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Mini-Review

Are Opioids Really Needed After Pediatric Surgery? A Mini-Review

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Abstract

Achieving adequate pain control during the post-operative period is imperative to the recovery of pediatric patients undergoing urologic surgery. While opioids are highly effective at post-operative pain management, their use comes at the cost of potential negative consequences including addiction, respiratory depression, and even death. Appropriate opioid stewardship is necessary to reduce the serious risks associated with pediatric opioid use. Option to reduce opioid use in ERAS protocols, directed provider education, use of non-opioid analgesics, regional anesthesia, and other supportive and system-based measures. Considering these alternatives can aid healthcare providers in delivering pain management that is both safe and effective.

Keywords: Opioid Analgesics; Urology; Pain Management; Opioids.

Introduction

Appropriate management of post-operative pain is critical to prevent complications and ensure a successful recovery. This is especially important in pediatric urology as children are likely to experience moderate to severe pain following laparoscopic, open, and endoscopic procedures [1]. Failure to adequately address pain may result in the development of chronic pain and negative behavioral consequences later in life [2]. Additionally, prolonged pain following urologic procedures can lead to increased anxiety for patients and parents, adversely affecting follow-up for patients with chronic conditions that require long-term care and frequent invasive procedures [1].

While opioids are the mainstay of postoperative pain management, their use may have negative consequences. The addictive potential of opioids can result in misuse, increasing the risk of serious side effects including respiratory depression and hypoxia. Death from opioid misuse has reached epidemic proportions in the United States and the pediatric mortality rate from prescription and illicit opioid use has increased by over 250% between 1999 and 2016 [3]. As surgical procedures are a common source of exposure to opioids for children and adolescents [4], health care providers are tasked with balancing the comfort and recovery of their patients against the harms of opioid over-prescribing. The goal of this article is to discuss the current state of opioid use, the problems associated with opioid use in children, and discuss non-opioid alternatives available to manage pain and improve overall safety in the pediatric population after urologic surgery.

The Current State of Opioid Use

The affinity for opioid use has likely been fueled by their efficacy in treating acute pain combined with prescriber concern for patient pain levels and comfort. It was previously thought that prescribing opioids in the acute postoperative period presented little risk to patients with early literature reporting that addiction was rare in patients treated with opioids [5]. Since then, increasing amounts of evidence have documented the short- and long-term risks of using opioids to treat pain, and in 2017 the United States Department of Health and Human Services declared the national opioid crisis to be a public health emergency. Even with growing awareness of the risks associated with opioids, a majority of pediatric urologist's report feeling comfortable prescribing opioids

after urologic surgery [1].

The most used opioids to treat acute pain in children are morphine, hydromorphone, fentanyl, oxycodone, and hydrocodone. Morphine has multiple routes of administration making it easy to use in many circumstances, with parenteral administration frequently used in the acute inpatient setting after surgery [6,7]. Fentanyl is more potent than morphine and is commonly used for procedural sedation for its rapid onset and short duration [8]. Oxycodone and hydrocodone are most commonly used as oral medications for treating acute pain once patients are discharged home [9].

What are the Problems with Opioid Use?

Though highly effective at reducing pain, opioids have several serious risks associated with their use. The most common short-term adverse effects include nausea, vomiting, sedation, respiratory depression, decreased gastrointestinal motility, and constipation [10,11]. These negative side effects can worsen due to genetic variations in drug metabolism. For instance, children with ultra-rapid CYP2D6 metabolism are faced with an increased risk of life-threatening respiratory depression and even death [12].

Opioid exposure in children may also have long-term risks extending into adulthood. Using prescription opioids in higher dosages or for longer time periods has been linked to an increased risk of addiction, opioid use disorder, overdose, and death later in life [13-15]. Despite patient-reported pain remaining steady, opioid prescription rates have dramatically increased with the number of opioids prescribed in 2017 six times those prescribed in 1999 [16]. The opioid epidemic is often associated with adults; however, this crisis also affects children. Pediatric deaths related to opioid misuse have risen more than 2.5 times since 1999 [3].

