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Standard procedure for the pharmacotherapy of pain in childhood

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Physicians of all specialties encounter patients in pain. The basis of the philosophy of caring children is not to question the existence of pain but to predict, prevent, and adequately treat it. Acute pain services implement preventive and multimodal analgesic treatment to increase the analgesic effect at the lowest possible doses to minimize undesirable effects of individual drugs. However, this service cannot be provided in all hospitals 24 hours a day. This study provides a clear, color-coded recommendation for pain relief in children, which provides a quick, rational, and safe choice of analgesics or their safe and effective combinations and dosage for each age group.

Keywords: preventive analgesia; multimodal principle of drug therapy pain; children.

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Стандартный подход к фармакотерапии боли у детей

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В клинической практике педиатры часто встречаются с острой и хронической болью у детей. Основным принципом оказания помощи является умение предвидеть и предотвращать появление боли, не ставя ее наличие под сомнение, а также всегда эффективно бороться с ней. В терапии боли используют превентивную и мультимодальную аналгезию, которая позволяет при минимально возможных дозировках получить максимальный эффект с наименее выраженными побочными проявлениями. В статье представлены стандартные рекомендации, которые на основании объективной оценки интенсивности боли позволяют быстро выбрать подходящий анальгетик для детей соответствующей возрастной группы.

Ключевые слова: превентивная аналгезия; мультимодальный принцип фармакотерапии боли; дети.

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BACKGROUND

Pain in children is not an independent nosological unit, but is associated with unpleasant anxious experiences and fear. Physiological response to painful stimuli in children and newborns is accompanied by various hormonal, metabolic, and cardiopulmonary changes, in which severity is comparable to those in adults and may even exceed them. Pain perception in children is individual. Children often react differently to the same sensitive stimuli.

Acute pain

Sudden pain can be an acute illness or injury manifestation, which serves as a signal of imminent body damage. Such pain has positive significance, definite cause, and can be permanent and disappear after cause elimination. Pain is associated with increased activity of the autonomic nervous system, similar to an acute stress response. Acute and persistent pain compels the patient to visit a doctor. Pain becomes chronic if left untreated.

Causes of acute pain in children

The most common causes of acute pain in children include trauma and common infectious childhood diseases, which are manifested by headache or toothache, sore throat, earache, stomach-ache, and acute abdominal pain. Severe headaches can be a sign of encephalitis, meningitis, hemorrhage, or hypertension. Decompensated congenital heart defects, myocarditis, arrhythmia, Kawasaki syndrome, pneumonia, and pneumothorax are accompanied by chest pain. Severe pain in the musculoskeletal system can be associated with joint cavity or muscle hemorrhage, arthritis, osteomyelitis, myositis, transient synovitis of the hip joint, post-infectious

arthritis, and reactive non-infectious arthritis. Acute pain is noted in preoperative and postoperative periods. Pain during procedures is due to the nature of diagnostic and therapeutic measures.

Objective pain assessment

The first prerequisite for effective analgesia is an objective assessment of pain intensity using rating scales. Noting pain intensity changes is recommended during treatment to monitor the efficiency and duration of analgesia in medical history.

Pain intensity in newborns is assessed considering physiological changes and behavioral responses. Physiological changes include tachycardia, tachypnea, increased blood pressure, and hidropoiesis. Typical behavioral responses include anguished facial expressions, incessant crying, and sudden and active limb movements (in particular, lower limb flexion). In the preverbal stage of children aging 0–3 years, pain intensity is determined by the Face, Legs, Activity, Cry, Consolability (FLACC¹) behavioral pain scale, which include facial expression, lower extremity position, child's activity, cry, and consolability (Table 1). Pain assessment result of an appropriate scale must be accurately documented.

Pain intensity in older children is assessed using the VAS. The Wong-Baker scale is the most widely used pain assessment tool in preschool children (Fig. 1). In adolescents, like adults, the FLACC pain intensity assesses subjectively and/or using numerical scales. Pain sensation perception in adolescents is influenced by mental and emotional factors.

¹ FLACC — Face, Legs, Activity, Cry, Consolability).

