Also see RxFiles: CHRONIC PAIN - Pain Overview and An Approach to Pain Assessment & Management Planning,

Overview

- Similarities exist for pain management across the lifespan; however, the pediatric population requires special consideration to ensure:
 - o Full pain assessment occurs even when challenges with a child's ability to verbally communicate are present.
 - Management strategies are individualized to be realistic and support daily function.
 - o **Active participation** of the child, to the extent possible, in their own multimodal pain management strategies.
- Use age-appropriate language: might say "hurt" instead of "pain", especially in younger children; ask yes/no questions for child 3-4yrs

assessment

General

Approach to

Management

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* consider the

underlying pain

(e.g. neuropathic,

General approach

- Prioritize the child's self-report of pain (can generally be done by age 3-4yrs) as the primary source for gathering info about pain experience o Other useful sources of information include observation, family/caregiver reports, and clinical context
- o Ask caregivers how to best communicate with the child (e.g. assistive technology, pictures) & what their behaviour is like when not in pain • Anticipate painful procedures (e.g. lab work, IV insertion, vaccination) & proactively establish a pain coping & management plan
- Pain management plans should be individualized and family-centred (consider what strategies might be useful/feasible in current circumstance) o Invite the child's participation in pain management strategies (encourages active self-management, helps build trust in healthcare encounters) o Promote active engagement - empower family members to assess & help manage pain at home

Common challenges

- Pain is commonly under-recognized & under-treated in pediatrics (Myth: children do not feel pain as their nervous system is not developed.4)
- o More difficult to assess pain in very young (pre-verbal) & children with an impairment that impacts verbal communication (e.g. non-verbal)
- o Children may restrain their pain behaviours, or struggle to know how to communicate their experience (e.g. adverse childhood experiences might influence pain perception & expression)
- o Caregivers are often very skilled at interpreting behaviour, however they may also under- and over-report pain for a variety of reasons (e.g. minimizing the pain or reflecting their own distress)
- Limited evidence to direct medication management (e.g. high placebo effect, questions about cannabinoids without evidence-based answers)
- Tendency to underdose medication (e.g. due to lack of parent/caregiver understanding of toxicity, dosing without weight-based calculation)⁵

ACUTE PAIN (e.g. acute otitis media, MSK injury, fracture, appendicitis, burns) All will experience acute pain at one time or another. Introduction Addressing early can improve a provider's ability to evaluate & diagnose the cause, support faster recovery, and possibly prevent sensitivity to future pain. / Prevalence 1/5 children who undergo major surgery will develop chronic pain in adulthood.² Location, quality (what makes it worse/better, words to describe), duration, context (recent relevant events/changes), functional consequences, pain intensity, + physical exam. Self-report scales to assess pain intensity:3,9 Faces Pain Scale-Revised (FPS-R) Age \geq 4-7 yrs (some suggest \geq 3 yrs); **Assessment** See online extra. ask about "how they feel inside" (not how they look) Numerical Rating Scale (NRS-11) | Age \geq 6 yrs; ensure numeric competency. *for comparison Color Analogue Scale (CAS) Age \geq 8 vrs; uses colour, size, and number gradients. use the same - Limitations if pre-verbal, non-verbal, different language, & hearing/seeing challenges tool to reassess Observational/Behavioural tools (if self-report not possible) with caregiver's assessment: 1,3,42 follow-up Neonatal Facial Coding System (NFCS) For neonates, 0-4 mos (also chronic pain). *explain the Face/Legs/Activity/Cry/Consolability (FLACC) | Age 2 mos – 7 yrs. results of

See online extra. Revised version (r-FLACC) for 4-19yrs with neurological impairment/non-verbal. Evaluation Enfant, DOuLeur (EVENDOL) Age 0-7 yrs. - Note medication toxicity & withdrawal can be associated with pain behaviors - rule/out. Assessment tools generally studied for hospital use, less studied in outpatient settings.³

- Documenting pain score associated with \uparrow analgesic use & \checkmark acute pain.8
- Multimodal Management is Key! 1.3.5,32,38,42.44 Include a combination of analgesic strategies: 1) Physical, 2) Psychological, & 3) Pharmacological. Emphasize active self-directed techniques. Using a "3P Approach" can ↑coping & pain threshold - educate patients & caregivers on the role for combinations of strategies.

Physical: As appropriate, consider heat, ice/cold compress, splinting, elevation, massage, bandage +/- dressing (immobilizing area can ↓ pain), caregiver holding/cuddling/rocking. Psychological: Consider use of distraction, breathing exercises, providing information & reassurance, virtual reality, counsel regarding anticipated pain severity & duration (when able). Pharmacological (see Tables 1&2): 1st line - NSAID or acetaminophen as monotherapy (if not CI), for most mild-moderate acute pain. NSAIDs may be preferred for acute dental pain. 41

- If monotherapy not effective (e.g for mod-severe pain), may switch to or add the other. May give one around the clock, with other PRN for breakthrough, or give both on scheduled basis.
- For mod-severe pain, may add immediate-release opioid to other optimized analgesics for short period (i.e. ≤5 days, longer period after surgery/trauma may be required); Not used as monotherapy.³⁹ o Screen youth for substance use (e.g. CRAFFT); risk factors for OUD in peds not well established.⁵⁶
- Triptan for acute migraine: Almotriptan 6.25-12.5mg po, may rpt x1^{>12yrs} (√HC indication; See online extra)
- Topical agents may be considered (e.g. lidocaine, capsaicin) for some types of pain.
- In acute care, consider other approaches (e.g. adjuvants ketamine/dexmedetomidine/nitrous oxide, nerve blocks, other administration routes such as IV or intranasal, epidural +/- patientcontrolled analgesia), as appropriate.

Physical: Physical therapy, physical activity, repositioning, yoga, passive stretching, warm baths, massage, mobility aids, square breathing, weighted blankets, vibratory stimulation, acupuncture, transcutaneous electrical nerve stimulation, occupational therapy (sensory rehabilitation, \uparrow ability to engage in ADLs and self-care).

Psychological: Reassure & validate that pain is real, educate regarding pain science & realistic goals for management strategies (focus on function before pain intensity), address "catastrophizing" & fear-avoidance behaviors. Normalize life through the "4 S's": sports, social, sleep, & school (see online extra). 45 Add CBT, Acceptance & Commitment Therapy, music therapy, guided imagery, mindfulness. **Consider multidisciplinary program referral if available, when high impact on function without improvement from multimodal strategies. **

Pharmacological (see Table 2): Trials for use in peds are low/very low QE, benefits often extrapolated from adult use. 44,50,5 • Acetaminophen / NSAID: Consider PRN → primary HA (caution: medication overuse HA) or acute-on-chronic pain.

