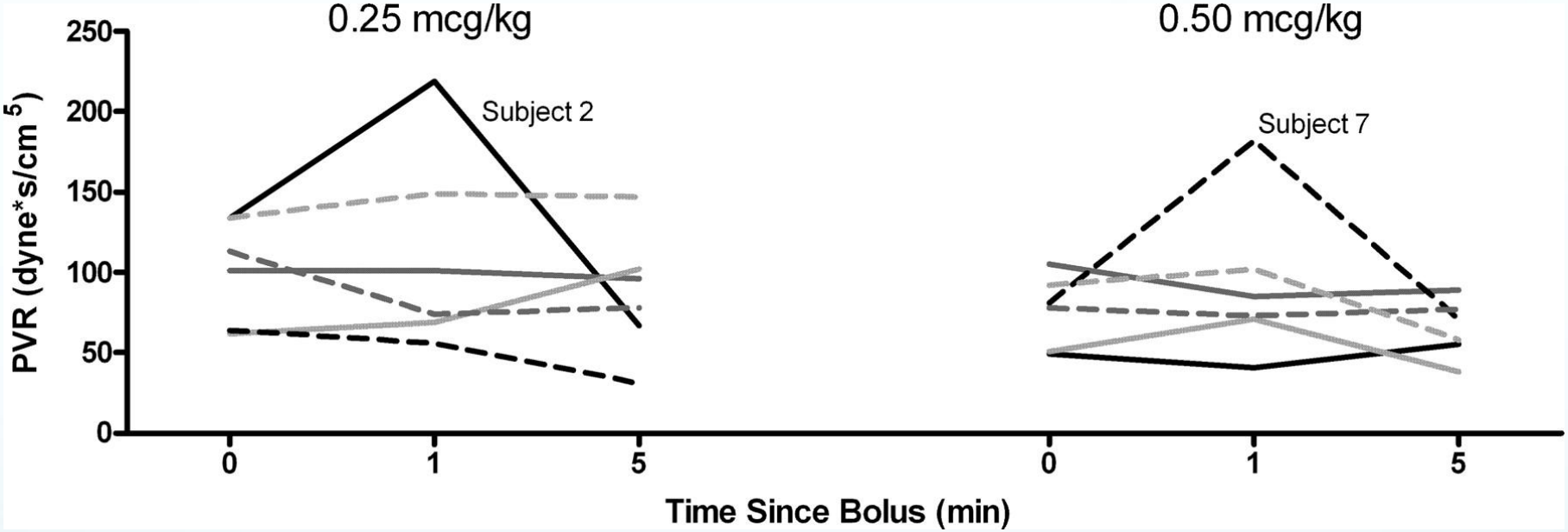
Pulmonary vascular resistance (PVR) over time for both dexmedetomidine doses.



