

DR GEORGE A CHALKIADIS (Orcid ID : 0000-0002-5613-1654)

DR SUSAN M GOOBIE (Orcid ID : 0000-0001-8697-089X)

Editor : Brian Anderson

Article type : Editorial

Manuscript Title:

Are Opioids Pediatric Anesthesiologists' Sword of Damocles?

With great power comes great responsibility and risk.

Article Category:

Editorial

Authors:

George Chalkiadis 1, Susan Goobie 2, Suellen Walker 3

Affiliations:

George Chalkiadis:

1. Department of Paediatric Anaesthesia and Pain Management, Royal Children's Hospital, Melbourne, Australia
2. Murdoch Children's Research Institute, Melbourne, Australia
3. University of Melbourne, Melbourne, Australia

Susan Goobie:

1. Department of Anesthesiology, Critical Care and Pain Medicine, Boston Children's Hospital, Boston, USA
2. Harvard Medical School, Boston, USA

Suellen Walker:

1. Clinical Neurosciences, UCL GOS Institute of Child Health, London, UK

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/PAN.13659](https://doi.org/10.1111/PAN.13659)

This article is protected by copyright. All rights reserved

2. Department of Anaesthesia and Pain Medicine, Great Ormond St Hospital NHS Foundation Trust, London, UK

Author for Correspondence:

George Chalkiadis, Department of Paediatric Anaesthesia and Pain Management, 50 Flemington Rd, Parkville, Victoria 3052, Australia. Telephone: +61393455233, Fax: +61393456003, Email: george.chalkiadis@rch.org.au

Should paediatric anaesthesiologists change their practice regarding opioid use in children perioperatively? Societal concerns regarding the “opioid epidemic” have led some anaesthesiologists **to advocate for** opioid-free anesthesia; this is not the solution to that problem.

There are numerous factors that underpin the safe and effective use of opioids for perioperative pain in children including the availability of different opioid preparations, protocols for titration and delivery systems such as patient-controlled analgesia, improved knowledge about the developmental pharmacodynamic and pharmacokinetic profiles of opioids, and increasing evidence related to the relative benefit and harm in different patient populations and clinical settings. The latter are well summarised in the Society for Pediatric Anesthesia (SPA) evidence-based recommendations for perioperative use of opioids in children¹ in this issue of *Pediatric Anesthesia*.

It is an undisputed fact that adequate perioperative analgesia is essential to minimise acute stress responses and physiological instability, and facilitate mobilisation and recovery. There is increasing awareness of potential long-term effects of pain and tissue injury on developing pain pathways, and the risk of persistent post-surgical pain following major surgery in later childhood². The benefits of multimodal analgesia techniques to improve analgesia and/or minimise opioid requirements and dose-related side-effects are well-established and outlined in the SPA document and in previous international evidence-based guidelines.^{1,3,4} However, there is a need to distinguish between ‘opioid-sparing’ and ‘opioid-free’ anesthesia. Avoiding opioids at the cost of uncontrolled pain is unacceptable. Alternative analgesia modalities may not be adequate or feasible for all patients, and the use of opioids remains an essential part of pain management regimens for many children.⁵

Increased numbers of opioid-related deaths in recent years have prompted some to coin the terms “opioid crisis” and “opioid epidemic”, with significant political and media attention focussing on the

potential for misuse or diversion of prescription analgesics. Increases in opioid-related deaths have been reported in children of all ages, particularly related to heroin and illicit synthetic opioids in 15-19 year olds,⁶ but the limitations of data indicating an 'epidemic' have been recently summarised.⁷ This is not to underplay the public health issues related to opioid misuse, the potential impact on care and well-being of children and/or families with substance abuse disorders,⁸ or the lack of childproof packaging and risk of accidental overdose with access to drugs prescribed for adults in the household.⁶ However, health care professionals or families should not fear appropriate medical use of opioids. The evidence that use of intraoperative opioids causes, or is even associated with long-term abuse in adults is scant and, to our knowledge, completely lacking in children. It is certainly inappropriate to propose a change of intra-operative anesthesia practice without such evidence. We could also find no evidence that judicious and responsible prescribing of opioids for children in the acute postoperative period when acetaminophen and NSAIDs provide insufficient analgesia, leads to substance use disorder.