Opioid over-prescribing is one contributing factor to the opioid crisis. Patients are often prescribed more opioids than they need after surgery [17-19]. This poses a serious risk to children as even when patients and/or families take medications correctly, a surplus of household opioids can progress to unintentional ingestion by young children. Accidental ingestion was the primary reason for overall childhood opioid exposure between 2000-2015 [20-22]. Leftover household medications also increase opioid availability to teenagers, leading to increased risk for intentional or persistent opioid use. According to National Poison Control, 71.5% of teenage opioid exposures from 2000-2015 were related to suicide, abuse, or misuse [22]. A reduction in opioid prescriptions is needed to decrease the number of opioids available in a household at any given time.

In addition, prescribing opioids to pediatric patients is associated with future opioid misuse even among patients with no prior drug experience and those who disapproved of illegal drug use [23,24]. Filling multiple opioid prescriptions is more likely in adolescents prescribed opioids for postsurgical pain management compared to adolescents prescribed opioids for nonoperative pain. In one study, 4.8% of opioid-naïve adolescents and young adults continued to fill opioid prescriptions between 90-180 days after operations. The matched control group of nonsurgical patients only showed persistent opioid use at a rate of 0.1%. The likelihood of future opioid misuse is significantly increased with persistent opioid use after surgery [25]. Thus, postoperative pain management may provide a door to future opioid dependence in children and young adults.

Appropriate opioid stewardship among physicians is necessary to reduce the serious risks associated with pediatric opioid use. One study found physicians were the source of opioids in 11-38% of opioid misuse cases in children and adolescents. Furthermore, 75% of young adults who use intravenous opioids reported opioid misuse that began with prescription opioids [26]. Of adolescents with nonfatal overdoses, 11% have been prescribed an opioid in the past year [10]. Pediatric urologists and other healthcare providers play a crucial role in maintaining safe opioid prescribing practices.

Ways to Reduce Opioid Use

Opioid prescribing practices for children undergoing surgical procedures vary greatly and there is no general agreement on best practices for managing acute pain after urologic procedures [27]. Acknowledging the importance of adequate pain control in children while addressing the consequences associated with opioid use creates a unique challenge for healthcare providers when managing acute surgical pain in pediatric patients. Fortunately, there are several ways to change opioid prescribing patterns as well as pharmacological and non-pharmacological treatment modalities for the management of post-operative pain that can reduce opioid exposure and prevent both the immediate and long-term negative consequences associated with opioid use.

1. Changing prescribing patterns

One way to reduce opioid exposure is to reduce the number of opioids prescribed. Carolan et al found that opioids were not routinely needed in 72% of pediatric patients after urologic surgery and that the strongest predictor for requiring postoperative opioids was age. Specifically, children undergoing penile and endoscopic procedures did not regularly require opioids [28].

Protocol-driven changes to opioid prescribing patterns are another way to potentially reduce opioid exposure after surgery. Enhanced recovery after surgery (ERAS) protocols are a multimodal approach aimed at improving surgical outcomes and reducing hospital stays, post-surgical complications, and healthcare costs. These protocols are often implemented at a hospital-wide level and many ERAS protocols have a focus on reducing opioid use by utilizing multiple classes of analgesics in a synergistic manner

to enhance pain management after various procedures [29]. Many studies have shown that opioid prescriptions significantly decrease post-discharge when ERAS protocols are implemented with one study showing up to a 40% reduction in opioid prescribing outcomes [30,31]. This suggests that a system-wide approach to pain management after urologic surgery can lead to successful reductions in opioid prescribing rates.

Recent evidence has also shown that directed provider education effectively reduces opioid prescriptions after pediatric urologic surgery [27,28]. Mittal et al found that utilizing a standardized pain management protocol after outpatient urologic surgery, which included adequate prescriber education, lead to a reduction in the number of patients receiving opioid prescriptions from 43.9% to 2.3% [27]. Carolan et al reported a similar trend with fewer pediatric patients receiving opioids after urologic surgery (55% to 28%) following provider education on overall prescribing data and which patients required opioids after surgery [28].

Changes to opioid prescribing patterns can also be affected by policies made at the regional, state, or national levels. There are several reports of successful reductions in outpatient opioid prescriptions in states where government mandates limit how opioids can be prescribed to minors [32,33]. While these policies do not necessarily improve pain control or reduce the need for opioids, they may reduce the overprescribing of opioids in cases when they are not needed, in turn decreasing the potential for opioid abuse and misuse. Collectively, this information is promising given that reductions in post-operative opioid prescriptions have not resulted in increased rates of negative post-operative pain outcomes such as pain scores, emergency room or urgent care visits for pain, or phone calls to providers regarding pain [27, 31, 34].