Table 1. Pain assessment scale for newborns, infants, children under 3 years of age, and children with delayed psychomotor development — “behavioral scale” (visual analog scale [VAS]) [2, 3]

Parameter	0 points	1 point	2 points
Face	Neutral facial expression	Rarely grimace or knitted eyebrows. Unsociability. No interest is expressed	Chin shaking frequently or constantly, jaw clenching
Legs	Normal position, relaxed	Inability to find a normal position, constantly moving legs, legs tense	Kicking or raising legs
Activity	Calm normal lying position, free movements	Writhing, shifting back and forth, tense	Bending, rigidity, twitching
Cry	Absence of cry (during sleep or wakefulness)	Groaning or whimpering, sometimes complains	Cry for a long time, screams or sobs, often complains
Consolability	Satisfied, calm	Calms down from touching, hugging, talking. Can be distracted	Difficult to calm down

Note. The monitoring is performed for 1–5 min. Each parameter is rated from 0 to 2 points. Total score ranges from 0 to 10 points on the VAS. VAS 1–3 (mild pain): patient reports pain only upon request, without a grimace of pain, and are fully focused. VAS 4–7 (moderate pain): patient emotionally complains of pain with a grimace of pain. VAS 8–10 (severe pain): patient seeks a relief position, has a grimace of pain, groans, and experiences stress.

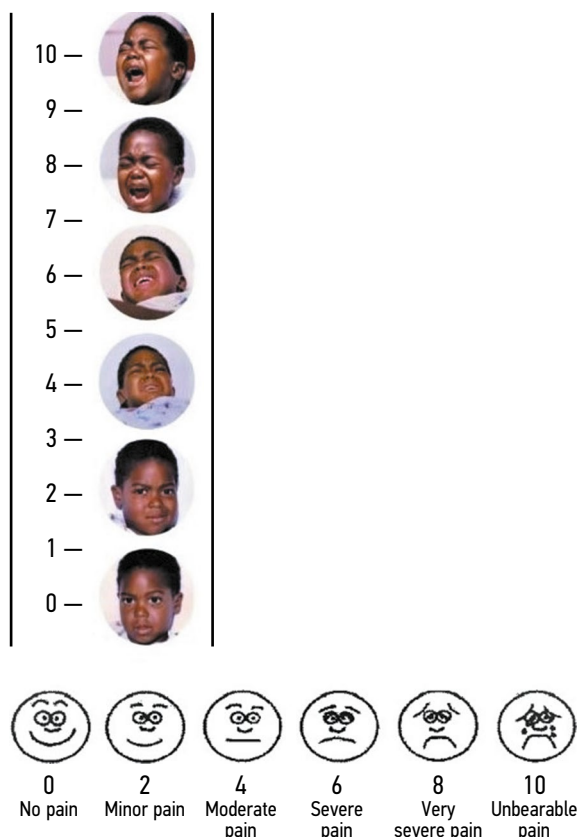


Fig. 1. Assessment scales of pain for children in preschool and school age [2, 3]

Pain degree

VAS 1–3 indicates low pain intensity. The patient informs the presence of pain only in response to a question, fully concentrated on the conversation, without grimace of pain. VAS 4–7 indicates moderate pain, the patient complains emotionally of pain, can hardly concentrate on the conversation, and has an expression of pain on the face. VAS 8–10 signals severe, unbearable pain. A patient with a face twisted in pain seeks a position of rest, groans loudly, and experiences stress.

Pharmacological principles of pain management

The World Health Organization (WHO) recommends a three-staged approach to pain management (WHO’s pain relief ladder) (Fig. 2).

- The pain relief ladder consist the following steps:
- 1) **non-opioid analgesics:** paracetamol;
 - 2) **oral or parenteral feeble opioid analgesics or non-steroidal analgesics:** codeine, tramadol, diclofenac, ibuprofen, etc.;
 - 3) **parenteral potent opioids:** morphine, fentanyl, etc.

The most effective principles for perioperative pain suppression while maintaining its effect in the postoperative period include intrathecal or epidural administration of opioids, peripheral or central nerve block, which are part of anesthetic procedures (Fig. 3).

In pain management, adjuvants can be used in addition and as necessary, which are elements of maintenance or combination therapy. These agents include antidepressants, anxiolytics, antihistamines, and antiepileptic drugs which can suppress the central nervous system activity. Anesthetic and neurosurgical measures can also be used as adjuvants [1–4].