- Gabapentinoid, TCA ?for neuropathic-type or chronic widespread MSK (e.g. juvenile fibromyalgia) pain.
- Opioids rarely indicated (exception: may use OAT in OUD): may use for acute flares/acute-on-chronic pain. o Avoid use for primary HA, centrally mediated abdominal pain syndrome, chronic MSK pain.^{39,45} o Avoid abrupt/rapid discontinuation if on stable, long-term dose.
- Traditional medicines & other culturally relevant healing practices may be utilized, as requested.
- Consider dietary supplements (e.g. magnesium 9mg/kg/day po divided TID; Max: 600mg/day for migraine prevention).

- CHRONIC PAIN (i.e. lasting > 3 months) (e.g. chronic headache, abdominal pain, low back pain, spasticity) • Estimates suggest 11-38% of children will experience chronic pain, with prevalence generally being higher in girls than boys, and increasing with age.¹
- Evidence suggests chronic pain associated with adverse childhood experiences.⁶
- Anxiety & depression in youth with chronic pain are >3x greater than in those without pain.
- Complete a biopsychosocial assessment: In addition to location, quality, duration, etc ... Also consider social determinants of health, emotional components of pain (e.g. mental health, "catastrophizing", beliefs about pain), sensitivity to sounds/smells/touch, impact on daily life (e.g. play, school, socialization, sleep, family life), prior & current strategies trialed (e.g. movement, mind, medications), language & cognitive abilities, values & preferences.
- Little evidence for use of NRS-11, yet may be used at initial assessment (FPS-R not recommended)

Self-report scales generally to assess pain interference with function in life: 1,10			
Bath Adolescent Pain Questionnaire (BAPQ)	Age 10-19 yrs, parent version also an option		
Pediatric Pain Interference Scale (PPIS)	Age 8-17 yrs, available as short form		
Pediatric Pain Questionnaire (PPQ)	Age 4-16 yrs, parent & child screening tool		
Pediatric Pain Profile (PPP)	Age 1-18yrs with severe neurological impairment		

- No validated behavioural tools for use in chronic pain (might use NFCS, EVENDOL).
- Additional tools may be found at: Holland Bloorview Kids Rehab Hospital Tools for Assessing Chronic Pain.
- Assess other related comorbid conditions, and treat concurrently (e.g. mental health, constipation).
- Assess values, preferences, & goals (strive to relieve symptoms & ↑ function).

Needle Pain & Other Common Minor Procedures (e.g. vaccination, IV insertion, NG tube insertion)^{11,22}

Parent: be present, engage child in non-procedure talk, assist with child's position for comfort (sitting upright on or beside parent), apply numbing cream for child (Topical anaesthetic: OTC; apply prior to appointment; may \$\psi\$ pain 40%; see Table 1), avoid saying "it's ok" or "it will be over soon". Avoid giving oral analgesics/antipyretics to infant / child pre-emptively (ineffective & may \$\psi\$ vaccine immune response). \$^{52}\$ Video for parents here.

Neonate/infant: 12-17 swaddle, feed at the breast 2-3min pre-procedure, if BF not feasible (e.g. NPO, CI, parent unavailable), give oral sucrose 24% soln (e.g. TootSweet; home made=1 sugar pack/cube in 10mL H₂O) 1-2min pre-procedure & repeat PRN + sucking.

Topical anesthetics: Not well studied in term/pre-term neonates, however used. 24 Tetracaine & liposomal lidocaine have fast onset & not associated with methemoglobinemia, but in very young (including preterm) lidocaine/prilocaine has the most evidence. Systemic toxicity (cardiac & CNS-seizures) possible 3 but rare with appropriate use. If used, apply small amount of cream for shortest period necessary for onset (& avoid patch).

Age ≥1yr:18.19 Upright position, age-appropriate distraction / psychological techniques²⁰ - very useful: toys, books, bubbles, TV, music, humour, imagery, deep breathing, blowing a pinwheel. Topical anesthetic (See Table 1); ?Vapoccolant Spray PAIN EASE OTC; onset ≤60 seconds, risk of over-cooling & may startle young child.²³

Older child (≥4yr): add preparation/information: brief description, what to expect - feels cold/warm, little pinch, will help you! Choose words such as "pressure/immunization/poke", instead of "pain/shot/needle". Cough Trick, 21 cool-vibrating device (e.g. Buzzy). 30

Resources: 1) BC Centre for Disease Control – Reducing Immunization Injection Pain;
2) Immunize Canada – Pain Management During Immunizations for Children;
3) Toronto SickKids – CARD System, Learning hub. See online extras: for information about

Drugs for Procedural Sedation & Other Local Anesthesthetics (for open wounds, infiltration)

Table 1: Topical Anesthetics ("numbing cream/patch")²² OTO

✓ Skin anesthetic prior to venipuncture or cannulation. Use of **AMETOP** for vaccination is off-label.

(Strengths & formulations) Dura	nset (O) ation (D) Adverse Events AE / Contraindications CI time (M)*	Additional Comments	Cost/Pack
Iiposomal Iidocaine O: 30 r (15-4 MAXILENE 4 4% crm (5, 30g tube)	than lidocaine/ prilocaine. No safety data for child <2yo however used. Caution if heart block/	Occlusion <u>not</u> required (but may use to protect area from rubbing) Minimally vasoactive Methylparaben free	\$60, 30g 4% crm \$70, 30g 5% crm
Iidocaine + prilocaine	hr skin blanching / erythema). Caution if heart block/severe	Occlusive dressing required Do not cut patch Preservative free	\$65, 30g \$ 15 , 2 patch
tetracaine (also called amethocaine) AMETOP 4% gel (1.5g single use tube, 12g) W: 1-4 (depend D: 30-4 M: 2 h	A45 min AE: vasodilation (may cause more erythema, edema than lidocaine products; skin blistering (rare) CI: Neonates <1mos (including preterm corrected to 1mos, see note at left)	Occlusive dressing required Store refrigerated Methylparaben preservative (caution: hypersensitivity)	\$15, 1.5g

General Comments: Effectiveness: Few head-to-head studies, however compared to lidocaine/prilocaine for IV insertion: linosomal lidocaine as effective 25,26 & tetracaine as effective, possibly more effective (Cochrane review withdrawn by authors). Not likely effective for heel poke. A Cream Application: Use on intact skin only, avoid contact with mucous membranes, child's fingers, & ingestion. Amount applied on planned site(s) for 0-3mos: 0.5g (size of a 5-cent coin); for ≥4mos: 1-2g (up to size of a 2-dollar coin). Cover with occlusive dressing (e.g. Tegaderm) or plastic wrap secured with tape, as required, up to the maximum application time (see above*). Wipe off prior to procedure. Resource: How to apply.

