Pain Medicine Journal

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Preemptive, preventive, мультимодальная аналгезия: звенья в одном механизме лечения послеоперационной боли?

Британо-украинский симпозиум

17-20 апреля - 2019

г. Киев

Дмитриев Д.В.

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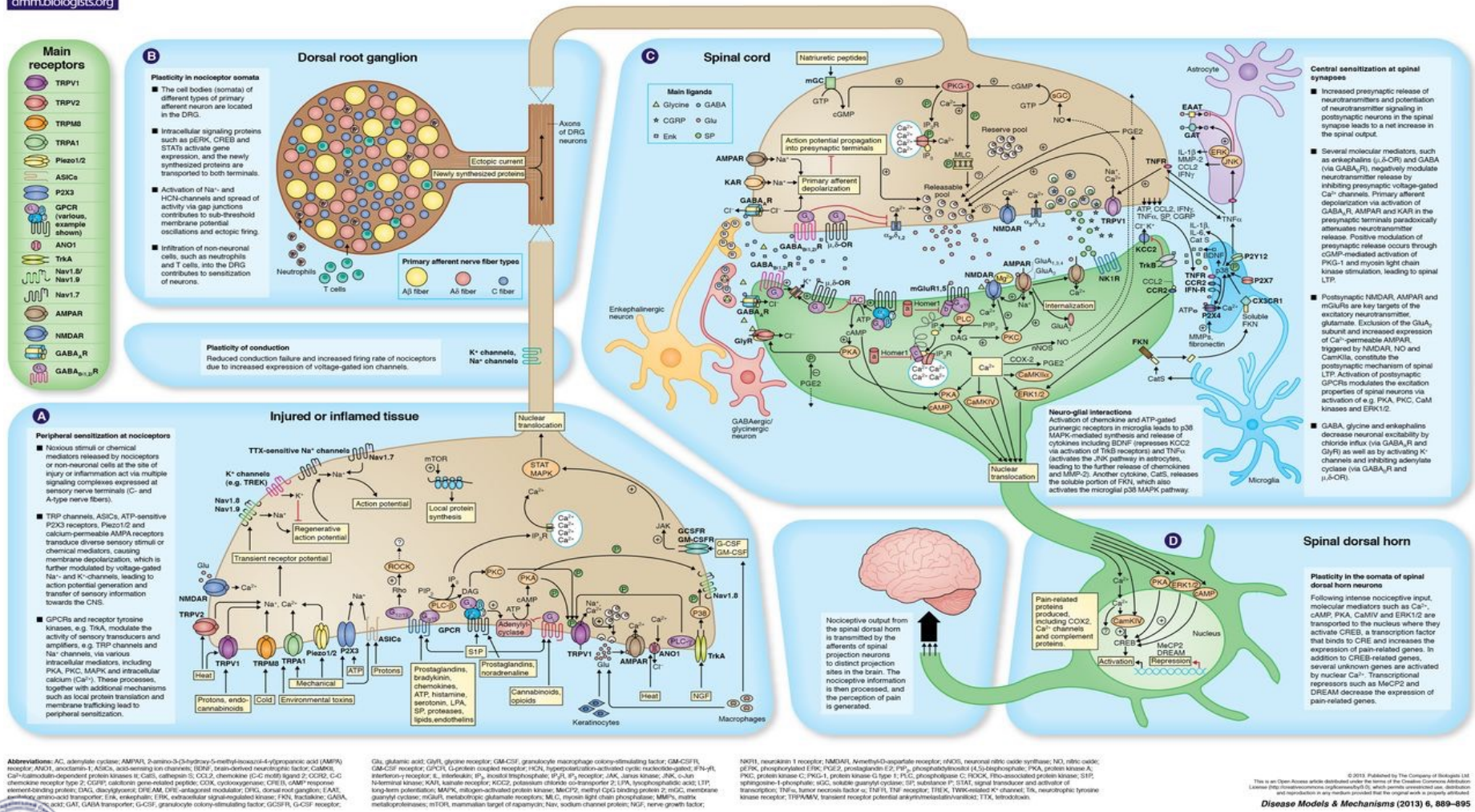
DMM Disease Models & Mechanisms dmm.biologists.org

Pain hypersensitivity mechanisms at a glance

Vijayan Gangadharan and Rohini Kuner



Abbreviations: AC, adenylate cyclase; AMPAR, 2-amino-3-(3-hydroxy-5-methyl-isoxazol-4-yl)propanoic acid (AMPA) receptor; ANO1, anoctamin-1; ASICs, acid-sensing ion channels; BDNF, brain-derived neurotrophic factor; CaMKII, Ca2+/calmodulin-dependent protein kinases II; CatS, cathepsin S; CCL2, chemokine (C-C motif) ligand 2; CCR2, C-C chemokine receptor type 2; CGRP, calcitonin gene-related peptide; COX, cyclooxygenase; CREB, cAMP response element-binding protein; DAG, diacylglycerol; DREAM, DRE–antagonist modulator; DRG, dorsal root ganglion; EAAT, excitatory amino-acid transporter; Enk, enkephalin; ERK, extracellular signal-regulated kinase; FKN, fractalkine; GABA, γ-aminobutyric acid; GAT, GABA transporter; G-CSF, granulocyte colony-stimulating factor; GCSFR, G-CSF receptor; Glu, glutamic acid; GlyR, glycine receptor; GM-CSF, granulocyte macrophage colony-stimulating factor; GM-CSFR, GM-CSF receptor; GPCR, G-protein coupled receptor; HCN, hyperpolarization-activated cyclic nucleotide-gated; IFN-γR, interferon-γ receptor; IL, interleukin; IP$_3$, inositol trisphosphate; IP$_3$R, IP$_3$ receptor; JAK, Janus kinase; JNK, c-Jun N-terminal kinase; KAR, kainate receptor; KCC2, potassium chloride co-transporter 2; LPA, lysophosphatidic acid; LTP, long-term potentiation; MAPK, mitogen-activated protein kinase; MeCP2, methyl CpG binding protein 2; mGlC, membrane guanylyl cyclase; mGluR, metabotropic glutamate receptors; MLC, myosin light chain phosphatase; MMP, matrix metalloproteinases; mTOR, mammalian target of rapamycin; Nav, sodium channel protein; NGF, nerve growth factor; NKR1, neurokinin 1 receptor; NMDAR, N-methyl-D-aspartate receptor; nNOS, neuronal nitric oxide synthase; NO, nitric oxide; pERK, phosphorylated ERK; PGE2, prostaglandin E2; PIP$_2$, phosphatidylinositol (4,5)-bisphosphate; PKA, protein kinase A; PKC, protein kinase C; PKG-1, protein kinase G type 1; PLC, phospholipase C; ROCK, Rho-associated protein kinase; S1P, sphingosine-1-phosphate; sGC, soluble guanylyl cyclase; SP, substance P; STAT, signal transducer and activator of transcription; TNFα, tumor necrosis factor α; TNFR, TNF receptor; TREK, TWIK-related K+ channel; TrkA, neurotrophic tyrosine kinase receptor; TRPM/M/V, transient receptor potential ankyrin/melastatin/vanilloid; TTX, tetrodotoxin.