Pain drug treatment strategy and approach in children

The main principle of pain drug treatment is not only prevention, but also effective suppression. The type of analgesic and its dosage should be selected individually, taking into account the nature of medical manipulation, pain intensity, age, and concomitant diseases. Drug of choice depends on pain intensity objectified using rating scales. Relying on the principle of multimodal analgesia is recommended in pain management strategy selection. Combined use of non-opioid and opioid analgesics seems rational, as it enables the usage of multilevel pharmacological mechanisms of pain suppression. A practical advantage of multimodal analgesia is the ability to achieve the highest analgesic effect with minimal dosages, which helps in side effects risk reduction. Preventive analgesia, that is, the use of an analgesic before a painful procedure, significantly reduces drug dosage and minimizes their side effects. For example, systemic administration of analgesics is combined with preoperative infiltrative or regional anesthesia.

Conventional analgesics and adjuvants are used in pain pharmacotherapy. Top to bottom procedures are observed, that is, from invasive techniques and potent

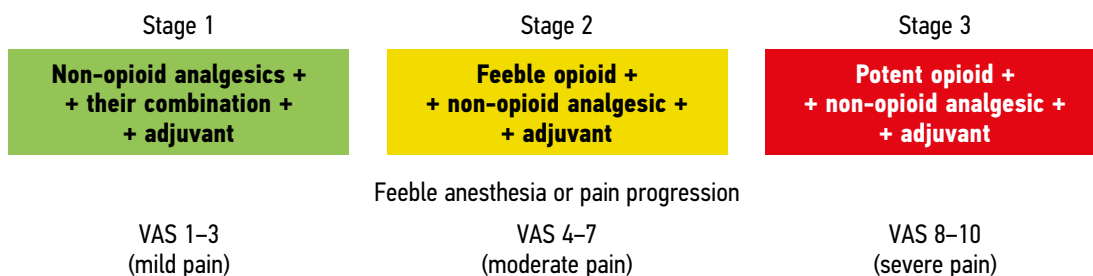


Fig. 2. The pain relief ladder. VAS — visual analog scale. Adjuvants — drugs with analgesic effect from other pharmacological groups, for example glucocorticoids, antispasmodics, muscle relaxants, etc. [2, 3]

Sedation

(Minor painless diagnostic procedures: magnetic resonance imaging, computed tomography)

Mild pain VAS 1–3

(Minor procedures, minor gynecological, urological, and plastic interventions)

Paracetamol + metamizol + sedation**Paracetamol + metamizol****Paracetamol + sedation****Paracetamol****Moderate pain VAS 4–7**

(ENT procedures, appendectomy, herniotomy, gynecological surgeries, neurosurgical manipulations)

Opiate + NSAIDs + Paracetamol + sedation**Opiate + NSAIDs + Paracetamol****Paracetamol + NSAIDs + sedation****Paracetamol + NSAIDs****Paracetamol + sedation****Paracetamol****Severe pain VAS 8–10**

(Surgeries in the epigastric region, kidneys, chest, spine, perianal region, bones, and joints)

Regional anesthesia +/- Opiate + NSAIDs + Paracetamol + sedation**Opiate + NSAIDs + Paracetamol + sedation****Opiate + NSAIDs + Paracetamol****Paracetamol + NSAIDs + sedation****Paracetamol + NSAIDs****Paracetamol + sedation****Paracetamol****Fig. 3.** Severity of pain and combination of analgosedation in children during or after painful diagnostic, therapeutic, or surgical procedures. ENT — Ears, nose, and throat; VAS — visual analog scale; NSAIDs — non-steroidal anti-inflammatory drugs

analgesics to simpler methods of administering less potent pain medications to effectively suppress acute pain. Drug combinations depend on pain syndrome intensity, and are prescribed at regular intervals for 48–72 h after a painful procedure (Table 2). Opiates are canceled first with decreased analgesic load. Effective analgesia-sedation is aimed at pain intensity reduction to 3–4 points as assessed according to a ten-level VAS.