Allergy: True allergy to local anesthetic is rare (ester more common than amide); often due to preservative. Avoid tetracaine if ester or PABA allergy. Cross-reactivity between amide and ester anesthestics unlikely. If reaction, may trial different class (i.e. if allergy to tetracaine, reasonable to trial lidocaine instead) & use formulation without preservative if available/suitable.

Table 2: Ora	al ,	Enteral Medic	ation for	Pain	Mana	gemen	t in Pediatric Patients1,38,45
_							

Generic/TRADE (Strengths & formulations)	Initial Dose & Maximum ^{31,42,43} (po unless otherwise indicated)	Adverse Events AE / Contraindications CI / Monitoring M	Comments	Cost/30d
acetaminophen TYLENOL X ▼ OT Susp 160mg/5mL; Drops infant 80mg/mL;	Initial: 10-15mg/kg q4-6hr (up to 1000mg/dose).	AE: Well tolerated. <u>Caution</u> : ?↑ hepatotoxicity risk if	• Lower max (e.g. 60mg/kg/day or less) for premature/ newborns³1; may give drops pr for doses ≤80mg	\$12/120 x 325mg tabs
Chew-tab 80, 160mg; Tab 325mg; Supp 120, 325mg Caution: Ingredient of many products! Unintentional duplication may occur.	Max: 75mg/kg/day ^{term≥10days} 4000mg/day, or 5 doses per 24hr. Supp pr : 15- <u>20</u> mg/kg	malnourished or dehydrated M: liver enzymes (with chronic use)	•Toxic single dose <6yrs: ≥200mg/kg •Rectal admin has erratic absorption & slower time to peak effect vs po (pr 2-5hrs vs po <1hr)³¹	\$12/100mL x 160mg/5mL
ibuprofen ADVIL, MOTRIN ▼ OT Susp 20mg/mL; Drops infant 40mg/mL; Chew-tab 100mg; Tab 200mg approxen g Susp 25mg/mL (ALEVE OTC ≥12yrs, Tab 220mg▼) (Stronger prescription strengths avail. for bot)		Caution: renal risk with dehydration, NSAID-induced asthma, & ? bleeding disorder • Some concern: long-term use may restrict healing fractures	•Generally, 1 st line for mild-moderate acute pain, used with other agents for mod-severe pain. •Max 14day/mos for migraine (prevent medication overuse HA) •Celecoxib ^{FDA approval} : JIA >2yrs 10-25kg: 50mg po BID (100mg cap smallest form available on CDN market, not indicated for this use in Canada)	\$15/100 x 200mg tabs \$12/100mL x 100mg/5mL \$17/100 x 220mg tabs \$60/474mL x 125mg/5mL
morphine DOLORAL, MS-IR, STATE Liquid 1, 2mg/mL; Tab 5, 10mg	K Initial : 0.2 -0.5mg/kg q4hr ^{>6mos} (up to 5 -10mg/ dose) Max : Generally limit to <mark>50mg/day</mark>	misuse risk. <u>Caution</u> : Hx of substance use	 Morphine initial dose for infant ≤ 6mos in monitored setting: 0.08-0.1mg/kg po q4hr May use for acute mod-severe pain in addition to 	5-10mg po q4h prn x 30 tabs \$14-17
HYDROmorphone DILAUDID, g Liquid 1mg/mL; Tab 1, 2mg (Stronger prescription strengths avail. for bot	or ≥50kg: 1-2mg/dose q4hr	depressants, ³⁹ OSA	other analgesics (not for monotherapy). See Q&As for prescribing considerations Do not stop abruptly after regular use (taper).	1-2mg po q4h prn x 30 tabs \$14-16
(Stronger prescription strengths avail. for both gabapentin NEURONTN, g Cap 100, 300, 400mg; Tab 600, 800mg	300mg/ dose), titrated to TID. Ma x: <mark>35-</mark> 50mg/kg/day	AE: Sedation, dizziness, wt gain, misuse risk. <u>Caution</u> : Concurrent	 Open capsules and sprinkle; gabapentin suspension may also be compounded by some pharmacies Off-label; may trial for neuropathic pain, fibromyalgia, 	100-300mg po HS \$11-13 300mg po bid-tid \$16-19
pregabalin LYRICA, g Cap 25, 50, 75, 150, 300mg	Initial: 1-1.75mg/kg daily (up to 50mg/dose), titrated to BID-TID Max: 14mg/kg/day or 600mg/day	CNS depressants (e.g. opioids) Pregabalin dose for juvenile fibromyalgia	spasticity, as used in adults (but not well studied) ^{46,47,49} Do not stop abruptly after regular use (taper). Livis initial: 25-75mg daily to BID; Max: 450mg/day ⁵⁴	25-75mg po HS \$14-19 75-150mg po bid \$28-35
amitriptyline ELAVIL, g Tab 10,25,50mg; 75mg ^X	Initial: 0.1-0.25mg/kg HS (up to 10mg/dose), titrated. Max: 0.5-2mg/kg HS or 50-100mg/day	Caution: ↓sz threshold, cardiac	 May crush amitriptyline tabs (admin immediately) but film coated (does not disperse well) & bitter taste; nortriptyline caps may be opened & sprinkled 	10-25mg po HS \$11-12 50-100mg po HS \$14-17
nortriptyline AVENTYL	Initial: 0.2-0.25mg/kg HS (up to 10mg/dose), titrated.	QTc, suicidality, with other	•Off-label; may trial for migraine proph (not effective?) ⁴⁸ , neuropathic pain, as used in adults (but not well studied) ⁴⁷	10-25mg po HS \$21-31 50mg po HS

Q&As

Is alternating acetaminophen with ibuprofen appropriate? It can be. Since the mechanisms of action differ, they may be used concurrently, however monotherapy sufficient & preferred when possible. Combination may ↑ risk of administration errors & AE (e.g. renal). If used, advise caregiver to verify each dose & write down time of each administration to keep track.

Are opioids the most effective option for acute pain?

The evidence suggests they are not. Ibuprofen may be more effective than acetaminophen/codeine for MSK injury.³³ Oral ibuprofen 10mg/kg = to oral morphine 0.5mg/kg for post-op ortho pain³⁴ & extremity fracture

What are some considerations when prescribing opioids for pediatric patients?³⁹ • Generally, acute pain limit <5days.

pain³⁵ plus morphine is associated with more AE.