Disease Models & Mechanisms (2013) 6, 889–895

Vijayan Gangadharan, and Rohini Kuner Dis. Model. Mech. 2013;6:889-895

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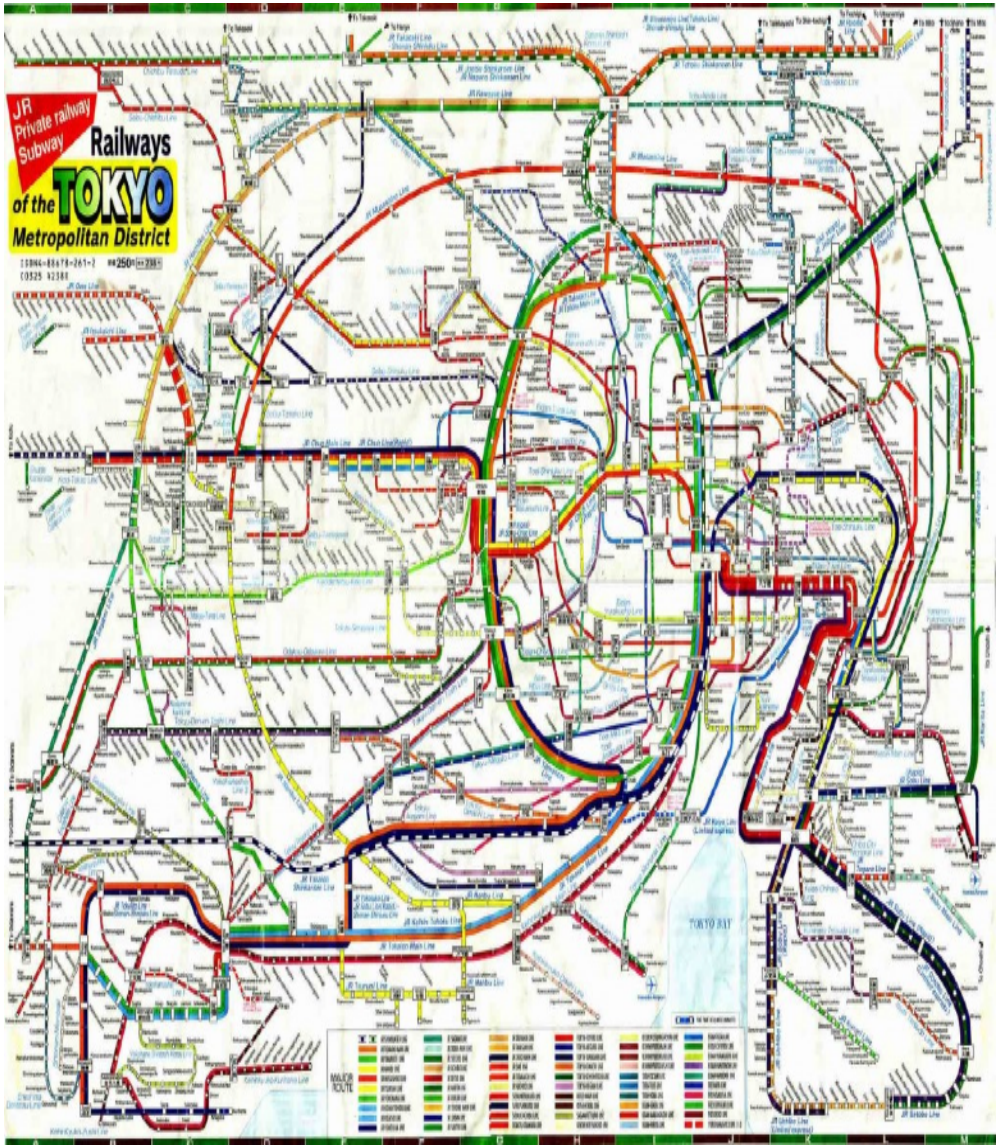

Pain Medicine Journal

ORIGINAL ARTICLE

Pain in hospitalized children: A prospective cross-sectional survey of pain prevalence, intensity, assessment and management in a Canadian pediatric teaching hospital

Elsa M Taylor MBChB FANZCA[1], Kristina Boyer RN MSc[2], Fiona A Campbell BSc MD FRCA[3]

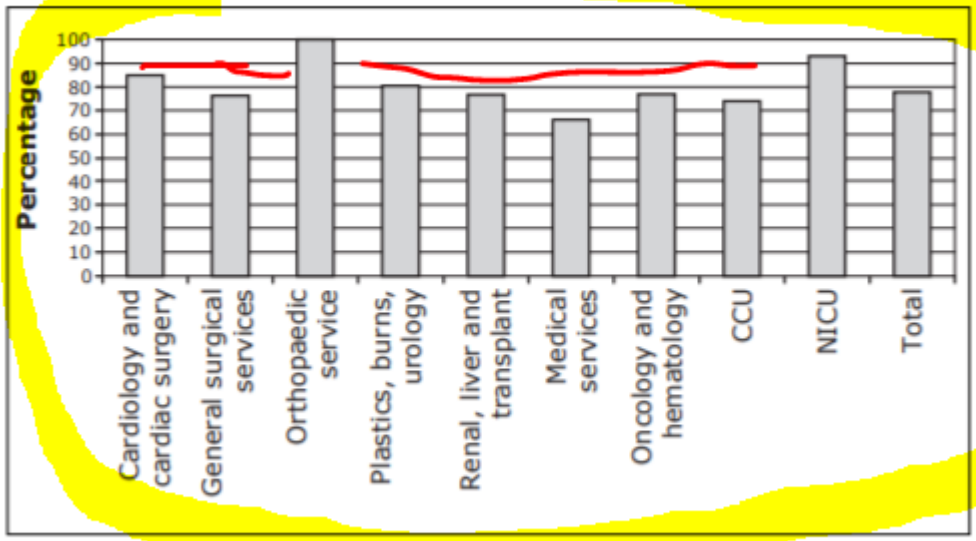

Figure 1) *Prevalence of pain during admission by service. CCU Critical care unit; NICU Neonatal intensive care unit*

Вывод.