2. Non-Opioid Analgesia

An important strategy for reducing opioid exposure is the use of non-opioid analgesics such as acetaminophen, non-steroidal anti-inflammatory agents (NSAIDs), gabapentinoids, adrenergic agents, and some antidepressants [35,36]. NSAIDs and acetaminophen in both enteral and parenteral administrations have been shown to be successful at treating postoperative pain and reducing opioid use [1,37,38]. Prior studies have also shown that pain may be managed entirely with non-opioid analgesics after orchiopexy and inguinal hernia repair [1, 39]. Additionally, NSAIDs and acetaminophen can be used in combination as an alternative to opioids. These two medications have greater efficacy in combination than when used alone [40].

In addition, there are several studies documenting the safety and efficacy of ketorolac for postoperative pain control in children undergoing urologic procedures. Ketorolac is an NSAID that can be administered parenterally, making it an ideal choice for treating pain in the acute postoperative period. Although many urologists report feeling comfortable prescribing ketorolac to children after surgery, and despite its proven benefits for treating pain, it is still infrequently used [1,41,42]. NSAIDs are relatively safe to use in children, especially when compared to the risks of opioids, however, they are associated with potential renal injury and therefore their use may be limited in patients with renal or upper urinary tract conditions.

Other non-opioid pharmacologic agents that can be used to treat postoperative pain include dexmedetomidine, a selective a2-adrenergic agonist, and ketamine, an N-methyl-D-aspartate (NMDA) receptor antagonist. Dexmedetomidine has been shown to decrease postoperative pain and reduce opioid consumption when used in combination with other non-opioid analgesics [43,44]. Both dexmedetomidine and ketamine have been associated with fewer opioid-related complications such as respiratory and cardiovascular suppression while effectively treating acute postoperative pain [43,45,46].

3. Regional Anesthesia

Regional anesthesia is another modality for pain control that should be utilized in children undergoing urologic surgery to aid in the reduction of opioid use. This may include peripheral nerve blocks or neuraxial analgesia in the form of spinal or epidural injections. Regional anesthesia is not a novel technique as inguinal nerve blocks are a common regional anesthesia technique used by many pediatric urologists and anesthesiologists. There are many different methods of regional anesthesia and different options depending on the procedure. For example, in surgical cases for ureteral implantation, some providers choose local analgesia and others choose epidural anesthesia [1].

Spinal anesthesia is a method of neuraxial regional anesthesia involving intrathecal administration of anesthetic agents. Spinal anesthesia combined with continuous infusion of local anesthetic agents through a caudal catheter has been shown to reduce or avoid the use of opioids in the perioperative period for many procedures including ureteral implantations, ureterocele excision, ureteral repairs, hypospadias repairs, genitoplasty, and pyeloplasty [47]. Caudal blocks are another common technique that can effectively treat post-operative pain and reduce opioid use after urologic procedures. This method of regional anesthesia involves an injection of anesthetic agents into the sacral epidural space [48-50]. The effects of regional anesthesia can be augmented with drugs such as clonidine, ketamine, or midazolam, which have all been shown to significantly increase the duration of analgesia [51].

When neuraxial anesthesia is not necessary, peripheral nerve blocks may be used. For example, penile blocks can be used to manage pain without the need for opioids or further regional interventions in children undergoing hypospadias repair [52].

There is also evidence that the use of peripheral catheters to deliver continuous local analgesia can reduce opioid use. Continuous infusion of ropivacaine at incision sites has been shown to reduce opioid use by up to two-thirds after lower urinary tract reconstructive surgery. This technique may be helpful in pediatric patients undergoing complex urologic surgeries with longer expected hospital stays. It may also be a reasonable alternative for many pediatric urology patients with conditions such as spina bifida and other forms of spinal dysraphism who are not able to receive neuraxial anesthesia [53].

Non-Pharmacologic Options for Pain Control

In addition to non-opioid and regional analgesia, there are several non-pharmacologic methods for managing postoperative pain that may reduce the need for opioids. These include techniques to manage preoperative anxiety, implementing the support of Certified Child Life Specialists, and emphasizing caretaker education on pain management at home. Each of these methods has been associated with reduced pain scores in the postoperative period [54-56]. Other non-pharmacological methods to reduce postoperative pain include comfort measures such as swaddling, warm and/or cold compresses, distraction techniques, and family support. Finally, with the adoption of less invasive surgical techniques for pediatric urologic surgery, there may be a further reduction in the need for postoperative opioids.