- Start with lowest immediate release dose (syrup, tab) & reassess/titrate/taper as appropriate.
- Counsel re: potential AE & management. Be prepared to prevent opioid AE & treat as soon as they happen (e.g. nausea, constipation, itch).
- Advise re: <u>locked</u> storage & proper disposal. Consider caregiver-observed administration. Educate about non-medical substance use (& risks of sharing / selling meds), & monitor for self-led dose escalations.^{39,64}
- Discuss overdose response & provide naloxone (See: <u>JAMA Parent Naloxone resource</u>).
- Avoid tramadol: Cl in <18yrs HC 2017
- Avoid codeine: Cl in <12yrs HC 2013 & in <18yrs post-op tonsil/adenoid removal HC 2016; also avoid if 12-18yrs with OSA, ↑BMI, severe lung dz³9; morphine toxicity risk in ultrarapid CYP2D6 metabolizers

Additional Resources: • https://kidsinpain.ca/

- BC Children's Hospital: <u>Pediatric Pain Guide for Caregivers</u>
- Zoe & Zak's Pain Hacks Book Series More at online extras!

Abbreviations: ==Exception Drug Status in SK x =Non-formulary in SK ♥=prior approval for NIHB ⊗=not covered by NIHB ▼=covered by NIHB SHT=serotonin ADLs=activities of daily living AE=adverse events BF=breastfeeding BID=twice daily BMI=body mass index cap=capsule CBD=cannabidiol CBT=cognitive behavioural therapy CI=contraindicated crm=cream CV=cardiovascular CYP=cytochrome d=day(s) DI=drug interaction dz=disease FDA=approved Food & Drug Admin. fx=function g=generic available G6PD=glucose-6-phosphate dehydrogenase HA=headache HC=Health Canada hr=hour(s) HS=bedtime HTN=hypertension hx=history IV=intravenous JAMA=Journal of the American Medical Association JIA=juvenile idiopathic arthritis max=maximum min=minute(s) MOA=mechanism of action mod=moderate mos=month(s) MSK=musculoskeletal N/V=nausea/vomiting NSAID=non-steroidal anti-inflammatory drug(s) OAT=opioid agonist therapy ODT=orally disintegrating tablet oint=ointment OSA=obstructive sleep apnea OUD=opioid use disorder PABA=para-aminobenzoic acid peds=pediatrics PI=placebo po=oral pr=per rectum PRN=as needed QE=quality of evidence QTc=corrected QT interval RCT=randomized controlled trial rpt=repeat s=second soln=solution SR=sustained release supp=suppository susp=suspension sx=symptoms sz=seizure tab=tablet TCA=tricyclic antidepressant(s) THC=delta-9-tetrahydrocannabinol TID=three times daily tx=treatment wks=weeks wt=weight yrs=years/years old

RxFiles On-Line Extras: PEDIATRIC PAIN

A Wiebe BSP, L Regier BSP, B Jensen BSP, B Kessler BSP © www.RxFiles.ca

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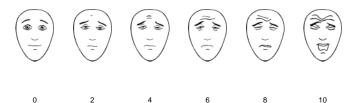
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Faces Pain Scale - Revised (FPS-R) - age 4+

This is a thumbnail image. The full-size FPS-R with instructions is available at https://www.iasp-pain.org/resources/faces-pain-scale-revised/. Numbers are not shown to children.



From: Hicks CL, von Baeyer CL, Spafford PA, Van Korlaar I, Goodenough B. The Faces Pain Scale - Revised. Toward a common metric in pediatric pain measurement. Pain 2001:93:173-183. ©2001 International Association for the Study of Pain. Reprinted with

FLACC SCALE – for assessing pain in very young children non-verbal; suitable for cognitively impaired				
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw	
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up	
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking	
Cry	No cry (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams or sobs, frequent complaints	
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort	

- ◆Each of the five categories (F) Face; (L) Legs; (A) Activity; (C) Cry; (C) Consolability is scored from 0-2, which results in a total score between zero and ten
- From The FLACC: A behavioral scale for scoring postoperative pain in young children, by S Merkel and others, 1997, Pediatr Nurse 23(3), p. 293-297. Copyright 1997 by Jannetti Co. University of Michigan Medical Center.

Drugs for Procedural Sedation (sedative/hypnotic adjuncts)

Monitor for procedural sedation & vital signs. Check protocols & be aware of guidelines/liability implications (institutional/departmental/professional). Should not be providing sedation & doing procedure.

N₂O:(50/50mix O2, demand valve) age ≥ 3: quick 3 min, short acting good for IV starts; CI: pneumothorax, bowel obstruction

•Midazolam: as adjunct prior to minor procedures: po onset 10-20min, duration 30-45min:

po: <20kg: 0.5-0.75mg/kg/dose; ≥20kg: 0.3-0.5mg/kg/dose; Max 10-20mg po;

no oral formulation commercially available in Canada – use injectable product given orally, or some pharmacies may compound oral suspension using injectable formulation

Note IV midazolam dose is MUCH lower than po dose!!! (1/10th the dose)

{IV: 0.05mg/kg/dose IV x1; repeat x1 PRN; onset 2-5min, duration 10-20min}; AE: disinhibition, apnea, paradoxical agitation;

Caution:

hepatic / renal fx; DI: CNS depressants:

dose of both.

{Nasal | limited study: use injectable product through Mucosal Atomization Device; faster onset but √sedation & duration than po; can be irritating to nasal mucosa; less effective than intranasal ketamine. 36}

•Ketamine: 0.5-2mg/kg IV (1mg/kg intranasal); onset 1-5min; duration 15-60min;

AE: nystagmus, dissociative (looks awake but is asleep; inform parents); vivid dreams x48hrs (add low dose midazolam if ≥10 yrs to prevent nightmares}; ↑BP, HR, salivation (co-administer atropine with 1st dose); rash common but transient.

Rare-Severe AE: laryngospasm, apnea, resp depression, recovery agitation,

Preserves pharyngeal & resp fx. CI: airway instability, URTI, ? TICP, TBP, acute globe injury, glaucoma, thyrotoxicosis, psych disorder. Age >1yr preferred; DI: CYP 2B6.

- Fentanyl: chest wall rigidity possible with midazolam
- •Propofol: CAUTION SIGNIFICANT TOXICITY! → metabolic acidosis; ↑BP, ↑death in ICU! Reserve for anaesthesia.