77 % отмечали боль в послеоперационном периоде

44 % отмечали выраженную боль в первые 24 часа после операции

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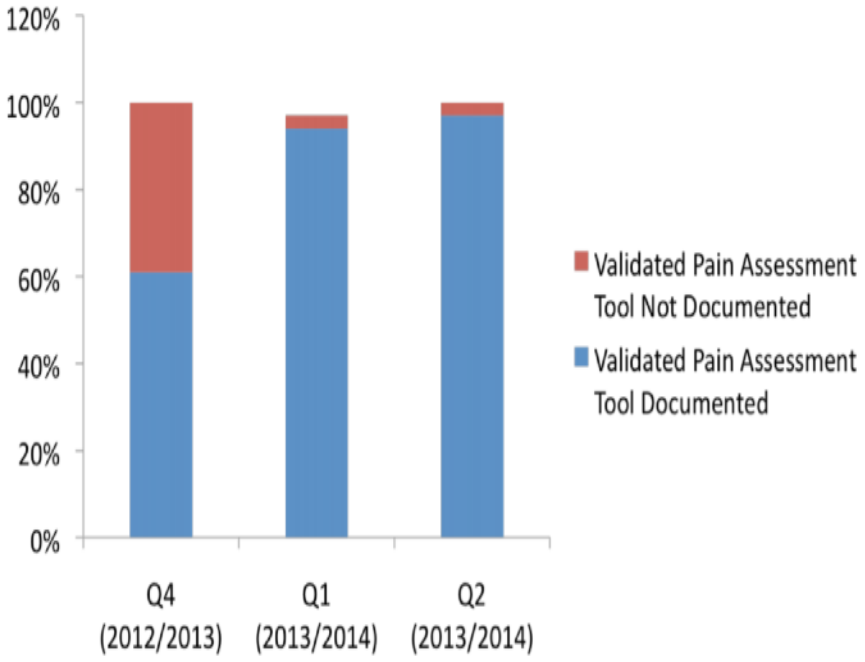
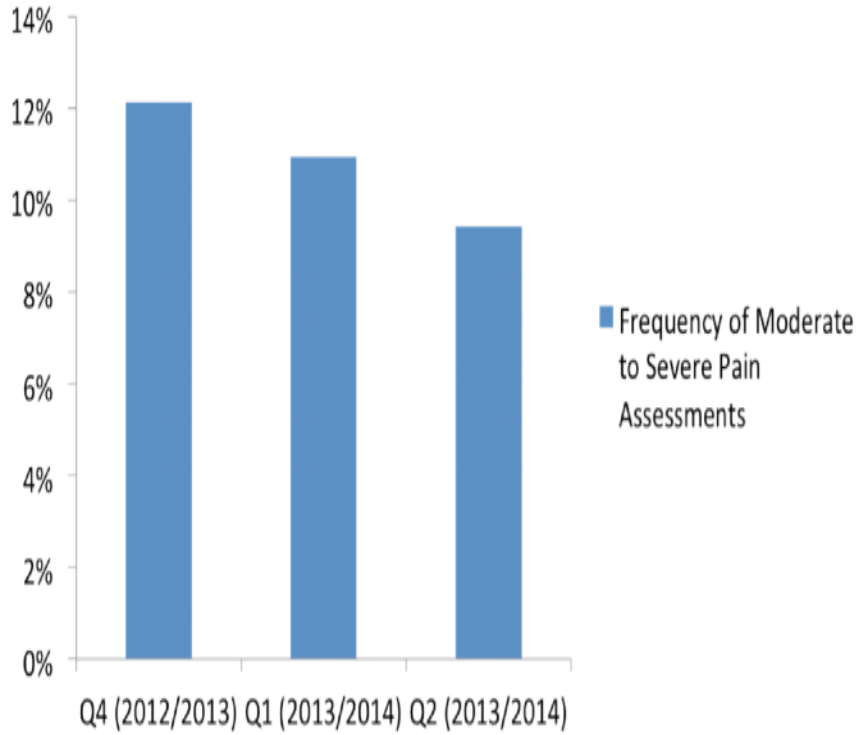
SK QIP – Surgical pain

Pain Assessment Documentation



Frequency of Moderate to Severe Pain

(i.e. number of assessments indicating moderate to severe pain)



Taylor EM, Boyer K, Campbell FA. Pain Res Manag. 2008 Jan-Feb;13(1):25-32.

Pain Medicine Journal

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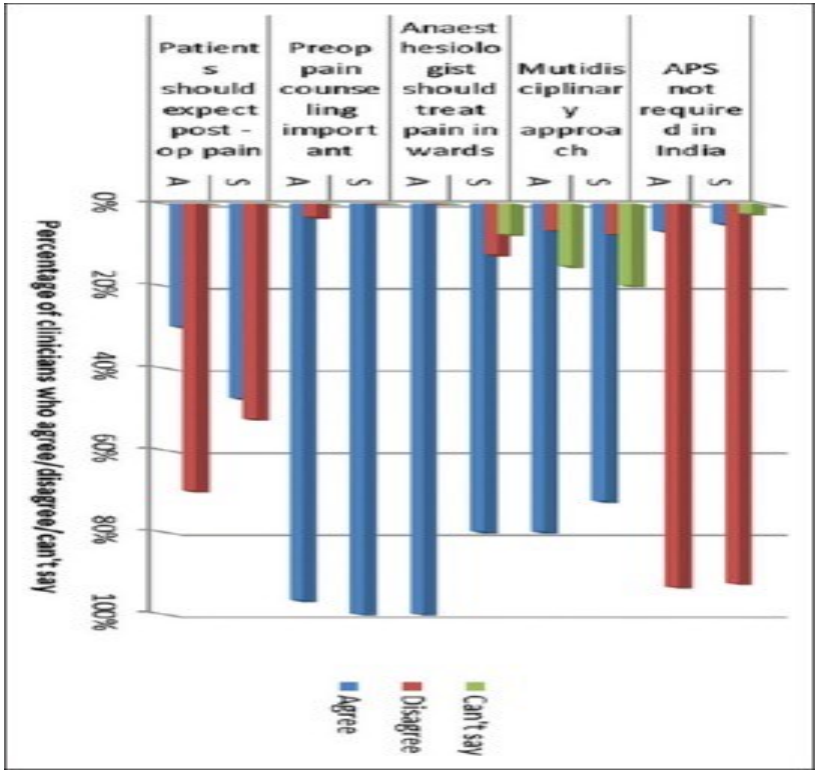
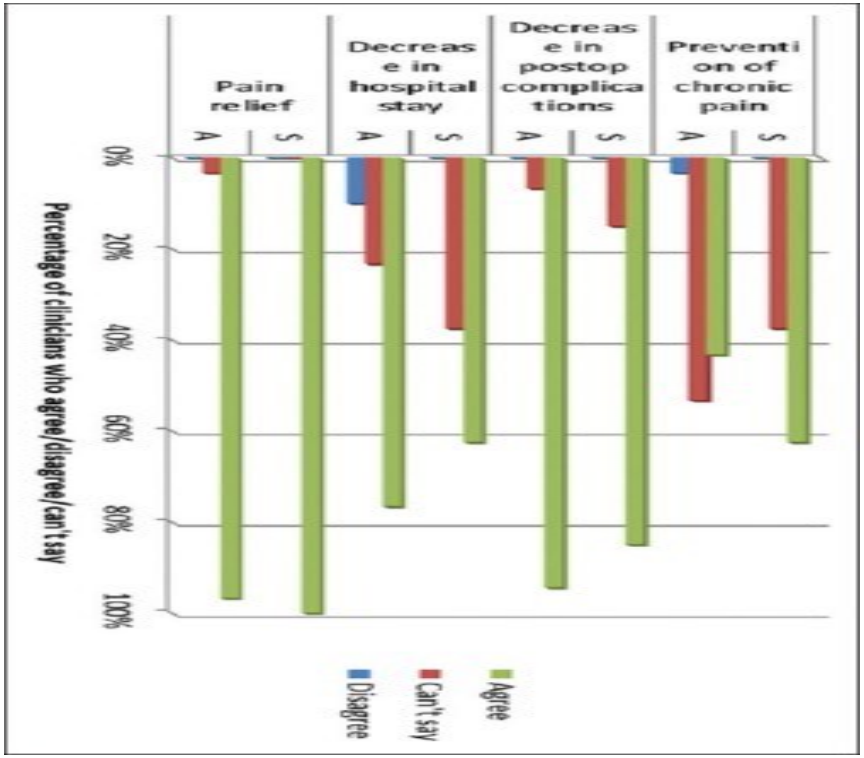
A MULTICENTRE SURVEY OF THE CURRENT ACUTE POST-OPERATIVE PAIN MANAGEMENT PRACTICES IN TERTIARY CARE TEACHING HOSPITALS IN MAHARASHTRA

S. Kh.Khatib, S.S. Razvi. Indian J Anaesth. 2017





Вывод. ***До 67 % отмечали боль в послеоперационном периоде, 38 % отмечали выраженную боль в первые 24 часа после операции***

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American Pain Society

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Available online at www.jpain.org and www.sciencedirect.com