Jooste E H et al. Anesth Analg 2010;111:1490-1496

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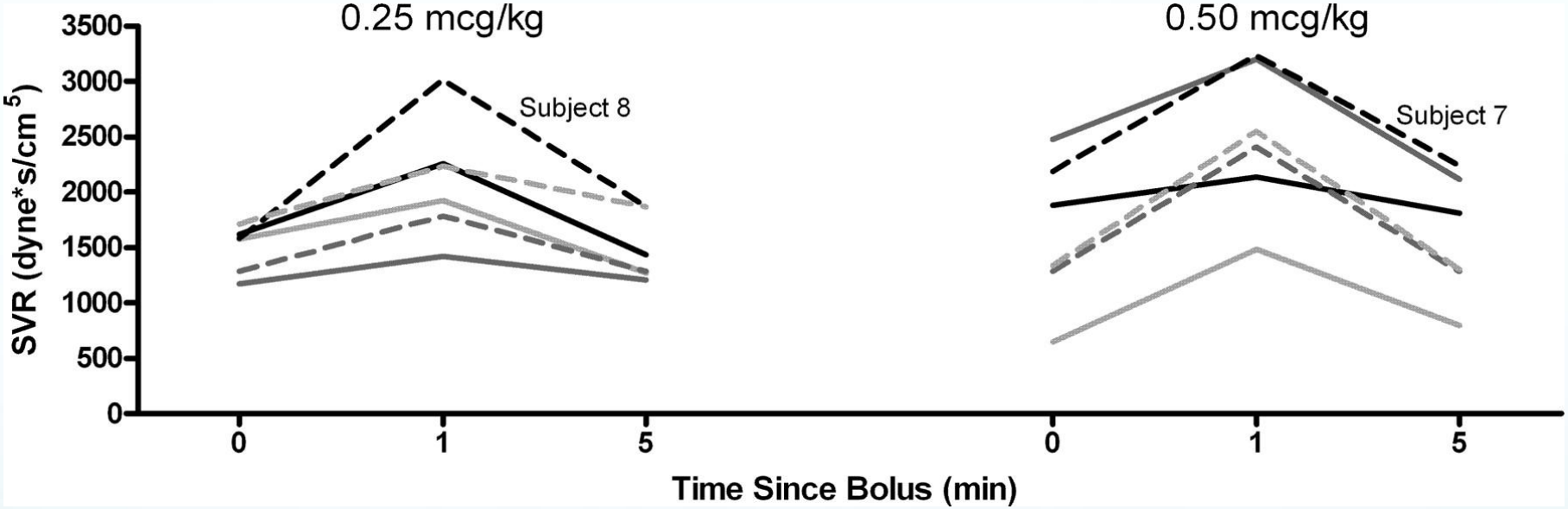
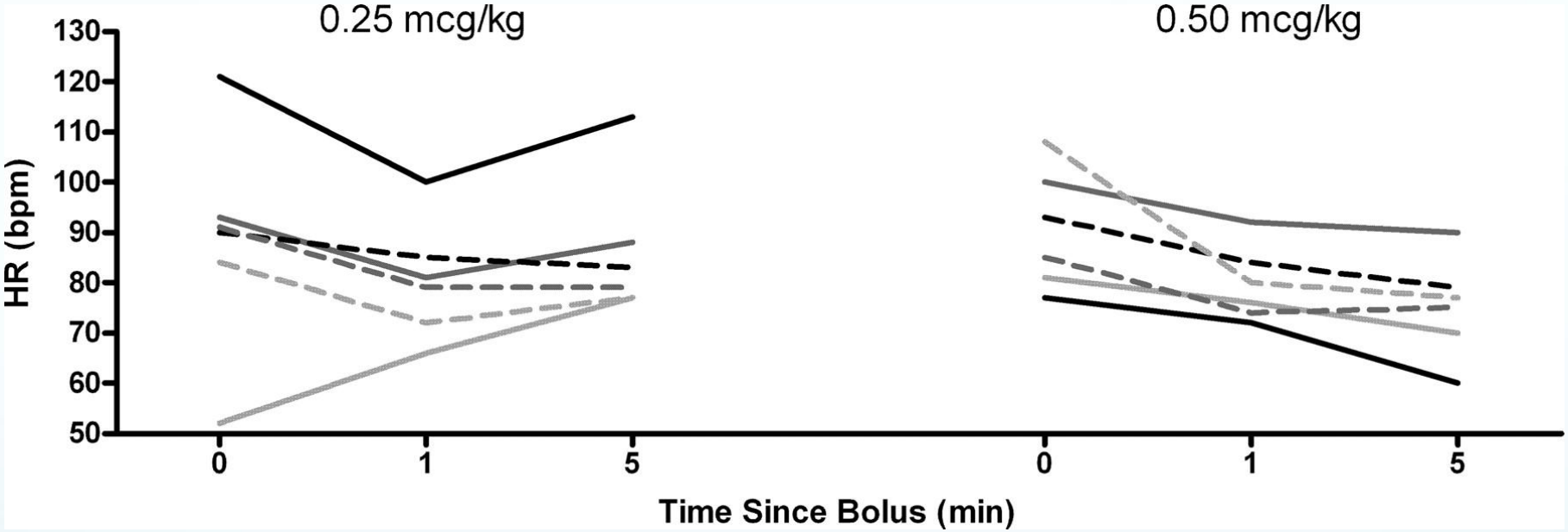
Systemic vascular resistance (SVR) over time for both dexmedetomidine doses, again showing the increase at 1 minute with a decrease back to baseline at 5 minutes.



Jooste E H et al. Anesth Analg 2010;111:1490-1496

ANESTHESIA & ANALGESIA

Heart rate (HR) changes over time for dexmedetomidine at both doses, highlighting the increase back to baseline in the 0.25 µg/kg dose, whereas the HR remains slow for the 0.5 µg/kg dose.



Jooste E H et al. Anesth Analg 2010;111:1490-1496

ANESTHESIA & ANALGESIA

Dexmedetomidine in Children: Current Knowledge and Future Applications

Keira P. Mason, MD,* and Jerrold Lerman, MD, FRCPC, FANZCA†

More than 200 studies and reports have been published regarding the use of dexmedetomidine in infants and children. We reviewed the English literature to summarize the current state of knowledge of this drug in children for the practicing anesthesiologist. Dexmedetomidine is an effective sedative for infants and children that only minimally depresses the respiratory system while maintaining a patent airway. However, dexmedetomidine does depress the cardiovascular system. Specifically, bradycardia, hypotension, and hypertension occur to varying degrees depending on the age of the child. Hypertension is more prevalent when larger doses of dexmedetomidine are given to infants. Consistent with its 2-hour elimination half-life, recovery after dexmedetomidine may be protracted in comparison with other sedatives. Dexmedetomidine provides and augments analgesia and diminishes shivering as well as agitation postoperatively. The safety record of dexmedetomidine suggests that it can be used effectively and safely in children, with appropriate monitoring and interventions to manage cardiovascular sequelae. (Anesth Analg 2011;113:1129–42)