Conclusions

Achieving adequate pain control during the post-operative period is imperative to the recovery of pediatric patients undergoing urologic surgery. For decades, opioids have been the primary agent prescribed for treating this population, but are they really needed? Although they are highly effective at treating acute pain in the postoperative period, opioid use comes at the cost of serious negative consequences including addiction, respiratory depression, and even death. To reduce opioid exposure and improve opioid prescribing patterns, it is important to consider a layered approach to pain management in the post-operative period for children undergoing urologic surgery. There are multiple strategies including ERAS protocols, directed provider education, non-opioid analgesics, regional anesthesia, and other supportive and system-based measures that have been proven to reduce opioid use. Though current guidelines regarding opioid prescribing for children are limited, improving these clinical practice guidelines, and considering non-opioid alternatives can aid healthcare providers in delivering pain management that is both safe and effective.

References

1. Morrison K, Herbst K, Corbett S, Herndon CD (2014) Pain management practice patterns for common pediatric urology procedures. Urology 83: 206-210.
2. Lovich-Sapola J, Smith CE, Brandt CP (2014) Postoperative pain control. Surg Clin North Am 95: 301-318.
3. Gaither JR, Shabanova V, Leventhal JM (2018) US National Trends in Pediatric Deaths From Prescription and Illicit Opioids, 1999-2016. JAMA Netw Open 1: e186558.
4. Ward A, De Souza E, Miller D, Wang E, Sun EC, et al. (2020) Incidence of and Factors Associated With Prolonged and Persistent Postoperative Opioid Use in Children 0-18 Years of Age. Anesth Analg 131: 1237-1248.
5. Porter J, Jick H (1980) Addiction rare in patients treated with narcotics. N Engl J Med 302: 123.
6. Dampier CD, Setty BN, Logan J, Ioli JG, Dean R (1995) Intravenous morphine pharmacokinetics in pediatric patients with sickle cell disease. J Pediatr 126: 461-467.
7. Boric K, Dosenovic S, Kadic AJ, Batinic M, Cavar M, et al. (2017) Interventions for postoperative pain in children: An overview of systematic reviews. Paediatr Anaesth 27: 893-904.
8. Badina L, Norbedo S, Barbi E (2006) Procedural sedation and analgesia in children. Lancet 367: 1900-1901.
9. Fischer B, Argento E (2012) Prescription opioid related misuse, harms, diversion and interventions in Canada: a review. Pain Physician 15: ES191-203.
10. Harbaugh CM, Gadepalli SK (2019) Pediatric postoperative opioid prescribing and the opioid crisis. Curr Opin Pediatr 31: 378-385.
11. Chung CP, Callahan ST, Cooper WO, Dupont WD, Murray KT, et al. (2018) Outpatient Opioid Prescriptions for Children and Opioid-Related Adverse Events. Pediatrics 142: e20172156.
12. Packiasabapathy S, Sadhasivam S (2018) Gender, genetics, and analgesia: understanding the differences in response to pain relief. J Pain Res 11: 2729-2739.
13. Centers For Disease Control And Prevention Public Health Service U S Department Of Health And Human Services (2016) Guideline for Prescribing Opioids for Chronic Pain. J Pain Palliat Care Pharmacother 30: 138-140.
14. Crystal DT, Blankensteijn LL, Ibrahim AMS, Brownstein GM, Reed LS, et al. (2020) Quantifying the Crisis: Opioid-Related Adverse Events in Outpatient Ambulatory Plastic Surgery. Plast Reconstr Surg 145: 687-695.
15. Seth P, Rudd RA, Noonan RK, Haegerich TM (2018) Quantifying the Epidemic of Prescription Opioid Overdose Deaths. Am J Public Health 108: 500-502.
16. Kolodny A, Courtwright DT, Hwang CS, Kreiner P, Eadie JL, et al. (2015) The prescription opioid and heroin crisis: a public health approach to an epidemic of addiction. Annu Rev Public Health 36: 559-574.
17. Monitto CL, Hsu A, Gao S, Vozzo PT, Park PS, et al. (2017) Opioid Prescribing for the Treatment of Acute Pain in Children on Hospital Discharge. Anesth Analg 125: 2113-2122.
18. Huang JS, Kuelbs CL (2018) Clinician opioid prescribing practices and patient utilization of prescribed opioids in pediatrics. J Opioid Manag 14: 309-316.
19. Tepolt FA, Bido J, Burgess S, Micheli LJ, Kocher MS (2018) Opioid Overprescription After Knee Arthroscopy and Related Surgery in Adolescents and Young Adults. Arthroscopy 34: 3236-3243.
20. The CBHSQ Report. 2013.