Guidelines on the Management of Postoperative Pain

Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council

Roger Chou,[*] Debra B. Gordon,[†] Oscar A. de Leon-Casasola,[‡] Jack M. Rosenberg,[§] Stephen Bickler,[¶] Tim Brennan,[‖] Todd Carter,[**] Carla L. Cassidy,[††] Eva Hall Chittenden,[‡‡] Ernest Degenhardt,[§§] Scott Griffith,[¶¶] Renee Manworren,[‖‖] Bill McCarberg,[***] Robert Montgomery,[†††] Jamie Murphy,[‡‡‡] Melissa F. Perkal,[§§§] Santhanam Suresh,[¶¶¶] Kathleen Sluka,[‖‖‖] Scott Strassels,[****] Richard Thirlby,[††††] Eugene Viscusi,[‡‡‡‡] ary A. Walco,[§§§§] Lisa Warner,[¶¶¶¶] Steven J. Weisman,[‖‖‖‖] and Christopher L. Wu[‡‡‡]

Pain Medicine Journal

Table 3. Options for Components of Multimodal Therapy for Commonly Performed Surgeries

Type of Surgery	Systemic Pharmacologic Therapy	Local, Intra-articular or Topical Techniques*	Regional Anesthetic Techniques*	Neuraxial Anesthetic Techniques*	Nonpharmacologic Therapies†
Thoracotomy	Opioids‡ NSAIDs§ and/or acetaminophen Gabapentin or pregabalin§ i.v. ketamine¶		Paravertebral block	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Cognitive modalities TENS
Open laparotomy	Opioids‡ NSAIDs§ and/or acetaminophen Gabapentin or pregabalin§ i.v. ketamine¶ i.v. lidocaine	Local anesthetic at incision i.v. lidocaine infusion	Transversus abdominis plane block	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Cognitive modalities TENS
Total hip replacement	Opioids‡ NSAIDs§ and/or acetaminophen Gabapentin or pregabalin§ i.v. ketamine¶	Intra-articular local anesthetic and/or opioid	Site-specific regional anesthetic technique with local anesthetic	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Cognitive modalities TENS
Total knee replacement	Opioids‡ NSAIDs§ and/or acetaminophen Gabapentin or pregabalin§ i.v. ketamine¶	Intra-articular local anesthetic and/or opioid	Site-specific regional anesthetic technique with local anesthetic	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Cognitive modalities TENS
Spinal fusion	Opioids‡ Acetaminophen† Gabapentin or pregabalin§ i.v. ketamine¶	Local anesthetic at incision		Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Cognitive modalities TENS
Cesarean section	Opioids‡ NSAIDs§ and/or acetaminophen	Local anesthetic at incision	Transversus abdominal plane block	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Cognitive modalities TENS
CABG	Opioids‡ Acetaminophen Gabapentin or pregabalin§ i.v. ketamine¶				Cognitive modalities TENS

Abbreviation: CABG, coronary artery bypass grafting.
NOTE. Blank cells indicate techniques generally not used for the procedure in question.
*Intra-articular, peripheral regional, and neuraxial techniques typically not used together.
†Use as adjunctive treatments.
‡Use i.v. PCA when parenteral route needed for more than a few hours and patients have adequate cognitive function to understand the device and safety limitations.
§ be administered preoperatively.
¶ basis of panel consensus, primarily consider for use in opioid-tolerant or otherwise complex patients.

Pain Medicine Journal

Caliskan et al. BMC Anesthesiology 2013, 13:34
http://www.biomedcentral.com/1471-2253/13/34

BMC Anesthesiology

RESEARCH ARTICLE Open Access

The efficacy of intravenous paracetamol versus dipyrone for postoperative analgesia after day-case lower abdominal surgery in children with spinal anesthesia: a prospective randomized double-blind placebo-controlled study

Esra Caliskan[1,3*], Mesut Sener[1], Aysu Kocum[1], Nesrin Bozdogan Ozyilkan[1], Semire Serin Ezer[2] and Anis Aribogan[1]

Methods: Sixty children scheduled for elective lower abdominal surgery under spinal anesthesia were randomized to receive either intravenous paracetamol 15 mg/kg, dipyrone 15 mg/kg or isotonic saline. The primary outcome measure was pain at rest, assessed by means of a visual analog scale 15 min, 30 min, 1 h, 2 h, 4 h and 6 h after surgery. If needed, pethidine 0.25 mg/kg was used as the rescue analgesic. Time to first administration of rescue analgesic, cumulative pethidine requirements, adverse effects and complications were also recorded.

Results: There were no significant differences in age, sex, weight, height or duration of surgery between the groups. Pain scores were significantly lower in the paracetamol group at 1 h ($P = 0.030$) and dipyrone group at 2 h ($P = 0.010$) when compared with placebo. The proportion of patients requiring rescue analgesia was significantly lower in the paracetamol and dipyrone groups than the placebo group (vs. paracetamol $P = 0.037$; vs. dipyrone $P = 0.020$). Time to first analgesic requirement appeared shorter in the placebo group but this difference was not statistically significant, nor were there significant differences in pethidine requirements, adverse effects or complications.

Conclusion: After lower abdominal surgery conducted under spinal anesthesia in children, intravenous paracetamol appears to have similar analgesic properties to intravenous dipyrone, suggesting that it can be used as an alternative in the early postoperative period.

Pain Medicine Journal

Pediatric Anesthesia

Pediatric Anesthesia ISSN 1155-5645

ORIGINAL ARTICLE

Opioid-sparing effects of perioperative paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) in children

Ivan Wong[1,2], Celia St John-Green[2] & Suellen M. Walker[1,3]

Keywords
pain; postoperative; child; analgesics; opioid; analgesics; non-narcotic; anti-inflammatory agents; nonsteroidal

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Section Editor: Per-Arne Lonnqvist

Accepted 4 March 2013

doi:10.1111/pan.12163

Summary

Background and Objectives: Perioperative pain in children can be effectively managed with systemic opioids, but addition of paracetamol or nonsteroidal anti-inflammatory drugs (NSAIDs) may reduce opioid requirements and potentially improve analgesia and/or reduce adverse effects.
Methods: A systematic literature search was conducted to identify trials evaluating postoperative opioid requirements in children and comparing NSAID and/or paracetamol with placebo. Studies were stratified according to design: continuous availability of intravenous opioid (PCA/NCA) vs intermittent 'as needed' bolus; and single vs multiple dose paracetamol/NSAIDs. Primary outcome data were extracted, and the percentage decrease in mean opioid consumption was calculated for statistically significant reductions compared with placebo. Secondary outcomes included differences in pain intensity, adverse effects (sedation, respiratory depression, postoperative nausea and vomiting, pruritus, urinary retention, bleeding), and patient/parent satisfaction.
Results: Thirty-one randomized controlled studies, with 48 active treatment arms compared with placebo, were included. Significant opioid sparing was reported in 38 of 48 active treatment arms, across 21 of the 31 studies. Benefit was most consistently reported when multiple doses of study drug were administered, and 24 h PCA or NCA opioid requirements were assessed. The proportion of positive studies was less with paracetamol, but was influenced by dose and route of administration. Despite availability of opioid for titration, a reduction in pain intensity by NSAIDs and/or paracetamol was reported in 16 of 29 studies. Evidence for clinically significant reductions in opioid-related adverse effects was less robust.
Conclusion: This systematic review supports addition of NSAIDs and/or paracetamol to systemic opioid for perioperative pain management in children.