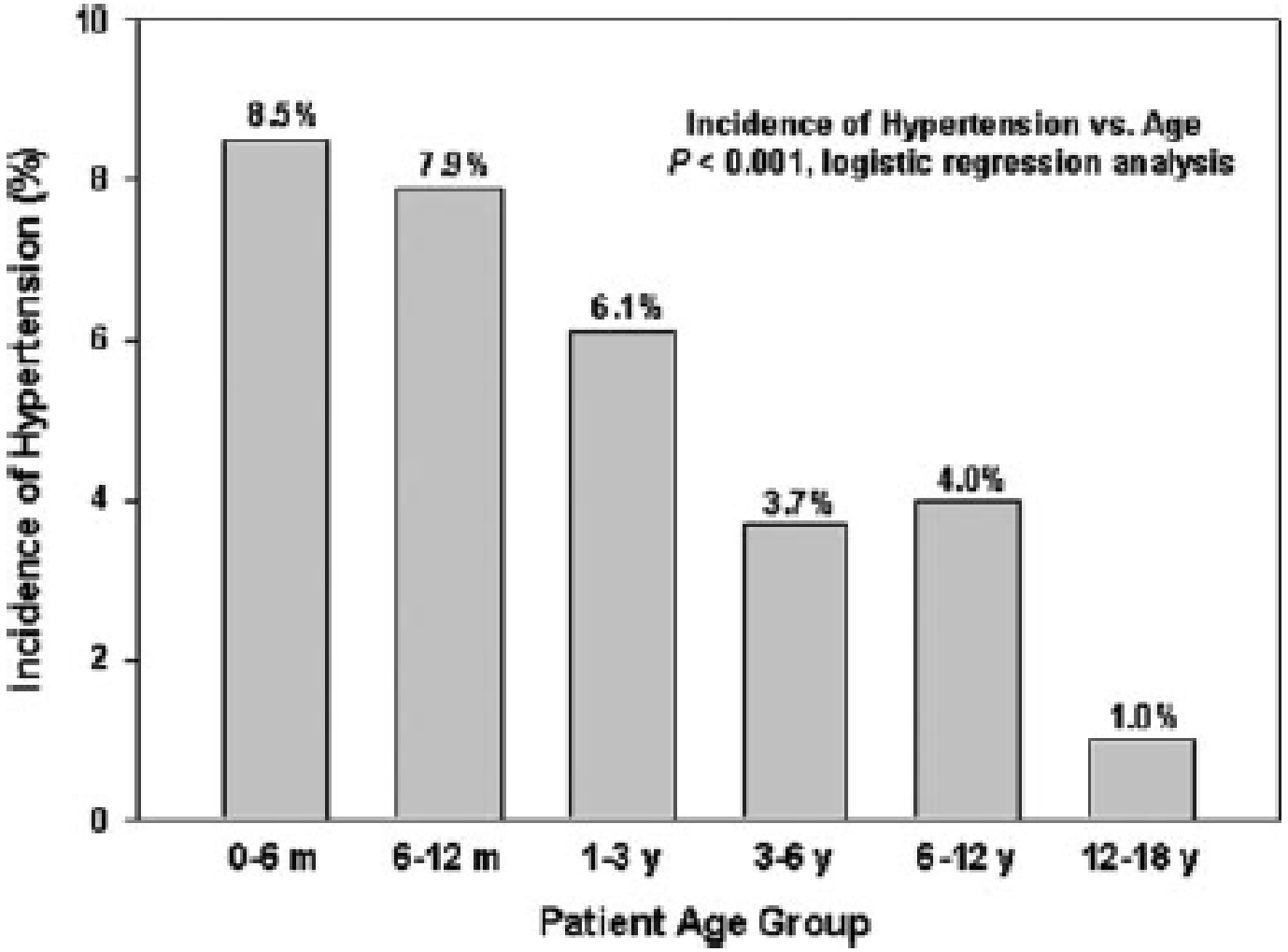


Figure 4. Three-thousand five-hundred twenty-two children received dexmedetomidine per protocol: initial bolus of 3 μg/kg dexmedetomidine over 10 minutes, followed by a continuous infusion of 2 μg/kg/h to maintain a Ramsay Sedation Score (RSS) of 4. If at any point during the sedation, the child failed to achieve or maintain RSS 4, this bolus could be repeated up to 2 more times. The most frequent incidence of hypertension occurred in children <1 year of age who received more than 1 bolus ($P < 0.001$). From Mason,[53] publisher permission obtained.

Perioperative Use of Dexmedetomidine Is Associated With Decreased Incidence of Ventricular and Supraventricular Tachyarrhythmias After Congenital Cardiac Operations

Constantinos Chrysostomou, MD, Joan Sanchez-de-Toledo, MD, Peter Wearden, MD, PhD, Edmund H. Jooste, MD, Steven E. Lichtenstein, MD, Patrick M. Callahan, MD, Tunga Suresh, MD, Elizabeth O'Malley, CCP, LP, Dana Shiderly, CRNP, Jamie Haney, MS, Masahiro Yoshida, MD, Richard Orr, MD, Ricardo Munoz, MD, and Victor O. Morell, MD

Departments of Critical Care Medicine, Cardiac Intensive Care Unit, Cardiothoracic Surgery, and Anesthesiology, Children's Hospital of Pittsburgh of the University of Pittsburgh School of Medicine and the Department of Bioengineering, Cardiovascular Systems Laboratory, Swanson School of Engineering, University of Pittsburgh, Pittsburgh, Pennsylvania; and the Department of Critical Care Medicine, Cardiac Intensive Care Unit, Hospital Vall d'Hebron, Barcelona, Spain

Background. Postoperative tachyarrhythmias remain a common complication after congenital cardiac operations. Dexmedetomidine (DEX), an α-2 adrenoreceptor agonist, can have a therapeutic role in supraventricular tachyarrhythmias for cardioversion to sinus rhythm or heart rate control. Whether routine perioperative use of DEX decreases the incidence of supraventricular and ventricular tachyarrhythmias was studied.

Methods. In this prospective cohort study, 32 pediatric patients undergoing cardiothoracic operations received DEX and were compared with 20 control patients who did not receive DEX.