Other Local Anesthetics* Comments: 45 minutes for good effect; Avoid mucous membranes 45 minutes 65		
	LET lidocaine 4% */ epinephrine 0.1% / tetracaine 0.5%	 Topical anaesthetic for open wounds esp facial/scalp if <5cm in length; max
	Eninephrine (E): ↑ hemostasis ↑ anaesthetic duration: (compound)	1) mix with cellulose form gel, apply to wound, cover - occlusive dre

2) place LET soaked cotton ball into wound; apply pressure x20min AVOID: digits, nose tip, ear, penis (2° necrosis end artery). Methylcellulose / epinephrine 0.05% / cocaine 11.8% Mixed solution with methylcellulose forms gel, preventing running; LET preferred! Local Infiltration: 1) warm anaesthetic 37°C, 2) use smaller gauge needle (e.g. 27 or 30-gauge), 3) inject at slow rate, proximal borders 1st, from

inside wound edge, 4) pre-treat with topical anaesthetic, 5) consider buffering (sodium bicarb 9mL mix with 1mL 1mEq/mL bicarb) for less pain, 6) pressure Mepivacaine: local onset 6-10min; duration 1-3hrs; Lidocaine (L): local onset rapid; duration 30min Bupivacaine (B): local onset 8-12min;

{duration 1-2hr if regional block}; Age 3yrs+ ✓ if Age <3yrs or weight <13.6kg, use [0.5-1.5%]; - little vasodilation & epinephrine seldom needed [L: 0.5%, 1%, 2%; L+E: 1%, 2%; (L+E no preservative:1.5%)]

duration 4- 6hr; Age 12yrs+ ✓ CI: sulfite allergy [B: 0.25%, 0.5%; B+E: 1%, 2%]

Systemic toxicity (cardiac & CNS-seizures) possible but rare with appropriate use: (careful with dose & site)

Normalizing the 4 S's for Chronic Pain Management: Sports, Social, Sleep, & School⁴⁵

"First your life gets back to normal, then your pain decreases — unfortunately it's not the other way around... sometimes pain may even increase, before it gets better." — the 4 S's need to return to normal parameters before pain resolution could or should be expected.

- Friedrichsdorf, et al.

- 1) **Sports** address physical therapy, emphasize restoration of activity (e.g. exercise, participation in sports)
- 2) **Social** validate & acknowledge feelings of being misunderstood, work with psychologist/family therapist to build coping strategies and develop strategies for integration with others in social settings
- 3) Sleep address insomnia through education and establishment of healthy routines (e.g. waking at consistent time in the morning, eating breakfast, personal hygiene, attendance at school, avoidance of napping, avoidance of screen time at least 1 hour prior to bedtime, maximum weekend "sleep in" of 1-2 hours on weekend).
- 4) **School** Ensure daily attendance, work with school to establish support (e.g. time-limited breaks), address teasing/bullying, potential learning concerns

Cannabis in Child & Adolescent Populations for Chronic Pain^{60,62,63}

- Cannabis products in Canada available for pediatric access include prescribed cannabinoids (e.g. nabilone CESAMET® cannabidiol oral solution EPIDIOLEX & Ø, nabiximols SATIVEX & Ø) and cannabis for medical purposes authorized by a prescriber (many products, including whole dried flower, oils, capsules).
 - o The two most well known (& studied) cannabinoids are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD).
- While the evidence base is growing for use of cannabinoid products in a variety of pediatric indications (e.g. CBD for drug-resistant epilepsy, namely Dravet & Lennox-Gastaut syndromes), there is insufficient evidence to support its efficacy (& no dosing information) for chronic pain.⁶⁰
 - Cannabis use in pediatrics is off-label for all indications (exception: EPIDIOLEX indicated for drug resistant epilepsy≥2yrs)
 - o Chronic headache in adolescents study underway: CBD (using THC:CBD 1:25 extract) po 0.2mg/kg/day titrated to max 1mg/kg/day.61
- Safety considerations include:
 - o Longer-term safety data in pediatrics is limited to purified CBD
 - o <u>Most common short-term AE associated with CBD</u>: drowsiness, fatigue, ↓appetite, diarrhea, vomiting, ↑ liver transaminases, ?thrombocytopenia, irritability/agitation
 - DI: CBD inhibits CYP2C19 enzyme may ↑ levels of clobazam, citalopram
 - o <u>Potential AE associated with THC</u>: ↓memory, hypotension, euphoria, nausea/cannabis-hyperemesis syndrome, dizziness, fatigue, ↑appetite, ?negative impact on brain development (noted of concern with non-medical use of high concentrations of THC).
 - o Advise against: smoking (respiratory risks, difficult to standardize dose), edibles (difficult to standardize dose, products tend to have high THC:CBD content)
- Cost can be a barrier to access (generally, not covered)
- Place in therapy: Generally, <u>possibly</u> consider trial of cannabis for chronic pain after multiple other management strategies (pharm & non-pharm) have been trialed and insufficiently effective, the risks vs benefits have been examined and shared decision-making utilized, in consultation with a specialist in pediatric chronic pain management. Ensure goals of therapy clearly defined, & monitor for AE.
- Resource: Counselling Adolescents & Parents about Cannabis (Canadian Pediatric Society, 2020)
- See RxFiles chart: Cannabinoids: Overview for more information.

Migraine Management with Triptans – MOA: Selective 5HT-1 receptor agonists.

Agents with HC/FDA indication for pediatrics/adolescents listed below. See RxFiles chart: MIGRAINE: Acute Therapy for more, including information about other triptans.

Place in therapy: Generally, first trial lifestyle modification (e.g sleep, physical activity, regular meals, hydration), headache diary (e.g. triggers, symptoms, duration, severity, medication effect) +/- CBT

- Next, treat early (within <1hr of onset) with NSAID (e.g. ibuprofen studied QE=low, pain-free within 2hrs NNT=4⁵⁷). May add acetaminophen if needed +/- an antiemetic. ⁵⁹
- If ineffective, reasonable to trial triptan for mod-severe migraine in pediatrics ≥6yrs. Consider trial of alternate triptan or add NSAID (e.g. ibuprofen, naproxen) to triptan if not helpful after 2-3 times.⁵⁸
- Counsel about medication overuse headache (Limit NSAID/acetaminophen to ≤14days/mos & triptans to ≤9days/mos).
 Consider prophylactic agent if ≥3-6 migraines/month.