Pain Medicine Journal

Accepted: 14 March 2018

DOI: 10.1111/pan.13373

http://doctorthinking.org

SPECIAL INTEREST ARTICLE

WILEY Pediatric Anesthesia

Postoperative pain management in children: Guidance from the pain committee of the European Society for Paediatric Anaesthesiology (ESPA Pain Management Ladder Initiative)

Maria Vittinghoff[1] | Per-Arne Lönnqvist[2] | Valeria Mossetti[3] | Stefan Heschl[1] | Dusica Simic[4] | Vesna Colovic[5] | Dmytro Dmytriiev[6] | Martin Hölzle[7] | Marzena Zielinska[8] | Anna Kubica-Cielinska[8] | Elizabeth Lorraine-Lichtenstein[9] | Ivana Budić[10] | Marijana Karisik[11] | Belen De Josè Maria[12] | Francesco Smedile[13] | Neil S. Morton[14]

TABLE 8 Dosage suggestions for systemic analgesia

Basic level	Intermediate level	Advanced level	Dosage suggestions
Rectal NSAIDs (Nonsteroidal anti-inflammatory drugs)			
Ibuprofen	Ibuprofen	Ibuprofen	10 mg kg^{-1} every 8 h
Diclofenac	Diclofenac	Diclofenac	1 mg kg^{-1} every 8 h
Naproxen	Naproxen	Naproxen	5-7.5 mg kg^{-1} every 12 h
Oral NSAIDs			
Ibuprofen	Ibuprofen	Ibuprofen	10 mg kg^{-1} every 8 h
Diclofenac	Diclofenac	Diclofenac	1 mg kg^{-1} every 8 h
Intravenous NSAIDs			
		Ketorolac	0.5-1 mg kg^{-1} kg up to 30 mg for a single intraoperative dose 0.15-0.2 mg kg^{-1} (max 10 mg) every 6 h (short-term therapy, maximum 48 h)
		Ketoprofen	1 mg kg^{-1} every 8 h

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TABLE 4 Pyloromyotomy

Pyloromyotomy (open and laparoscopic)[138,152,153]	Intraoperative	Postoperative
Basic level	• Fentanyl or opioid of choice.[49-53] • Rectal paracetamol[154] • Local wound infiltration/local port-side infiltration by the surgeon of a long-acting local anesthetic.[54,139,155,156]	• Intravenous fentanyl or other suitable agent (if available) to treat breakthrough pain in the PACU.[49-53] • Oral or rectal paracetamol in adequate dosing during the entire postoperative period.[44-46]
Intermediate level	• Intravenous paracetamol or rectal NSAID.[58,59,154,157] • Landmark-based caudal blockade with long-acting local anesthetics ± adjunct clonidine if available.[158]	• Intravenous nalbuphine or other suitable agent (if available) to treat serious breakthrough pain in the PACU.[56,57,143] • Oral or rectal NSAIDs (eg, ibuprofen) and/or paracetamol in adequate dosing during the entire postoperative period.[43]
Advanced level	• Intravenous metamizole or rectal NSAID. • Intravenous loading dose of paracetamol.[58,154] • Ultrasound-guided rectus sheath block or bilateral subcostal TAP or ultrasound-guided caudal blockade with long-acting local anesthetics combined with appropriate adjunct.[155,159-162]	• Intravenous nalbuphine or other suitable agent (if available) to treat breakthrough pain in the PACU. • Oral or rectal NSAIDs (eg, ibuprofen) and/or paracetamol in adequate dosing during the entire postoperative period. • intravenous nalbuphine or oral tramadol as rescue in the ward

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Rectal paracetamol (if rectal NSAID is not available)			
Paracetamol	Paracetamol	Paracetamol	20-40 mg kg^{-1} (15 mg kg^{-1} if <10 kg) Single loading dose in association with anesthesia; the higher dose is due to poor bioavailability from rectal route of administration
Oral paracetamol			
Paracetamol	Paracetamol	Paracetamol	10-15 mg kg^{-1} every 6 h
Intravenous paracetamol			
		Paracetamol	<10 kg: 7,5 mg kg^{-1} >10 kg: 15 mg kg^{-1} Intravenous preparation: 10 mg mL^{-1}
Intraoperative opioids depending on age and procedure			
Fentanyl	Fentanyl	Fentanyl	1-2 μg kg^{-1}
Morphine	Morphine	Morphine	25-100 μg kg^{-1} depending on age, titrated to effect
	Piritramide	Piritramide	0.1-0.15 mg kg^{-1}
	Alfentanil	Alfentanil	10-20 μg kg^{-1}
	Sufentanil	Sufentanil	0.5-1 μg kg^{-1} bolus
		Sufentanil	0.5-1 μg kg^{-1} bolus then continuous infusion of 0.5-1 μg kg^{-1} h^{-1}
		Remifentanil	0.05-0.3 μg kg^{-1} min^{-1}
Intraoperative use of ketamine/S-ketamine			
Ketamine/S-Ketamine	Ketamine/S-Ketamine	Ketamine/S-Ketamine	0.5 mg kg^{-1} may be used as adjunct to intraoperative opioids, consider reduced dose when using S-ketamine
Intraoperative/postoperative intravenous Metamizol			
		Metamizole	10-15 mg kg^{-1} every 8 h 2.5 mg kg^{-1} h^{-1} (continuous infusion following an intraoperative loading dose) (Due to the risk of agranulocytosis after long-term use metamizole is recommended for short term postoperative use in a hospital setting only)

Journal of Clinical Anesthesia

Journal of Clinical Anesthesia 25 (2013)

Effect of preemptive and preventive acetaminophen on postoperative pain score: a randomized, double-blind trial of patients undergoing lower extremity surgery

Gholamreza Khalili, Mohsen Janghorbani

Исследование преэмптив и превентив аналгезии с парацетамолом в ортопедии.

Гр. 1 – плацебо, Гр.2 Преэмптив, Гр.3 Превентив.