Results. Dexmedetomidine was started after anesthesia induction and continued intraoperatively and postoperatively for 38 ± 4 hours (mean dose, 0.76 ± 0.04 μg/kg/h). Ten control patients and 2 DEX patients sustained 16 episodes of tachyarrhythmias ($p = 0.001$), including a 25% vs 0% ($p = 0.01$) incidence of ventricular tachycardia and 25% vs 6% ($p = 0.05$) of supraventricular arrhythmias in the control and DEX group, respectively. Transient complete heart block occurred in 2 control patients and in 1 DEX patient. Control patients had a higher heart rate (141 ± 5 vs 127 ± 3 beats/min, $p = 0.03$), more sinus tachycardia episodes (40% vs 6%; $p = 0.008$), required more antihypertensive drugs with nitroprusside (20 ± 7 vs 4 ± 1 μg/kg; $p = 0.004$) and nicardipine (13 ± 5 vs 2 ± 1 μg/kg; $p = 0.02$), and required more fentanyl (39 ± 8 vs 19 ± 3 μg/kg; $p = 0.005$).

Conclusions. Perioperative use of dexmedetomidine is associated with a significantly decreased incidence of ventricular and supraventricular tachyarrhythmias, without significant adverse effects.

(Ann Thorac Surg 2011;92:964–72)

Table 1. Demographic and Intraoperative Patient Characteristics

Variable[a]	Control (n = 20)	DEX (n = 32)	*p* Value
Age, mon	2.6 (0.13–158)	4.8 (0.16–198)	0.29
Weight, kg	3.9 (2.6–99)	5.3 (2.6–83)	0.23
Female sex	12 (60)	11 (34)	0.13
Aristotle score	7.3 (4.0–14.5)	8.5 (3.0–14.5)	0.24
Length of stay, day			
CICU stay[b]	4 (1–16)	4 (1–20)	0.59
Hospital stay[c]	7 (3–19)	8 (3–45)	0.63
Intraoperative data			
CPB time, min	79 ± 9	93 ± 7	0.12
Aortic clamp time, min	30 ± 6	33 ± 6	0.84
Circulatory arrest time, min	31 ± 6	26 ± 4	0.57
Modified ultrafiltration, mL/kg	71 ± 5	65 ± 3	0.14
Dexmedetomidine LD, μg/kg	. . .	1 ± 0.1	. . .
Dexmedetomidine, μg/kg/h	. . .	0.5	. . .
Sufentanil, μg/kg/min	0.33 ± 0.06	0.28 ± 0.03	0.40
Fentanyl, μg/kg	25 ± 7	20 ± 4	0.85
Midazolam, mg/kg	0.33 ± 0.06	0.33 ± 0.05	0.69
Caudal block,	2 (10)	6 (19)	0.65
Epinephrine, μg/kg/min	0.06 ± 0.01	0.07 ± 0.01	0.92
Milrinone, μg/kg/min	0.88 ± 0.17	0.87 ± 0.17	0.85
Methylprednisolone, mg/kg	28 ± 1	29 ± 1	0.4
Magnesium sulphate, mEq/kg	0.4 ± 0.1	0.4 ± 0.1	0.4

[a] Continuous data are presented as median (range) and mean ± standard error; categoric data are presented as number (%). [b] Length of stay from operation to CICU discharge. [c] Length of stay from operation to hospital discharge.

CICU = cardiac intensive care unit; CPB = cardiopulmonary bypass; DEX = dexmedetomidine; LD = loading dose.

Table 3. Patients With Arrhythmias and Arrhythmia Episodes

Variable	Control	DEX	*p* Value
Tachyarrhythmias, No. (%)	10 (50)	2 (6)	0.001[a]
Episodes, No.			
Ventricular tachycardia	6	. . .	
Atrial ectopic tachycardia	3	. . .	
Junctional ectopic tachycardia	2	. . .	
Reentrant SVT	1	2	
Atrial bigeminy	1	. . .	
Junctional accelerated rhythm	. . .	1	
Bradyarrhythmias, No. (%)	2 (10)	2 (6)	0.85
Episodes, No.			
Complete AV block	1	2	
Sinoatrial node dysfunction	1	. . .	

[a] Statistically significant.

AV = atrioventricular; DEX = dexmedetomidine; SVT = supraventricular tachycardia.

Ann Thorac Surg
2011;92:964–72

Table 6. Cardiorespiratory and Sedation and Analgesic Requirements During the Postoperative Period

Variable[a]	Control (n = 20)	DEX (n = 32)	*p* Value
Intubated	13 (68)	20 (62)	0.49
Duration of intubation, days	3.5 ± 0.6	3.0 ± 0.8	0.5
Mortality	0	1 (3)	0.8
Inotropic/vasotropic support			
Epinephrine, μg/kg	0.56 ± 0.16	0.86 ± 0.25	0.38
Patients taking epinephrine	10 (53)	14 (44)	0.63
Milrinone, μg/kg	49 ± 5	37 ± 4	0.06
Patients taking milrinone	20 (100)	32 (100)	NA
Nitroprusside, μg/kg	20 ± 7	4 ± 1	0.004[b]
Patients taking nitroprusside	11 (58)	9 (28)	0.07
Nicardipine, μg/kg	13 ± 5	2 ± 1	0.02[b]
Patients taking nicardipine	6 (32)	9 (28)	0.9
Sedatives/analgesics			
Dexmedetomidine, μg/kg/h		0.76 ± 0.04	
Dexmedetomidine duration, hrs		38 ± 4	
Fentanyl, μg/kg	39 ± 8	19 ± 3	0.005[b]
Patients taking fentanyl	16 (84)	18 (56)	0.08
Morphine, mg/kg	0.03 ± 0.01	0.02 ± 0.01	0.7
Midazolam, mg/kg	0.09 ± 0.02	0.07 ± 0.02	0.55
Lorazepam, mg/kg	0.02 ± 0.01	0.02 ± 0.01	0.7
Chloral hydrate, mg/kg	25 ± 6	16 ± 4	0.23

[a] Continuous data are shown as mean ± standard error; categoric data as number (%). [b] Statistically significant.