Generic/TRADE	HC/FDA Indication	Initial Dose & Maximum ^{31,42,43}	Adverse Events AE /	Comments	\$/6 doses
(Strengths & formulations)	for Age	(po unless otherwise indicated)	Contraindications CI	Comments	*
almotriptan AXERT, g	✓ adolescent ^{≥12yrs}	6.25-12.5mg po; may repeat in 2hr;	AE: nausea, dizziness, facial	Only product with HC indication; for adolescents only	\$ <u>57</u> -25
Tab 6.25, 12.5mg = ≥12yrs ▼		MAX: 25mg/24hr.	flushing, chest discomfort,		
<u>riza</u> triptan MAXALT, g	■ USA: ODT child ≥6yrs	<40kg: 5mg po; ≥40kg: 10mg po x1	paresthesia	Time to peak effect of tablet faster than ODT (60-90min	\$34
Tab 5, 10mg ^{≥18yrs} ▼;		dose; no safety data for repeat dose,	CI: hx of stroke, peripheral	<u>90</u> -150min)	
RPD Tab (ODT) 5, 10mg ≈≥18yrs ▼		but some use. ⁵⁹	vascular disease,	DI: avoid with propranolol if weight <40kg &	
			uncontrolled HTN, Wolff-	√ rizatriptan dose for ≥40kg	
sumatriptan/naproxen sodium	USA : Tab	85/500mg po x1 dose; do not repeat	Parkinson-White syndrome,	Caution: do not exceed max naproxen 7-10mg/kg/dose.	\$80
SUVEXX Tab 85/500mg X ⊗	adolescent ^{≥12yrs}	dose.	ischemic CV disease,	High cost: could consider combination of sumatriptan +	
USA: TREXIMET			hemiplegic	naproxen as sole ingredient products, though off-label for	1
			migraine/migraine with	use in pediatrics.	
zolmitriptan ZOMIG	USA : Nasal spray	2.5- <u>5</u> mg spray in <mark>one</mark> nostril;		Fast relief: Nasal onset = 10-15min.	\$120
Tab 2.5mg, g \(\bigsim \geq 18yrs \bigve \cdot \);	adolescent ^{≥12yrs}	may repeat in 2 hr; MAX: 10mg/24hr.		Nasal route useful if nausea/vomiting.	
RAPIMELT Tab 2.5mg, g ≈≥18yrs ♥; Nasal spray 2.5mg ✗ ⊗, 5mg ≈≥18yrs ♥		Tabs off-label: <40kg: 2.5mg po;			\$22-33 if
ivasai spray 2.5mg ▼ ⊗, 5mg ■, 1		≥40kg: <mark>5mg</mark> ; may repeat in 2hr ⁵⁹			tabs

Other Pediatric Pain Resources:

- SaskPain.ca
- Opioids and Pain in Youth: A toolkit for health professionals 1) acute pain 2) chronic pain
- Therapeutic Management of an Acute Migraine Attack in Pediatrics
- Power over Pain Portal for Youth

Search Terms

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References - Pediatric Pain:

- 1. Trottier ED, Ali S, Dore-Bergeron MJ, et al. Best practices in pain assessment and management for children Position Statement. Canadian Paediatric Society. Paediatrics & Child Health. 2022;27:429–437.
- 2. Health Standards Organization. Pediatric Pain Management. National Standard of Canada. 2023. Accessed Oct 4, 2024 from: https://healthstandards.org/standard/pediatric-pain-management-can-hso-13200-2023-e/.
- 3. Villacres S, Chumpitazi CE. Acute Pediatric Pain Management in the Primary Care Office. Pediatr Ann. 2018;47(3):e124-e129. doi: 10.3928/19382359-20180222-01.
- 4. Anand KJ, Hickey PR. Pain and its effects in the human neonate and fetus. N Engl J Med. 1987 Nov 19;317(21):1321-9. {Also: Finley, G.A., Franck, L.S., Grunau, R.E., & von Baeyer, C.L. (2005). Why children's pain matters. International Association for the Study of Pain. Pain: Clinical Updates, XIII(4), 1-6.
- 5. Dlugosz CK, Chater RW, Engle JP. Appropriate use of nonprescription analgesics in pediatric patients. J Pediatr Health Care. 2006;20(5):316-25; quiz 326-8.
- 6. Tidmarsh LV, Harrison R, Ravindran D, et al. The Influence of Adverse Childhood Experiences in Pain Management: Mechanisms, Processes, and Trauma-Informed Care. Front Pain Res (Lausanne). 2022 Jun 10;3:923866. doi: 10.3389/fpain.2022.923866.
- 7. Dudeney J, Aaron RV, Hathway T, et al. Anxiety and Depression in Youth with Chronic Pain: A Systematic Review and Meta-Analysis. JAMA Pediatr. Published online September 09, 2024. doi:10.1001/jamapediatrics.2024.3039.
- 8. Drendel AL, Brousseau DC, Gorelick MH. Pain assessment for pediatric patients in the emergency department. Pediatrics. 2006 May;117(5):1511-8.
- 9. Birnie KA, Hundert AS, Lalloo C, Nguyen C, Stinson JN. Recommendations for selection of self-report pain intensity measures in children and adolescents: a systematic review and quality assessment of measurement properties. Pain. 2019 Jan;160(1):5-18. doi: 10.1097/j.pain.000000000001377.
- 10. Kingsnorth S, Townley A, Provvidenza C, et al. Pediatric Chronic Pain Assessment Tools Chronic pain assessment toolbox for children with disabilities. Ontario, CA. Section 3.0, Version 2. 2018. Accessed Oct 4, 2024, from: https://hollandbloorview.ca/sites/default/files/2019-06/Chronic%20Pain%20Assessment%20Tools%202018-04.pdf.
- 11. Taddio A, McMurtry CM, Shah V, et al. Reducing pain during vaccine injections: clinical practice guideline. CMAJ. 2015 Aug 24;187(13):975-982.. http://www.cmaj.ca/content/early/2015/08/24/cmaj.150391.full.pdf.
- 12. Shah PS, Aliwalas L, Shah V. Breastfeeding or breastmilk to alleviate procedural pain in neonates: a systematic review. Breastfeed Med. 2007 Jun;2(2):74-82.
- 13. Efe E, Ozer ZC. The use of breast-feeding for pain relief during neonatal immunization injections. Appl Nurs Res. 2007 Feb;20(1):10-6.
- 14. Stevens B, Yamada J, Ohlsson A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database Syst Rev. 2004;(3):CD001069.
- 15. Acad Emerg Med. 2006 Jun;13(6):617-22. Epub 2006 Apr 24. A randomized, controlled trial of sucrose analgesia in infants younger than 90 days of age who require bladder catheterization in the pediatric emergency department. Rogers AJ, Greenwald MH, Deguzman MA, Kelley ME, Simon HK.
- 16. Harrison D, et al. Efficacy of sweet solutions for analgesia in infants between 1 and 12 months of age: a systematic review. Arch Dis Child. 2010 Jun;95(6):406-13.
- 17. Pillai Riddell RR, Bucsea O, Shiff I, et al. Non-pharmacological management of infant and young child procedural pain. Cochrane Database of Systematic Reviews 2023, Issue 6. Art. No.: CD006275. DOI: 10.1002/14651858.CD006275.pub4.
- 18. Schechter NL, Zempsky WT, Cohen LL, McGrath PJ, McMurtry CM, Bright NS. Pain reduction during pediatric immunizations: evidence-based review and recommendations. Pediatrics. 2007 May;119(5):e1184-98.
- 19. Taddio A, Manley J, Potash L, Ipp M, Sgro M, Shah V. Routine immunization practices: use of topical anesthetics & oral analgesics. Pediatrics 2007;120(3):e637-43.
- 20. Uman LS, Chambers CT, McGrath PJ, Kisely S. Psychological interventions for needle-related procedural pain and distress in children and adolescents. Cochrane Database of Systematic Reviews. 2006 Oct 18;(4):CD005179.0.
- 21. Wallace DP, Allen KD, Lacroix AE, et al. The "Cough Trick," a Brief Strategy to Manage Pediatric Pain From Immunization Injections. Pediatrics. 2010 Jan 11.
- 22. Trottier ED, Dore-Bergeron MJ, Chauvin-Kimoff L, et al. Managing pain and distress in children undergoing brief diagnostic and therapeutic procedures Position Statement. Canadian Paediatric Society. Paediatrics & Child Health. 2019;24(8):509-521.
- 23. Farion KJ, Splinter KL, Newhook K, Gaboury I, Splinter WM. The effect of vapocoolant spray on pain due to intravenous cannulation in children: a RCT. CMAJ. 2008;179:31-6.
- 24. Foster JP, Taylor C, Spence K. Topical anaesthesia for needle-related pain in newborn infants. Cochrane Database Syst Rev. 2017 Feb 4;2(2):CD010331. doi: 10.1002/14651858.CD010331.pub2.
- 25. Koh JL, Harrison D, Myers R, et al. A randomized, double-blind comparison study of EMLA and ELA-Max for topical anesthesia in children undergoing intravenous insertion. Paediatr Anaesth. 2004 Dec;14(12):977-82. doi: 10.1111/j.1460-9592.2004.01381.x.
- 26. Eichenfield LF, Funk A, Fallon-Friedlander S, et al. A clinical study to evaluate the efficacy of ELA-Max (4% liposomal lidocaine) as compared with eutectic mixture of local anesthetics cream for pain reduction of venipuncture in children. Pediatrics. 2002 Jun;109(6):1093-9. doi: 10.1542/peds.1093.6.1093.
- 27. Lander JA, Weltman BJ, So SS. EMLA and amethocaine for reduction of children's pain associated with needle insertion. Cochrane Database Syst Rev. 2006 Jul 19;(3):CD004236. doi: 10.1002/14651858.CD004236.pub2. Update in: Cochrane Database Syst Rev. 2014 Mar 13;(3):CD004236. doi: 10.1002/14651858.CD004236.pub3.
- 28. Eggleston ST, Lush LW. Understanding allergic reactions to local anesthetics. Ann Pharmacother. 1996 Jul-Aug;30(7-8):851-7.
- 29. Maulidi H. McNair C. Seller N et al. Arrhythmia associated with tetracaine in an extremely low birth weight premature infant. Pediatrics. 2012 Dec:130(6):e1704-7, doi: 10.1542/peds.2011-1743.
- 30. Su HC, Hsieh CW, Lai NM, et al. Using Vibrating and Cold Device for Pain Relieves in Children: A Systematic Review and Meta-analysis of Randomized Controlled Trials. J Pediatr Nurs. 2021 Nov-Dec;61:23-33. doi: 10.1016/j.pedn.2021.02.027.
- 31. Uptodate Lexidrug. Drug Product Monographs. Accessed Oct 16, 2024 from: https://www.wolterskluwer.com/en/solutions/uptodate/pro/lexidrug.
- 32. Children's Healthcare Canada (CHS). Acute Pain A Toolkit for health professionals. Accessed Oct 16, 2024 from: https://www.childrenshealthcarecanada.ca/en/networks-and-hubs/suap-acute-pain.aspx.
- 33. Clark E, Plint AC, Correll R, et al. A randomized, controlled trial of acetaminophen, ibuprofen, and codeine for acute pain relief in children with musculoskeletal trauma. Pediatrics. 2007 Mar;119(3):460-7. Comment in: Evid Based Med. 2007;12(5):144. Pediatrics. 2007;120(1):237; author reply 237-8.
- 34. Poonai N, et al. Oral morphine versus ibuprofen administered at home for postoperative orthopedic pain in children: a randomized controlled trial. CMAJ.2017 Oct 10;189(40):E1252-E1258.
- 35. Poonai N, Bhullar G, Lin K, et al. Oral administration of morphine versus ibuprofen to manage postfracture pain in children: a randomized trial. CMAJ. 2014;186(180:1358-1363.
- 36. Nasal Midazolam for Sedation in Pediatric Patients Prior to Invasive Procedures. CADTH HTIS. March 2008. Available from: https://www.cda
 - amc. ca/sites/default/files/pdf/htis/Nasal%20Midazolam%20for%20Sedation%20in%20Pediatric%20Patients%20Prior%20Invasive%20Procedures%20Clinical%20Safety%20and%20Ef.pdf. and the control of the control
- 37. Emslander HC. Local and topical anesthesia for pediatric wound repair: a review of selected aspects. Pediatr Emerg Care. 1998 Apr;14(2):123-9.
- 38. Chumpitazi CE, Chang C, Atanelov Z, et al. Managing acute pain in children presenting to the emergency department without opioids. J Am Coll Emerg Physicians Open. 2022 Mar 12;3(2):e12664. doi: 10.1002/emp2.12664.
- 39. Hadland SE, Agarwal R, Raman SR, et al. American Academy of Pediatrics. Opioid Prescribing for Acute Pain Management in Children and Adolescents in Outpatient Settings: Clinical Practice Guideline. Pediatrics 2024; e2024068752. 10.1542/peds.2024-068752
- 40. Kelley-Quon LI, Kirkpatrick MG, Ricca RL, et al. Guidelines for Opioid Prescribing in Children and Adolescents After Surgery: An Expert Panel Opinion. JAMA Surg. 2021;156(1):76–90. doi:10.1001/jamasurg.2020.5045.
 41. Carrasco-Labra A, Polk DE, Urquhart O, et al. Evidence-based clinical practice guideline for the pharmacologic management of acute dental pain in children. The Journal of the American Dental Association, 2023;154(9):814 825.e2.
- 42. Hauer J, Houtrow AJ, Pain Assessment and Treatment in Children With Significant Impairment of the Central Nervous System. Pediatrics. June 2017;139(6): e20171002. 10.1542/peds.2017-1002.
- 42. readed 3, routing way, rain assessment and readment in clinicate in with against in parameter in the central nervous system, recussed out 24, 2024 from: 1,133(0), readment of the central nervous system recussed out 24, 2024 from: 1,230(0), readment of the central nervous system recussed out 24, 2024 from: 1,230(0), readment of the central nervous system recussed out 24, 2024 from: 1,230(0), readment of the central nervous system recussed out 24, 2024 from: 1,230(0), readment of the central nervous system recussed out 24, 2024 from: 1,230(0), readment of the central nervous system recussed out 24, 2024 from: 1,230(0), readment of the central nervous system recussed out 24, 2024 from: 1,230(0), readment of the central nervous system recussed out 24, 2024 from: 1,230(0), readment of the central nervous system recussed out 24, 2024 from: 1,230(0), readment of the central nervous system recussed out 24, 2024 from: 1,230(0), readment of the central nervous system recussed out 24, 2024 from: 1,230(0), readment of the central nervous system recussed out 24, 2024 from: 1,230(0), readment of the central nervous system recursed in the cen
- 44. Guidelines on the management of chronic pain in children. Geneva: World Health Organization;2020. Available from: https://www.who.int/publications/i/item/9789240017870.
- 45. Friedrichsdorf SJ, Giordano J, Dakoji KD, et al. Chronic Pain in Children and Adolescents: Diagnosis and Treatment of Primary Pain Disorders in Head, Abdomen, Muscles and Joints. Children. 2016;3(4):42. doi: 10.3390/children3040042.
- 46. Egunsola O, Wylie CE, Chitty KM, et al. Systematic review of the efficacy and safety of gabapentin and pregabalin for pain in children and adolescents. Anesth Analg. 2019;128(4):811–819.