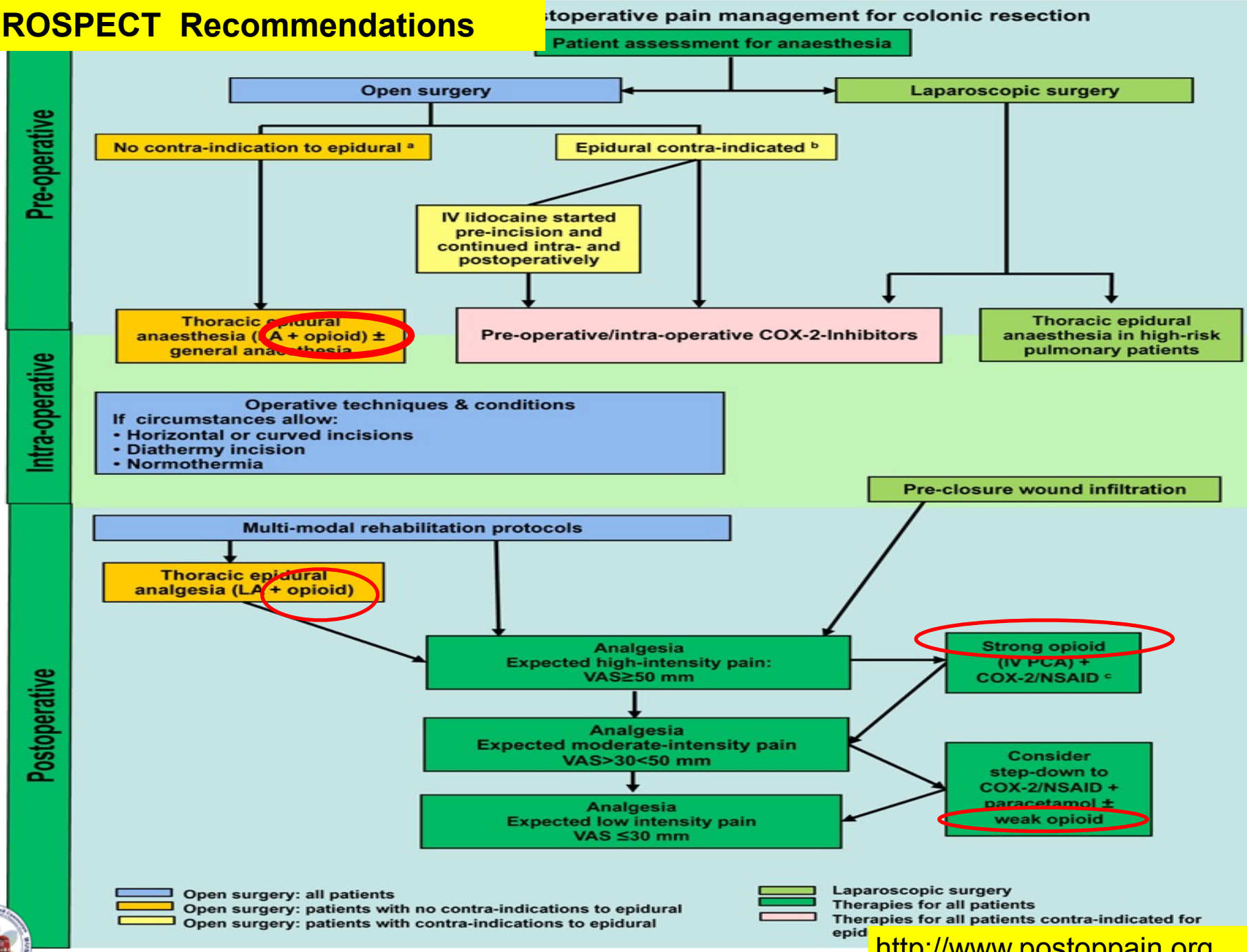
Парацетамол за 30-40 мин до начала операции.

Оценка интенсивности боли, потребность в обезболивании (меперидин)

	Treatment groups			*P*-value*
	Preemptive	Preventive	Normal saline	
Patients (n)	25	25	25	-
VRS at 6 hrs	2.72 (1.27)	2.87 (1.96)	4.48 (1.04)	0.001
VRS at 12 hrs	4.08 (1.66)	4.42 (1.82)	4.24 (1.45)	0.775
VRS at 18 hrs	2.92 (1.06)	2.96 (1.34)	3.17 (1.05)	0.727
VRS 24 hrs	2.00 (1.48)	1.83 (0.83)	1.77 (1.41)	0.821
Postop meperidine (mg)	23.0 (20.3)	30.0 (22.8)	42.0 (15.7)	0.003
Time to first postop request for analgesic (min)	10.8 (4.4)	10.7 (4.3)	7.0 (3.3)	0.008

Заключение: больные после операций на н/конечностях под спинальной анестезией преемптив и превентив аналгезия с парацетамолом усиливает аналгезию и снижает послеоперационное потребление аналгетиков

PROSPECT Recommendations



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Pain Medicine Journal

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Pediatric Anesthesia

SYSTEMATIC REVIEW

Interventions for postoperative pain in children: An overview of systematic reviews

Krste Boric, Svjetlana Dosenovic, Antonia Jelicic Kadic, Marijan Batinic, Marija Cavar, Marjan Urlic, Nikolina Markovina, Livia Puljak

included 45 systematic reviews that evaluated interventions for postoperative pain in children. Out of 45 systematic reviews that investigated various interventions for postoperative pain in children, 19 systematic reviews (42%) presented conclusive evidence of efficacy. Positive conclusive evidence was reported in 18 systematic reviews (40%) for the efficacy of diclofenac, ketamine, caudal analgesia, dexmedetomidine, music therapy, corticosteroid, epidural analgesia, paracetamol, and/or nonsteroidal anti-inflammatory drugs and transversus abdominis plane block. Only one systematic review reported conclusive evidence of equal efficacy that involved a comparison of dexmedetomidine vs morphine and fentanyl. Safety of interventions was reported as conclusive in 14 systematic reviews (31%), with positive conclusive evidence for dexmedetomidine, corticosteroid, epidural analgesia, transversus abdominis plane block, and clonidine. Seven systematic reviews reported equal conclusive safety for epidural infusion, diclofenac intravenous vs ketamine added to opioid analgesia, bupivacaine, ketamine, paracetamol, and dexmedetomidine vs intravenous infusions of various opioid analgesics, oral suspension and suppository of diclofenac, only opioid, normal saline, no tment, placebo, and midazolam. Negative conclusive statement for safety was

Вывод.

Из 45 систематических обзоров, 19 (42%) для эффективности диклофенака, кетамина, каудальной анальгезии, дексмедетомидина, музыкальной терапии, кортикостероидов, эпидуральной аналгезии, парацетамола и / или нестероидных противовоспалительных препаратов и регионарной аналгезии.

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Journal of Pain Research

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ORIGINAL RESEARCH

Efficacy of preemptive analgesia on acute postoperative pain in children undergoing major orthopedic surgery of the lower extremities

This article was published in the following Dove Press journal:
Journal of Pain Research

Table 2 Postoperative pain scores determined using the r-FLACC pain scale

	Preemptive (n=23)	Control (n=24)	Median difference (95% CI)	*P*-value
r-FLACC				0.035[a]
PACU	0.0 (0.0–1.0)	1.5 (1.0–2.5)	−1.0 (−2.0 to −1.0)	0.001
6 hours	1.0 (0.0–2.0)	3.0 (2.0–4.0)	−2.0 (−3.0 to −1.0)	0.005
12 hours	1.0 (1.0–3.0)	2.0 (1.0–3.0)	0.0 (−1.0 to 0.0)	>0.999
24 hours	1.0 (0.0–2.0)	2.0 (1.0–3.0)	−1.0 (−1.0 to 0.0)	0.692
48 hours	0.0 (0.0–1.0)	1.0 (0.5–2.0)	−1.0 (−1.0 to 0.0)	0.351

Notes: Data are presented as median (interquartile range). [a]*P*-value of the group-by-time interaction in the nonparametric mixed model.
Abbreviations: PACU, postanesthesia care unit; r-FLACC, revised Face, Legs, Activity, Cry, and Consolability.

Table 4 Frequency of adverse events

	Preemptive (n=23)	Control (n=24)	*P*-value
PONV	11 (47.8)	9 (37.5)	0.474
Temporary discontinuation of PCA	3 (13.0)	1 (4.2)	0.348
Urinary retention	4 (17.4)	1 (4.2)	0.188
Transient motor blockade	1 (4.3)	3 (12.5)	0.609
Headache	1 (4.3)	0 (0.0)	0.489

Note: Data are presented as number of patients (%).
Abbreviations: PCA, patient-controlled analgesia; PONV, postoperative nausea and vomiting.