DEX = dexmedetomidine; NA = not applicable.

Pro: Dexmedetomidine Should Be Used for Infants and Children Undergoing Cardiac Surgery

R. Blaine Easley, MD,* and Joseph D. Tobias, MD†

THE LANDMARK WORK OF Anand et al[1,2] has documented the potential impact of anesthetic practice on morbidity and mortality after surgery for congenital heart disease. Nearly 20 years later, the anesthetic management of pediatric patients with congenital heart lesions is a delicate balance between the successful ablation of the harmful perioperative stress responses and the potential untoward sequelae of effective analgesia and sedation including prolonged ventilator dependence, adverse end-organ effects, and iatrogenic tolerance and dependency syndromes. Anesthesiologists remain intimately involved in the perioperative care of children undergoing cardiac surgery and continue to seek new modalities of perioperative analgesia and sedation in an attempt to limit these complications. Dexmedetomidine increasingly has been used by anesthesiologists and intensive care physicians to provide effective pain relief, sedation, and anxiolysis in critically ill infants and children while mitigating the adverse effects of ventilator and opioid dependency. Given its beneficial physiologic effects and limited adverse effect profile, there may be several potential applications for dexmedetomidine in the perioperative care of infants and children with congenital heart disease.

PHARMACOLOGY

Dexmedetomidine, a centrally acting α_2-adrenergic agonist, has similar physiologic properties to clonidine. However, when compared with clonidine, it has a higher specificity ratio for the α_2- versus the α_1-adrenergic receptor than clonidine (1,600:1 *v* 200:1, respectively) and a shorter half-life (2-3 hours *v* 8-12 hours for clonidine). Dexmedetomidine acts through a G-coupled protein receptor, decreasing intracellular adenylyl cyclase, cAMP, and cAMP-dependent protein kinase leading to dephosphorylation of ion channels. This results in reduced norepinephrine turnover and decreased central sympathetic outflow from the medullary vasomotor center with sympatholysis, decreased heart rate, and blood pressure. In addition, dexmedetomidine decreases renin and vasopressin levels, resulting in increased diuresis. The central stimulation of dexmedetomidine on parasympathetic outflow and inhibition of sympathetic outflow from the locus ceruleus lead to increased activity of inhibitory neurons of the γ-aminobutyric acid system, resulting in sedation and anxiolysis. Dexmedetomidine also inhibits the release of substance P from the dorsal horn of the spinal cord, leading to primary analgesic effects and potentiation of opioid-induced analgesia.[3] Through these mechanisms, dexmedetomidine provides sedation and anxiolysis, lowers the minimum alveolar concentration for inhalation agents,[4] decreases perioperative opioid requirements, decreases shivering responses,[5] and reduces the incidence of emergence delirium/agitation.[6] Currently, dexmedetomidine is Food and Drug Administration (FDA) approved only for short-term sedation (<24 hours) during mechanical ventilation of adult patients in an intensive care unit (ICU) setting. There is currently no FDA-approved usage in children. Despite this fact, there are more than 1,000 pediatric-aged patients reported in the literature who have received dexmedetomidine for a variety of clinical applications in and out of the operating room. The following discussion reviews the published reports of dexmedetomidine in infants and children with special emphasis on its use in patients with congenital heart disease.

CLINICAL EXPERIENCE WITH DEXMEDETOMIDINE

Previous reports in the pediatric population have shown the efficacy of dexmedetomidine as the sole agent for sedation during noninvasive radiologic procedures (computed tomography scan or magnetic resonance imaging). Although there are only 2 anecdotal reports in the literature of patients with cardiac lesions undergoing imaging,[7,8] 4 prospective studies of infants and children have shown it to be an effective agent in achieving and maintaining sedation during noninvasive diagnostic imaging procedures. The patients studied maintained spontaneous ventilation and required fewer doses of rescue medication (additional doses of medication to maintain immobility) compared with other sedation regimens including propofol or midazolam-based techniques. Dexmedetomidine also was effective in patients when other agents (midazolam and/or chloral

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Key words: dexmedetomidine, congenital heart disease, pediatric cardiac anesthesia, pediatric critical care

Table 1. Dexmedetomidine Dosing Regimen

Noninvasive procedures (cardiac MRI/CT)		
Loading dose:	Dexmedetomidine:	1-2 μg/kg IV over 10 minutes
Infusion:	Dexmedetomidine:	Following bolus completion, 0.5 μg/kg/hour IV
Rescue sedative:	Ketamine	1 mg/kg IV
	or midazolam:	0.1 mg/kg IV
Invasive procedures (cardiac catheterization)		
Loading dose:	Ketamine:	2 mg/kg IV with
	Dexmedetomidine:	1 μg/kg IV over 3 minutes
Infusion:	Dexmedetomidine:	2 μg/kg/hour IV for 30 minutes, then 1 μg/kg/hour
Rescue sedative:	Ketamine:	1 mg/kg IV bolus for movement/pain
Intraoperative procedures (cardiac surgery)		
Loading dose:	None	
Infusion:	Dexmedetomidine:	0.5 μg/kg/hour IV
Postoperative sedation (mechanical ventilation)		
Loading dose:	Dexmedetomidine:	0.5 to 1 μg/kg IV over 10-15 minutes (optional)
Infusion:	Dexmedetomidine:	0.5 to 1.5 μg/kg/hour IV

Pediatr Cardiol
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ORIGINAL ARTICLE

Is the Addition of Dexmedetomidine to a Ketamine–Propofol Combination in Pediatric Cardiac Catheterization Sedation Useful?