There is no doubt that opioids can be associated with significant and potentially life-threatening adverse effects. Regular assessment with titration of analgesia against individual response is an essential component of ongoing perioperative care, particularly in those at increased risk of respiratory depression (e.g., preterm-born neonates, obstructive sleep apnoea, co-morbidities, and potential sedative adjunct interactions).^{9,10} The dose and duration of each drug modality should be matched to the type, time-course and severity of pain. Reports of respiratory depression following use of oral morphine for a relatively brief procedure in neonates,¹¹ and worse neurodevelopmental outcome following infusion of morphine contributing to hypotension in ventilated neonate¹² highlight the need for judicious use and monitoring when opioids are used in high-risk populations. They should not be misinterpreted as a lack of safety or efficacy of opioids for perioperative pain.

An important potential source of prescription opioids is discharge medication. Local governance and education systems need to ensure that: discharge prescriptions are written by medical staff with adequate training and knowledge that should include psychosocial risk assessment; an appropriate formulation, dose, and limited number of doses are dispensed³; and parents have instructions for the safe storage of opioids and safe disposal of unused medication. This is an opportunity for pediatric anesthesiologists to continue to lead in ensuring responsible prescribing and dispensing of all analgesics both within the hospital and upon discharge. Improved knowledge of expected pain trajectories after commonly performed surgeries helps guide how much, what type and for how long analgesia will be necessary. It is desirable to provide regular follow-up of post-surgical patients, in

particular those undergoing surgeries where postoperative pain is expected to last several weeks and where adequate analgesia may facilitate rehabilitation and functional restoration. In line with this, secure electronic and real-time prescribing¹³ may help identify aberrant pain outcomes and inappropriate analgesic use or prescription to facilitate earlier intervention.

The SPA guidelines for the perioperative use of opioids support the appropriate and responsible use of opioids by pediatric anaesthesiologists for pediatric surgical patients. The opioid *sword of Damocles* places great power in the hands of the pediatric anesthesiologist; it can be appropriately drawn with noble purpose and without undue fear provided the potential risks are recognized, respected and managed responsibly.

Disclosure Statement:

Susan Goobie and Suellen Walker are editors of Pediatric Anesthesia.

Ethics: Not applicable

Funding: None received

Acknowledgements: The signatories have read the content of this editorial and have agreed to endorse its content.

References:

1. Cravero J, Agarwal R, Berde C, et al. The Society for Pediatric Anesthesiology recommendations for the use of opioids in children during the perioperative period. *Pediatric Anesthesia*. 2019;in press.
2. Rabbitts JA, Fisher E, Rosenbloom BN, Palermo TM. Prevalence and Predictors of Chronic Postsurgical Pain in Children: A Systematic Review and Meta-Analysis. *J Pain*. 2017;18(6):605-614.
3. Schug SA, Palmer GM, Scott DA, Halliwell R, Trinca J, Medicine. *Acute Pain Management: Scientific Evidence (4th Edition)*. Melbourne: ANZCA & FPM; 2015.
http://fpm.anzca.edu.au/documents/apmse4_2015_final

4. Association of Paediatric Anaesthetists of Great Britain and Ireland. Good practice in postoperative and procedural pain management, 2nd edition. *Paediatr Anaesth.* 2012;22 Suppl 1:1-79.
5. Veyckemans F. Opioid-free anaesthesia: Still a debate? *Eur J Anaesthesiol.* 2019;36(4):245-246.
6. Gaither JR, Shabanova V, Leventhal JM. US National Trends in Pediatric Deaths From Prescription and Illicit Opioids, 1999-2016. *JAMA Netw Open.* 2018;1(8):e186558.
7. Krane EJ, Weisman SJ, Walco GA. The National Opioid Epidemic and the Risk of Outpatient Opioids in Children. *Pediatrics.* 2018;142(2).
8. Feder KA, Letourneau EJ, Brook J. Children in the Opioid Epidemic: Addressing the Next Generation's Public Health Crisis. *Pediatrics.* 2019;143(1).
9. Howard RF, Lloyd-Thomas A, Thomas M, et al. Nurse-controlled analgesia (NCA) following major surgery in 10,000 patients in a children's hospital. *Paediatr Anaesth.* 2010;20(2):126-134.
10. Jay MA, Thomas BM, Nandi R, Howard RF. Higher risk of opioid-induced respiratory depression in children with neurodevelopmental disability: a retrospective cohort study of 12 904 patients. *Br J Anaesth.* 2017;118(2):239-246.
11. Hartley C, Moultrie F, Hoskin A, et al. Analgesic efficacy and safety of morphine in the Procedural Pain in Premature Infants (Poppi) study: randomised placebo-controlled trial. *Lancet.* 2018;392(10164):2595-2605.
12. Hall RW, Kronsberg SS, Barton BA, Kaiser JR, Anand KJ. Morphine, hypotension, and adverse outcomes among preterm neonates: who's to blame? Secondary results from the NEOPAIN trial. *Pediatrics.* 2005;115(5):1351-1359.
13. www2.health.vic.gov.au/public-health/drugs-and-poisons/safescript/about-safescript