Pediatric Anesthesia

Pediatric Anesthesia ISSN 1155-5645

ORIGINAL ARTICLE

Randomized controlled trial on preemptive analgesia for acute postoperative pain management in children

In-Kyung Song[1], Yong-Hee Park[2], Ji-Hyun Lee[1], Jin-Tae Kim[1], In Ho Choi[3] & Hee-Soo Kim[1]

Table 2 Intravenous patient-controlled analgesia data, pain scores, and emergence agitation score

Control group (n = 20) / Preemptive group (n = 21)	Postoperative hour(s)							
	0	1	2	4	8	12	24	48
IV-PCA Data								Total
Delivered volume (ml)								
Control	1.7 ± 1.8	1.7 ± 0.9	1.3 ± 0.8	1.6 ± 0.9		5.6 ± 2.1		31.4 ± 12.6
Preemptive	1.9 ± 1.1	1.9 ± 1.2	1.9 ± 1.1	1.7 ± 0.8		4.6 ± 2.2		28.3 ± 14.4
Frequency of pushing the button (n)								
Control	1.0 ± 1.7	2.8 ± 2.4	1.3 ± 2.1	0.8 ± 1.2		2.5 ± 2.9		14.9 ± 11.5
Preemptive	0.9 ± 1.1	2.4 ± 1.7	3.6 ± 3.7	0.7 ± 0.7		1.3 ± 1.6		14.6 ± 10.4
Effective count among the pushed attempts (n)								
Control	0.7 ± 1.2	1.2 ± 0.9	0.7 ± 0.9	0.6 ± 0.9		1.9 ± 2.0		10.9 ± 9.2
Preemptive	0.5 ± 0.6	1.4 ± 1.1	1.4 ± 1.1	0.7 ± 0.7		1.3 ± 1.6		10.2 ± 8.0
VRS								
Control		1.4 ± 1.1	0.9 ± 1.0	0.9 ± 0.9	1.4 ± 0.8		1.1 ± 1.0	0.7 ± 0.7
Preemptive		1.3 ± 0.8	1.1 ± 1.0	1.9 ± 1.4	1.4 ± 1.3	1.0 ± 1.0	0.7 ± 1.0	0.6 ± 0.6
WBFS								
Control		2.3 ± 1.0	2.0 ± 0.9	1.9 ± 1.5	2.1 ± 1.2		1.8 ± 1.8	0.8 ± 0.7
Preemptive		2.3 ± 1.4	2.0 ± 1.3	2.3 ± 1.3	2.4 ± 1.4	2.4 ± 1.8	1.3 ± 1.0	1.1 ± 0.9
EAS								
Control	10.1 ± 3.2	3.1 ± 2.1						
Preemptive	5.3 ± 4.8*	2.2 ± 2.4						

Values are mean ± SD. IV-PCA: intravenous patient-controlled analgesia, VRS: verbal rating scale, WBFS: Wong-Baker FACES® pain rating scale, EAS: emergence agitation score.

*P < 0.05 vs Control.

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Preemptive Analgesia with Paracetamol and Tramadol in Pediatric Adenotonsillectomy

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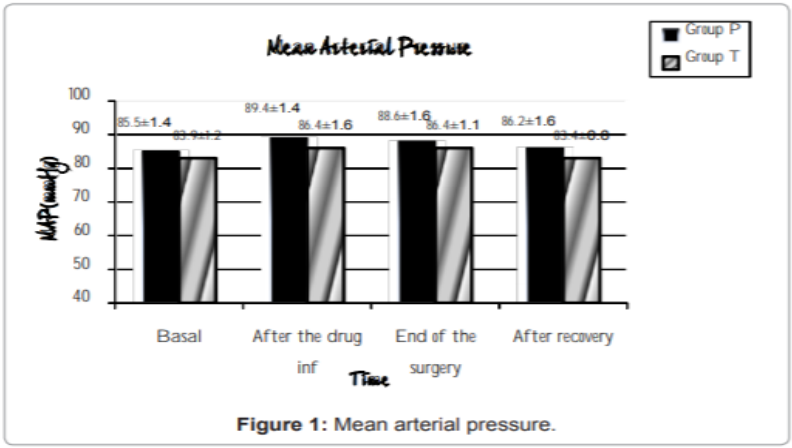

Figure 1: Mean arterial pressure.

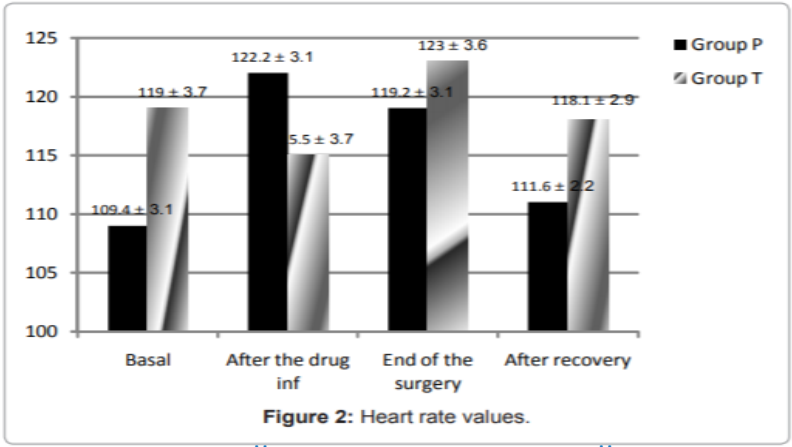

Figure 2: Heart rate values.

In conclusion, our findings indicate that preemptively administered i.v. paracetamol 15 mg kg^{-1} or tramadol 1 mg kg^{-1} in children undergoing adenotonsillectomy operation has no negative effects on intraoperative or postoperative hemodynamic parameters, ensures an effective analgesia during the postoperative period.

Preemptive i.v. paracetamol and tramadol were found to be efficient preemptive analgesics in adenotonsillectomy of children for postoperative analgesia.

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Table 3. Pain management data comparison between pre-emptive and preventive groups.

Group	Pre-emptive (n = 28)	Preventive (n = 27)	P-value
Children received fentanyl in PACU (%)	7 (27.6)	15 (58.6)	†0.0170*
Total IV fentanyl in PACU (μg)	6.6 ± 2.3	13.2 ± 4.7	‡0.0017**
Time of first fentanyl in PACU (min)	70.6 ± 37.3	37.1 ± 28.6	‡0.0432*
Treated with pain relief at home (%)	4 (13.8)	10 (38.0)	§0.0700

Values are presented as mean ± SD.
P-value by ‡Kruskal–Wallis rank test or †chi-square test; or §Fisher's exact test.
*$P < 0.05$ (significant) **$P < 0.01$ (significant).

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/ Özgün Araştırma

Effect of Pre-Emptive Paracetamol Infusion on Postoperative Analgesic Consumption in Children Undergoing Elective Herniorrhaphy

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Table 2. The analgesic drug consumption in the children undergoing elective herniorrhaphy

Drug	NA group, 2011 year	PA group, 2013 year	p
Sedative premedication (n)	10	8	0.799[¶]
Induction agents			
Sevoflurane via mask (n)	8	5	
Thiopental (n)	25	28	
Propofol (n)	26	26	
Etomidate (n)	1	0	0.603[¶]
Intraoperative opioid*	5.5±4.7	6.0±4.2	0.469
Postoperative opioid	0.3±1.0	0.9±1.6	0.014
Paracetamol pre-emptive dose (mg)	Not given	307.6±192.9	-
Paracetamol intraoperative (mg)	233±167.3	51.4±108.3	<0.001
Paracetamol postoperative (mg)	873.5±759.5	625.3±360.9	0.025
Paracetamol total (mg)	1157.8±908.8	983.0±536.4	0.202

NA: no pre-emptive analgesia; PA: pre-emptive analgesia. *opioid dose calculated as morphine equivalents. Two-tailed t test for continuous and [¶]Chi-square test for categorical data were performed; postoperative paracetamol was calculated as sum of the doses given in the recovery room and surgical ward until patients' discharge.