21. Post S, Spiller HA, Casavant MJ, Chounthirath T, Smith GA (2018) Buprenorphine Exposures Among Children and Adolescents Reported to US Poison Control Centers. Pediatrics 142: e20173652.

22. Allen JD, Casavant MJ, Spiller HA, Chounthirath T, Hodges NL, et al. (2017) Prescription Opioid Exposures Among Children and Adolescents in the United States: 2000-2015. Pediatrics 139: e20163382.

23. Miech R, Johnston L, O'Malley PM, Keyes KM, Heard K (2015) Prescription Opioids in Adolescence and Future Opioid Misuse. Pediatrics 136: e1169-1177.

24. McCabe SE, Veliz P, Schulenberg JE (2016) Adolescent context of exposure to prescription opioids and substance use disorder symptoms at age 35: a national longitudinal study. Pain 157: 2173-2178.

25. Harbaugh CM, Lee JS, Hu HM, McCabe SE, Voepel-Lewis T, et al. (2018) Persistent Opioid Use Among Pediatric Patients After Surgery. Pediatrics 141: e20172439.

26. Lankenau SE, Teti M, Silva K, Jackson Bloom J, Harocopos A, et al. (2012) Initiation into prescription opioid misuse amongst young injection drug users. Int J Drug Policy 23: 37-44.

27. Mittal S, Shukla AR, Sahadev R, Lee SY, Siu S, et al. (2020) Reducing post-operative opioids in children undergoing outpatient urologic surgery: A quality improvement initiative. J Pediatr Urol 16: 846.e1-846.e7.

28. Carolan AMC, Parker KM, Grimsby GM (2021) Opioid Use after Pediatric Urologic Surgery: Is It Really Needed? Urology 158: 184-188.

29. Ljungqvist O, Scott M, Fearon KC (2017) Enhanced Recovery After Surgery: A Review. JAMA Surg 152: 292-298.

30. Baxter KJ, Short HL, Wetzel M, Steinberg RS, Heiss KF, et al. (2019) Decreased opioid prescribing in children using an enhanced recovery protocol. J Pediatr Surg 54: 1104-1107.

31. O'Kelly F, Pokarowski M, DeCotiis KN, McDonnell C, Milford K, et al. (2020) Structured opioid-free protocol following outpatient hypospadias repair - A prospective SQUIRE 2.0-compliant quality improvement initiative. J Pediatr Urol 16: 647.e1-647.e9.

32. Villanueva J, Grajales V, Colaco M, Ayyash O, Chaudhry R, et al. (2021) Government Mandated Consent Dramatically Reduces Pediatric Urologist Opioid Utilization for Outpatient and Minor Emergency Surgeries. J Urol 205: 264-270.

33. Myrga JM, Macleod LC, Bandari J, Jacobs BL, Davies BJ (2020) Decrease in Urologic Discharge Opioid Prescribing after Mandatory Query of Statewide Prescription Drug Monitoring Program. Urology 139: 84-89.

34. Cardona-Grau D, Bush RA, Le HK, Huang J, Swords K, et al. (2019) Reducing Opioid Prescriptions in Outpatient Pediatric Urological Surgery. J Urol 201: 1012-1016.

35. Rove KO, Brockel MA, Saltzman AF, Dönmez MI, Brodie KE, et al. (2018) Prospective study of enhanced recovery after surgery protocol in children undergoing reconstructive operations. J Pediatr Urol 14: 252.e1-252.e9.

36. Gilron I (2016) Antidepressant Drugs for Postsurgical Pain: Current Status and Future Directions. Drugs 76: 159-167.

37. Zhu A, Benzon HA, Anderson TA (2017) Evidence for the Efficacy of Systemic Opioid-Sparing Analgesics in Pediatric Surgical Populations: A Systematic Review. Anesth Analg 125: 1569-1587.