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In conclusion, adding dexmedetomidine to a ketamine–propofol combination led to a reduction in the need for airway intervention and a decrease in movement during both local anesthetic infiltration and the procedure. Adding dexmedetomidine decreased the total consumption of propofol and shortened the recovery time.

Dexmedetomidine sedation for pediatric post-Fontan procedure patients

Natusko Tokuhira, MD; Kazuaki Atagi, MD; Hideki Shimaoka, MD; Atsushi Ujiro, MD; Yasunori Otsuka, MD; Michael Ramsay, MD, FRCA

Objective: The hemodynamic, respiratory, and sedative effects of dexmedetomidine (DEX) for pediatric patients post-Fontan surgery.

Design: Retrospective.

Setting: Single institutional intensive care unit.

Participants: Fourteen patients undergoing Fontan-type surgery.

Result: A retrospective review was conducted on 14 pediatric patients who had undergone a Fontan procedure for congenital heart disease. A vital component of postoperative management of these patients is to prevent an increase in pulmonary vascular resistance (PVR) that may lead to a serious reduction in cardiac output. DEX an alpha-2 adrenergic receptor agonist might offer an advantage over current sedation methods in preventing a rise in PVR. Nine patients received sedation with DEX and five patients in a control group were administered standard regimens of sedation and analgesia. The DEX group exhibited no evidence of an increased partial pressure of arterial carbon dioxide postoperatively as opposed to the control group. This lack of respiratory depression made the DEX group less likely to increase their PVR. However, the DEX group did experience a significant incidence of bradycardia that required the use of a cardiac pacemaker.

Conclusions: The results of this retrospective review of the role of DEX in the management of the post-Fontan surgical pediatric patient indicate some potential advantages. (Pediatr Crit Care Med 2009; 10:207–212)

KEY WORDS: pediatric critical care; postoperative sedation; alpha-2 agonists; dexmedetomidine; congenital heart surgery; Fontan procedure; hemodynamics; pulmonary vascular resistance

Table 2. Patient demographics in both groups

	Dexmedetomidine Group	Control Group
Patient	9	5
Age (yrs)	1.3 yrs (14 mos–11 yrs)	1.8 yrs (13 mos–15 yrs)
Sex (M:F)	6:3	4:1
Weight (kg)	8.2 (8.0–26.8)	9.3 (7.1–34.5)
Diagnosis	PPA (4), TA (1), DORV (1), SV (1), VSD (1), HLHS (1)	DORV (4), SV (1)

Data are median (range), or number of patients. No significant differences between the groups were present.

PPA, pure pulmonary artesia; TA, tricuspid atresia; DORV, double outlet right ventricle; SV, single ventricle; VSD, ventricular septal defect; HLHS, hypoplastic left heart syndrome.

Table 3. Postopertative data comparison between groups

	DEX Group	Control Group
Duration in intensive care unit (hrs)	87.3 ± 49.2	73.4 ± 37.9
Duration of DEX infusion (hrs)	84.2 ± 50.9	None
Duration of mechanical ventilation (hrs)	10.4 ± 5.5	11.1 ± 8.3
Analgesic/sedative		
IV continuous (except for DEX) (n)	0	1
IV push during intubation (n)	2	4
IV push until 24 hrs after extubation (n)	2	4
Pacing (n)	6	0