Conclusion

Pre-emptive analgesia with paracetamol infusion was proven to be efficient in terms of postoperative pain control but did not reduce the overall analgesic drug administration in children undergoing elective herniorrhaphy. Further studies investigating multimodal perioperative pain treatment using sedatives, nonpharmacological therapies and more active parental involvement in terms of decreased analgesic drugs consumption should be undertaken.

Preventive analgesia: Effect of small dose of ketamine on morphine requirement after renal surgery

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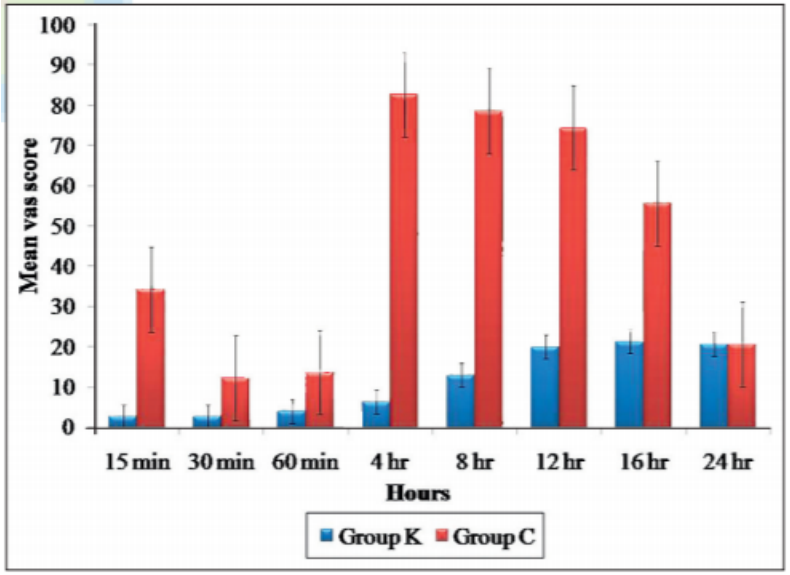

Figure 1: Mean VAS pain scores

Table 2: Postoperative analgesic requirement during 24 hours

	Group K	Group C	*P* value
TFA in hours (mean ± SD)	21.6 + 0.12	3.8 ± 0.7	<0.05
Total morphine consumption in 24 hrs (mean ± SD) in mg	5.8 ± 1.48	18.1 ± 1.6	<0.05
Number of patients requiring additional doses of morphine	5	30	<0.05

Home message

Для улучшения качества послеоперационного обезболивания необходимы:

- ***образовательные программы,***
- ***изменения политика государства и клиники в отношении лечения послеоперационной боли,***
- ***обеспечение оборудованием,***
- ***улучшение доступности опиоидов,***
- ***организацию СОБ,***
- ***разработанные локальные протоколы по периоперационному лечению болевого синдрома.***

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ANESTHESIA & ANALGESIA

The Value of "Multimodal" or "Balanced Analgesia" in Postoperative Pain Treatment

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Conclusions and Future Directions

From the available data on the postoperative use of multimodal pain therapy or balanced analgesia, this strategy seems advantageous, inasmuch as analgesic power may be enhanced. However, the expected gain

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REVIEW

Preventive analgesia for postoperative pain control: a broader concept

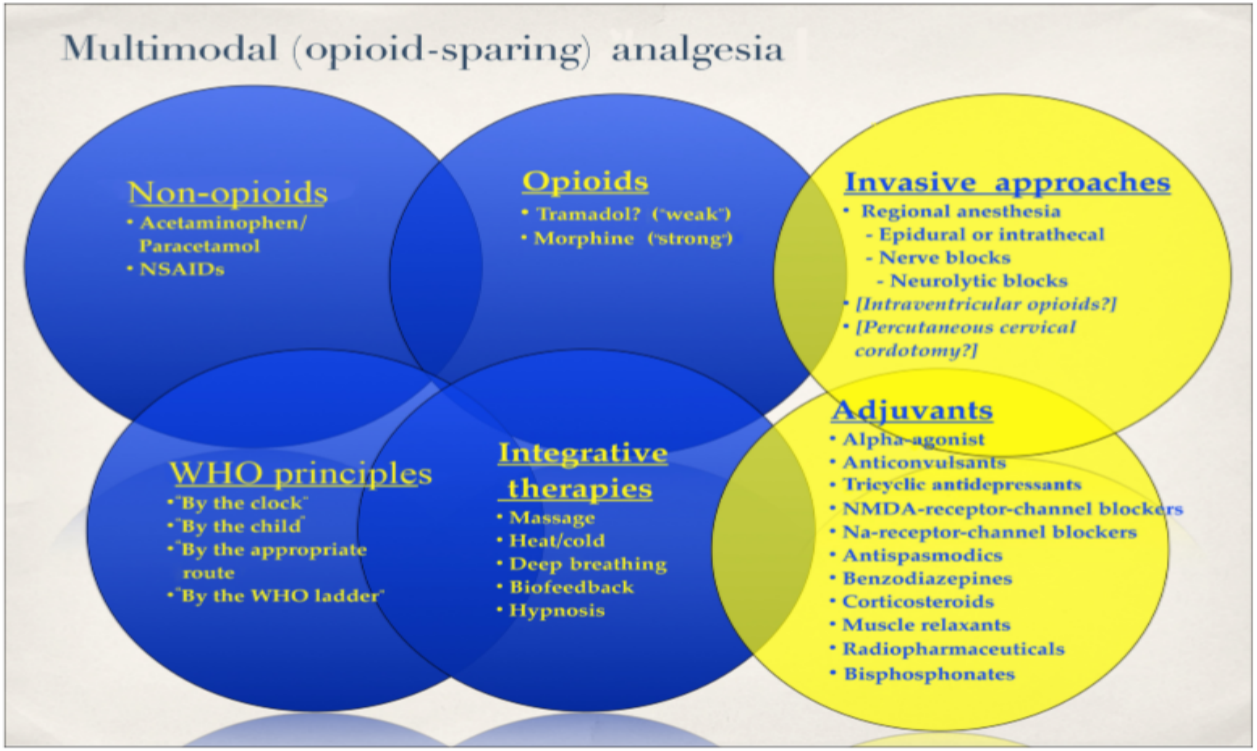

Figure 1 Managing children in acute cancer pain: multimodal "opioid-sparing" analgesia.
Notes: Blue circles show the standard approach; yellow circles show an advanced management approach in select cases.
Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs; WHO, World Health Organization; NMDA, *N*-methyl-D-aspartate.

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A nontoxic pain killer designed by modeling of pathological receptor conformations

V. Spahn[1,†], G. Del Vecchio[1,†], D. Labuz[1], A. Rodriguez-Gaztelumendi[1], N. Massaly[1,*], J. Temp[1], V. Durmaz[2], P. Sabri[2], M. Reidelbach[2], H. Machelska[1], M. Weber[2,‡], C. Stein[1,‡,§]

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A pain killer without side effects

Opioids are very strong and effective pain killers. However, they also have a range of well-known side effects and can cause addiction. Painful conditions such as inflammation or trauma are often associated with localized tissue acidification. Spahn *et al.* designed a novel opioid receptor agonist that, unlike clinically used opioids, best activates the receptors in such acidified tissues. In rat models of inflammatory pain, the new drug exerted strong pain relief essentially without the side effects of standard opioids.

Возможно скоро появится новый анальгетик равный по силе опиодам, но лишенный их недостатков

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