Signatories:

Mark Alcock
Department of Anaesthesia and Pain Management
Queensland Children's Hospital
Brisbane, Australia

Brian J Anderson
Department of Anaesthesiology
University of Auckland
Auckland, New Zealand

Karin Becke
Department of Anesthesiology and Critical Care Medicine
Cnopf Children's Hospital/Hospital Hallerwiese
Nuernberg, Germany

Charles Berde
Department of Anesthesiology, Critical Care and Pain Medicine
Boston Children's Hospital
Boston, USA

Patrick K. Birmingham MD
Department of Anesthesiology
Ann & Robert H. Lurie Children's Hospital of Chicago
Northwestern University Feinberg School of Medicine
Chicago, USA

Adrian Bosenberg
Department of Anesthesiology and Pain Management
Seattle Children's Hospital
Seattle, USA

Fiona Campbell
Department of Anesthesia and Pain Medicine
The Hospital for Sick Children
University of Toronto

Toronto, Canada

Joseph P. Cravero

Department of Anesthesiology, Critical Care, and Pain Medicine

Boston Children's Hospital

Harvard Medical School

Boston, USA

Andrew Davidson

Department of Paediatric Anaesthesia and Pain Management

Royal Children's Hospital

Murdoch Children's Research Institute

University of Melbourne

Jurgen C. de Graaff

Department of Anesthesiology

ErasmusMC - Sophia Children's Hospital

University Medical Center Rotterdam

Rotterdam, Netherlands

Thomas Engelhardt

Department of Anaesthesia

Royal Children's Hospital Aberdeen and School of Medicine

University of Aberdeen

Aberdeen, UK

Kenneth R. Goldschneider

Professor, Clinical Pediatrics and Anesthesia

Director, Pain Management Center

Cincinnati Children's Hospital Medical Center

Cincinnati, USA

Elliot J. Krane

Department of Anesthesiology, Perioperative and Pain Medicine

**Department of Pediatrics
Stanford University School of Medicine
Stanford Children's Health System
Palo Alto, USA**

**Stefan Lundeberg PhD
Pediatric Pain Treatment Service
Astrid Lindgren Children's Hospital
Karolinska University Hospital
Stockholm, Sweden**

**Greta M Palmer
Department of Paediatric Anaesthesia and Pain Management
Royal Children's Hospital
Murdoch Children's Research Institute
University of Melbourne
Melbourne, Australia**

**David Polaner
Department of Anesthesiology and Pain Management
Seattle Children's Hospital
University of Washington School of Medicine
Seattle, USA**

**Chandra Ramamoorthy
Department of Anesthesiology, Perioperative and Pain Medicine
Packhard Children's Hospital at Stanford
Palo Alto, USA**

**Navil F Sethna
Department of Anesthesiology, Critical Care and Pain Medicine
Boston Children's Hospital
Harvard Medical School**

Boston, USA

Mark Thomas

Department of Anaesthesia and Pain Medicine

Great Ormond St Hospital,

London, UK

Britta S von Ungern-Sternberg

Department of Anaesthesia and Pain Management

Perth Children's Hospital

University of Western Australia

Telethon Kid's Institute

Perth, Australia

Francis Veyckemans MD

Clinique d'Anesthésie Pédiatrique

Hôpital Jeanne de Flandre, CHRU de Lille,

Lille, France.

Laszlo Vutskits

Department of Pediatric Anesthesiology

University Hospitals of Geneva

Geneva, Switzerland

Gary A. Walco

Department of Anesthesiology and Pain Medicine

University of Washington School of Medicine

Seattle Children's Hospital

Seattle, USA

Steven J. Weisman,

Department of Anesthesiology and Department of Pediatrics

Children's Hospital of Wisconsin

Medical College of Wisconsin

Milwaukee, USA

Robert T. Wilder

Department of Anesthesiology and Perioperative Medicine

Mayo Clinic

Rochester, USA

Author Manuscript



Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:

Chalkiadis, G; Goobie, S; Walker, S

Title:

Are opioids pediatric anesthesiologists' sword of Damocles? With great power comes great responsibility and risk

Date:

2019-06-01

Citation:

Chalkiadis, G., Goobie, S. & Walker, S. (2019). Are opioids pediatric anesthesiologists' sword of Damocles? With great power comes great responsibility and risk. PEDIATRIC ANESTHESIA, 29 (6), pp.544-546. <https://doi.org/10.1111/pan.13659>.

Persistent Link:

<http://hdl.handle.net/11343/285945>

File Description:

Accepted version