Principles of effective pharmacotherapy for acute pain in children [2, 3] are as follows:

- the analgesic and its dosage are selected individually, depending on pain nature and intensity, as well as the age of the child and concomitant diseases;
- the analgesic is selected depending on pain assessment (intensity), which is performed using verbal, analog, numerical, and behavioral scales;
- use of multimodal (combined) analgesia with a preventive component (administration of an analgesic before a painful surgical procedure);
- analgesic administration at regular time intervals;
- opiates are canceled first with a decreased analgesic load;
- combinations with local and epidural anesthesia are advisable, as well as peripheral nerve blockade;

- the analgosedation is aimed at the VAS level of 3–4, when the patient can cough productively (effectively) and can be easily woken up.

In the modern university children's hospitals, the so-called acute pain management services provide effective evidence-based pain management. In the absence of treatment specialist for pain syndrome in children, clinical guidelines should be followed to objectively assess the pain intensity and choose a rational and safe method of analgesia.

From a practical point of view, each pediatric department should have clinical guidelines for pharmacotherapy of acute pain with precise indication of dosages for all categories of pediatric patients [3, 4].

ADDITIONAL INFORMATION

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Table 2. Principles of analgesics and sedatives administration in children

	Name	Route of administration	Age	Dosage	Maximum dosage	Administration interval	Side effects
Sedation	Midazolam	i.v.	0.5–5 years	0.05–0.1 mg/kg	6 mg/24 h	6 h	Paradoxical response
			6–12 years	0.025–0.05 mg/kg	10 mg/24 h		
	Chloral hydrate 10%	p.o., p.r.	0.5–12 years	0.3–0.5 mg/kg	10 mg/24 h	6–8 h	
			>28 days	0.5 ml/kg	–		
Opiates	Diazepam	i.v.	>0.5 years	0.1–0.2 mg/kg	–	6 h	–
	Piritramide	i.m. s/c	Adults	15–30 mg	–	6–8 h	–
			Children	0.05–0.2 ml/kg	–	6–8 h	–
		i.v.	Adults	7.5–22.5 mg slowly	–	6–8 h	–
			Children	0.05–0.1 mg/kg slowly	–	6–8 h	–
	Tramadol	i.v. p.o. p.r.	>0.5 year	1–2 mg/kg	8 mg/kg/24 h 400 mg/24 h	6–8 h	Nausea
ANALGESIA NSAIDs	Neodolpasse (diclofenac 75 mg + orphenadrine 30 mg)	i.v.	>14 years/40 kg	250 ml/infusion 2 h	–	12 h	–
	Diclofenac	p.o.	>12 years	1 ml/kg	3 mg/kg/24 h, 150 mg/24 h	8 h	–
	Ibuprofen	p.r.	>2 years/12.5 kg	10 ml/kg	–	6 h	–
			<12 years	5–10 ml/kg	40 mg/kg/24 h	6–8 h	–
	Metamizol	i.v.	>12 years	400–800 mg	2.4 g/24 h	6 h	–
			>3 mon./5 kg	10–15 mg/kg slowly	–	6 h	–
Paracetamol	p.r.	Adults	0.5–1 g	4–6 g/24 h	6 h	–	
		>10 kg	Initial 40 mg/kg Then 20 mg/kg	– –	6 h	–	
	p.o.	>10 kg	Initial 20 mg/kg Then 10–15 mg/kg	– –	4–6 h	Toxic dosage: 150 mg/kg/24 h (8 g/24 h)	
		>50 kg	1 g	4 g/24 h	6 h		
	i.v.	10–50 kg	10–15 mg/kg	60 mg/kg/24 h	6 h	–	
		<10 kg	7.5 mg/kg	30 mg/kg/24 h	6 h	–	
	p.o./p.r.	NB <32 WG	7.5 mg/kg	40 mg/kg/24 h	6 h	–	
		FTNB	–	60 mg/kg/24 h	–	–	
Infants		–	75 mg/kg/24 h	–	–		
		Children	–	100 mg/kg/24 h	–	–	

Note. FTNB — full-term newborns; NB — newborns; WG — week of gestation, i.m. — intramuscular, i.v. — intravenous, i/n — intranasal, p.r. — *per rectum*, p.o. — *per os*, s/c — subcutaneous.

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