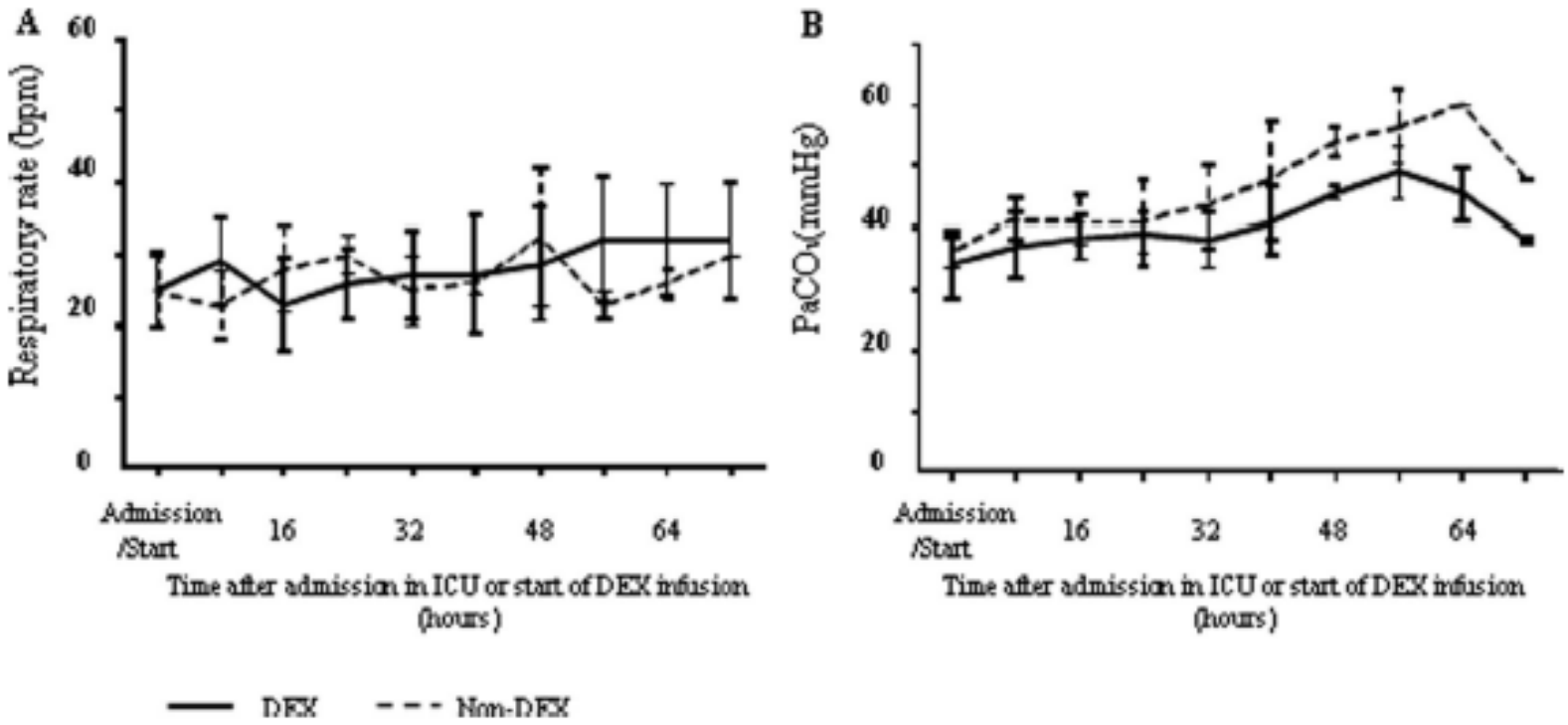
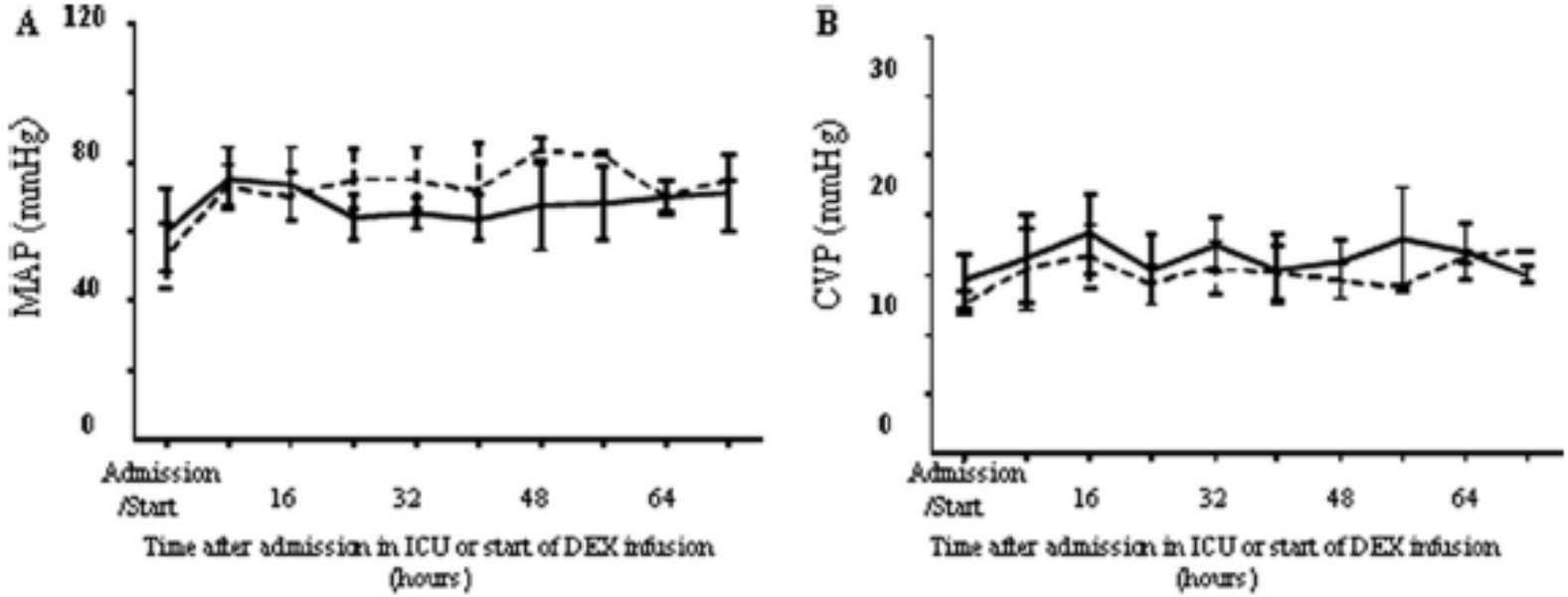


Figure 2. Respiratory profiles; respiratory rate and $Paco_2$ (mean ± SD). The DEX group did not show respiratory depression, and tended to have lower $Paco_2$ levels than the non-DEX group (not significant). *ICU*, intensive care unit; *DEX*, dexmedetomidine.