 47. Cooper TE, Heathcote LC, Clinch J, et al. Antidepressants for chronic non-cancer pain in children and adolescents. Cochrane Database Syst Rev. 2017 Aug 5;8(8):CD012535. doi: 10.1002/14651858.CD012535.pub2.
- 47. Cooper 1E, Heathcote LC, Clinch J, et al. Antidepressants for chronic non-cancer pain in children and adolescents. Cochrane Database Syst Rev. 2017 Aug 5;8(8):CD012535. doi: 10.1002/14651858.CD01.
- 48. Powers SW, Coffey CS, Chamberlin LA, et al. Trial of amitriptyline, topiramate, and placebo for pediatric migraine. New England Journal of Medicine. 2017 Jan 12;376(2):115-24.
- 49. Branstetter JW, Mantione J, Deangelo A, et al. Safety and Efficacy of Gabapentin for Pain in Pediatric Patients: A Systematic Review. Hosp Pediatr. 2024;14(1):e57-65.
- 50. Pharmacological Interventions for Chronic Pain in Pediatric Patients: A Review of Guidelines. Ottawa: CADTH; 2020 May. (CADTH rapid response report: summary with critical appraisal).
- 51. Eccleston C, Fisher E, Cooper TE, et al. Pharmacological interventions for chronic pain in children: An overview of systematic reviews. Pain 2019;160(8):1698–707.
- 52. Wysocki J, Center KJ, Brzostek J, et al. A randomized study of fever prophylaxis and the immunogenicity of routine pediatric vaccinations. Vaccine. 2017 Apr 4;35(15):1926-1935.
- 53. Upadhyaya HP, Arnold LM, Alaka K, et al. Efficacy and safety of duloxetine versus placebo in adolescents with juvenile fibromyalgia: results from a randomized controlled trial. Pediatr Rheumatol. 2019;17(1):1–10.
- 54. Arnold LM, Schikler KN, Bateman L, et al. Safety and efficacy of pregabalin in adolescents with fibromyalgia: a randomized, double-blind, placebo-controlled trial and a 6-month open-label extension study. Pediatr Rheumatol. 2016;14(1):46 Available from: http://ped-rheum.biomedcentral.com/articles/10.1186/s12969-016-0106-4.
- 55. Wang F, Van Den Eeden SK, Ackerson LM, et al. Oral magnesium oxide prophylaxis of frequent migrainous headache in children: A randomized, double-blind, placebo-controlled trial. Headache. 2003;43:601–610. doi: 10.1046/j.1526-4610.2003.03102.x.
- 56. Ahrari M, Ali S, Hartling L, et al. "Nonmedical Opioid Use After Short-Term Therapeutic Exposure in Children: A Systematic Review." Pediatrics. 2021;148(6):1.
- 57. Richer L, Billinghurst L, Linsdell MA, et al. Drugs for the acute treatment of migraine in children and adolescents. Cochrane Database Syst Rev. 2016 Apr 19;4(4):CD005220. doi: 10.1002/14651858.CD005220.pub2.
- 59. Migraine Canada. Pediatric Medication Dosing Advice. Therapeutic Management of an Acute Migraine Attack in Pediatrics (6-17 years). Accessed Nov 6, 2024, available from: https://migrainecanada.org/medication-dosing-advice/.
- 60. Kelly LE, Rieder MJ, Finkelstein Y. Medical cannabis for children: Evidence and recommendations. Paediatrics & Child Health May 2024;29(2):104-112. https://doi.org/10.1093/pch/pxad078.
- 61. Chhabra M, Lewis EC, Balshaw R, et al. A multi-centre, tolerability study of a cannabidiol-enriched Cannabis Herbal Extract for chronic headaches in adolescents: The CAN-CHA protocol. PLoS One. 2024 Sep 20;19(9):e0290185. doi: 10.1371/journal.pone.0290185.
- 62. Hagg L, Leung S, Carr R. Characterizing the Use of Nabiximols ($\Delta 9$ -Tetrahydrocannabinol-Cannabidiol) Buccal Spray in Pediatric Patients. Can J Hosp Pharm. 2023;76(3):216-20. https://doi.org/10.4212/cjhp.3349.
- 63. Chhabra M, Ben-Eltriki M, Mansell H, et al. Cannabinoids Used for Medical Purposes in Children and Adolescents: A Systematic Review and Meta-Analysis. JAMA Pediatr. 2024;178(11):1124–1135. doi:10.1001/jamapediatrics.2024.3045.
- 64. Chadi N, Walker-Harding L. COMMITTEE ON SUBSTANCE USE AND PREVENTION; Nonmedical Use of Controlled Medications by Adolescents and Young Adults: Clinical Report. Pediatrics December 2024; 154 (6): e2024069298. 10.1542/peds.2024-069298.