38. Hong J, Kim WO, Koo BN, Cho JS, Suk EH, et al. (2010) Fentanyl-sparing effect of acetaminophen as a mixture of fentanyl in intravenous parent-/nurse-controlled analgesia after pediatric ureteroneocystostomy. Anesthesiology 113: 672-677.

39. Stewart DW, Ragg PG, Sheppard S, Chalkiadis GA (2012) The severity and duration of postoperative pain and analgesia requirements in children after tonsillectomy, orchidopexy, or inguinal hernia repair. Paediatr Anaesth 22: 136-143.

40. Ong CK, Seymour RA, Lirk P, Merry AF (2010) Combining paracetamol (acetaminophen) with nonsteroidal antiinflammatory drugs: a qualitative systematic review of analgesic efficacy for acute postoperative pain. Anesth Analg 110: 1170-1179.

41. Chauhan RD, Idom CB, Noe HN (2001) Safety of ketorolac in the pediatric population after ureteroneocystostomy. J Urol 166: 1873-1875.

42. Routh JC, Graham DA, Nelson CP (2010) Ketorolac is underutilized after ureteral reimplantation despite reduced hospital cost and reduced length of stay. Urology 76: 9-13.

43. Gurbet A, Basagan-Mogol E, Turker G, Ugun F, Kaya FN, et al. (2006) Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. Can J Anaesth 53: 646-652.

44. Ohtani N, Yasui Y, Watanabe D, Kitamura M, Shoji K, et al. (2011) Perioperative infusion of dexmedetomidine at a high dose reduces postoperative analgesic requirements: a randomized control trial. J Anesth 25: 872-878.

45. Taittonen MT, Kirvelä OA, Aantaa R, Kanto JH (1997) Effect of clonidine and dexmedetomidine premedication on perioperative oxygen consumption and haemodynamic state. Br J Anaesth 78: 400-406.

46. Aspinall RL, Mayor A (2001) A prospective randomized controlled study of the efficacy of ketamine for postoperative pain relief in children after adenotonsillectomy. Paediatr Anaesth 11: 333-336.

47. Jayanthi VR, Spisak K, Smith AE, Martin DP, Ching CB, et al. (2019) Combined spinal/caudal catheter anesthesia: extending the boundaries of regional anesthesia for complex pediatric urological surgery. J Pediatr Urol 15: 442-447.

48. Tao B, Liu K, Wang D, Ding M, Yang N, et al. (2019) Perioperative effects of caudal block on pediatric patients in laparoscopic upper urinary tract surgery: a randomized controlled trial. BMC Pediatr 19: 427.

49. Noguchi S, Saito J, Nakai K, Kitayama M, Hirota K (2019) Efficacy of abdominal peripheral nerve block and caudal block during robot-assisted laparoscopic surgery: a retrospective clinical study. J Anesth 33: 103-107.

50. Allan CY, Jacqueline PA, Shubhda JH (2003) Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database Syst Rev 2003: CD003005.

51. Ansermino M, Basu R, Vandebeek C, Montgomery C (2003) Nonopioid additives to local anaesthetics for caudal blockade in children: a systematic review. Paediatr Anaesth 13: 561-573.

52. Kundra P, Yuvaraj K, Agrawal K, Krishnappa S, Kumar LT (2012) Surgical outcome in children undergoing hypospadias repair under caudal epidural vs penile block. Paediatr Anaesth 22: 707-712.

53. Chalmers DJ, Bielsky A, Wild TT, Siparsky GL, Wilcox DT (2015) Continuous local anesthetic infusion for children with spina bifida undergoing major reconstruction of the lower urinary tract. J Pediatr Urol 11: 72.e1-72.e5.

54. Kain ZN, Mayes LC, Caldwell-Andrews AA, Karas DE, McClain BC (2006) Preoperative anxiety, postoperative pain, and behavioral recovery in young children undergoing surgery. Pediatrics 118: 651-658.

55. Sanchez Cristal N, Staab J, Chatham R, Ryan S, Mcnair B, et al. (2018) Child Life Reduces Distress and Pain and Improves Family Satisfaction in the Pediatric Emergency Department. Clin Pediatr (Phila) 57: 1567-1575.

56. Vincent C, Chiappetta M, Beach A, Kiolbasa C, Latta K, et al. (2012) Parents' management of children's pain at home after surgery. J Spec Pediatr Nurs 17: 108-120.