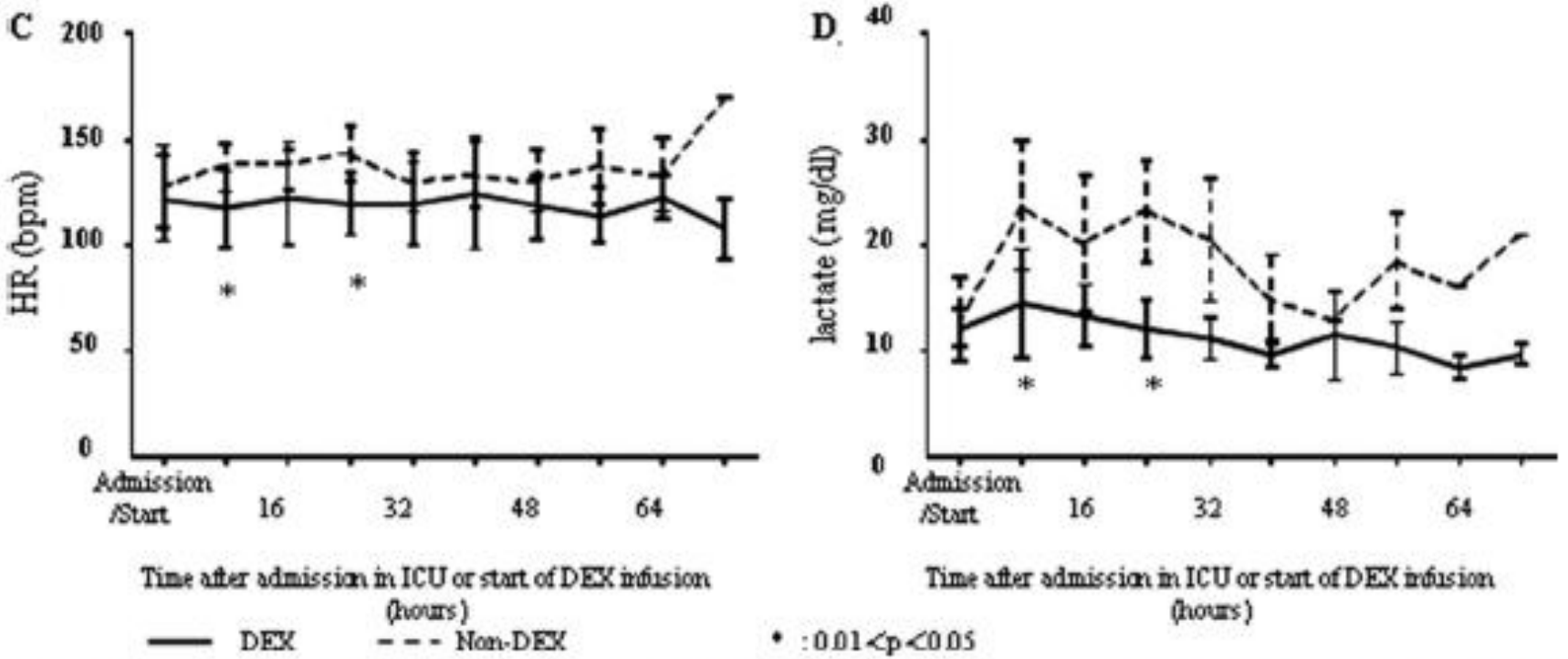


Figure 3. Hemodynamic profiles (*). The mean atrial pressure (*MAP*) and central venous pressure (*CVP*) were stable in both groups. Heart rate (*HR*) was lower in the DEX group with pacing, and lactate level was also lower in the DEX group. HR (mean ± SD). *ICU*, intensive care unit; *DEX*, dexmedetomidine.

This review indicates that DEX potentially might prevent elevations in PVR by providing sedation and analgesia without respiratory depression. Caution has to be emphasized in that hypotension and bradycardia may occur in the post-surgical patient and that treatment should be readily available.

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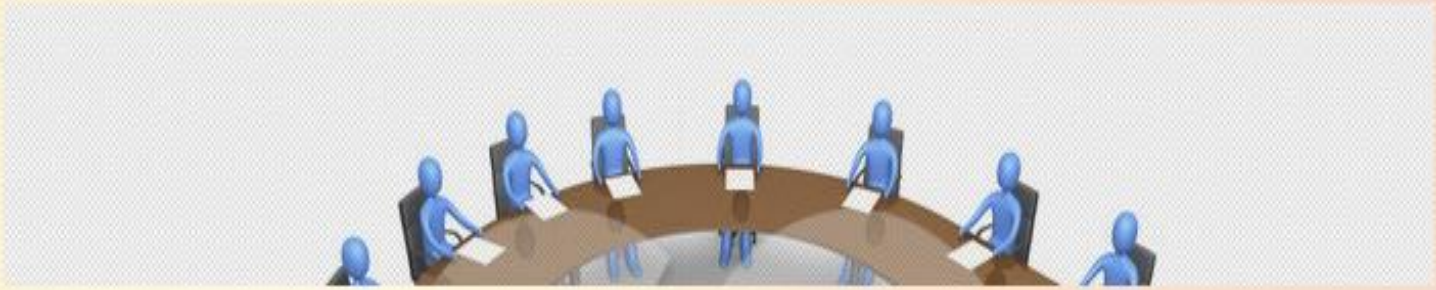

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