Medications for Facial Pain

legend
bold – compounding pharmacy
blue – controlled substance
italics – approval hurdles/ expensive

fast-acting as-needed medications for attacks / episodic worsening
attack / episodic worsening needs to announce itself

• sodium channel blocking anti-neuralgics	chewable carbamazepine 50-200 mg liquid oxcarbazepine 50-200 mg
• GABA-A-receptor enhancing benzodiazepine	orally-dissolving clonazepam 0.125-0.25 mg
• liquid gabapentin	liquid, 100-300 mg
• *orally dissolving –gepant*	rimegepant 75mg (anti-CGRP repurposing – fast onset !)
• *–gepant nasal spray*	zavegepant 10mg (anti-CGRP repurposing – fast onset !)
• **ketamine nasal spray**	**100-150mg/mL** *280mg/mL S-ketamine (Spravato)*
• **oxytocin nasal spray**	**240IU/mL (great safety)**
• lidocaine jelly, spray	

blood pressure: need to lower attack/ episodic worsening associated hypertension which can further aggravate pain
- fastest acting tablets: captopril 25 mg, clonidine 0.1 mg – joint management with family physician, cardio, hypertension
  15-30 min
- **[clonidine nasal drops or nasal spray – fast-acting, but inconsistent absorption]**
- for adjunct sedation: orally-dissolving clonazepam, liquid lorazepam

Medications for Facial Pain

regular meds I – tablet taken by mouth in regular intervals

sodium channel inhibiting compounds

carbamazepine 200-400mg 2-3x/d	regular tablet – extended release
oxcarbazepine 300-600mg 2-3x/d	regular tablet – extended release
eslicarbazepine 400mg 2x/d	MoA beyond carba - oxcarba
lacosamide 100-200mg 2x/d	**most potent sodium channel inhibitor, best safety - TME**
zonisamide 25-100mg 2-4x/d	not as potent, but no effect on body weight

lacosamide, zonisamide suitable in case of SIADH (low sodium) caused by carbamazepine, oxcarba

gabapentinoids

gabapentin 300-800mg and higher, 2-4x/d	regular tablet – extended release
pregabalin 150-450mg and higher, 2-4x/d	(weight)

lamotrigine

100mg 2-4x/d and higher dose	need slow dosing in

muscle-relaxing compounds with analgesic profile

baclofen 5-10mg (-20mg), 2-3x/d	good combination, very suitable in case of muscular tension
cyclobenzapril 5-10mg, 3x/d	good combination, very suitable in case of muscular tension

Medication for Facial Pain

regular meds II – tablet taken by mouth in regular intervals

analgesic SSRI/SNRI/NDRI

duloxetine	30-60 mg 1-2x/d	combination w gabapentinoids and/or sodium channel inhibitors capsules 20 mg lowest dose
venlafaxine	25-75mg 1-3x/d	can formulate lower dose; often works when duloxetine does not
vortioxetine	10-30mg/d	sometimes more punch than duloxetine
mirtazepine	15-30mg/d	can enhance weight; normalizes sleep
milnacipran	12.5-25mg 2-4/d	step-up vs duloxetine in comorbid fibromyalgia
bupropion	150-300mg/d	for mental health co-morbidities, NDRI rather than SNRI/SSRI (wean-off smoking)

cannabinoids

marinol	2.5-20 2-3x/d	slow dose-in; cannabinoid effects – can be helpful 3rd line agent

anti-inflammatories

indomethacine	25-50mg 2-3x/d	potent pan-COX-i (unwanted effects) – indicative of paroxysmal hemicrania in case there is striking effectiveness
meloxicam	7.5-15mg 1x/d	for treatment of inflammatory co-morbidities in case long-term tx needed

Medication for Facial Pain

regular meds III – tablet taken by mouth in regular intervals // nasal sprays

low-dose naltrexone

unique treatment - prevention medicine // in combination with a well-balanced standard regimen
superb safety profile
in my hands, has changed MANY lives
1-4.5(-6) mg/d better taken before bed
MoA: 1 = kick on endogenous opioid system, in sync w circadian rhythm
2 = gliotropic effect (via TLR-receptors on glial cells), also in sync w circadian rhythm
compounding pharmacy medication

ultra low-dose naltrexone 0.1-0.75 mg/d
for pts who do not tolerate regular ldNtx (comorbidity ?)

suggestion: ldNtx post-MVD, post-stereotactic radiosurgery ➔ prolong interval to pain recurrence ?
need clin study to address that question

nasal sprays containing oxytocin (24IU 2x/d) and ketamine (20mg 2-3x/d) can be tried (see treatment of attacks)
compound medications

Medication for Facial Pain

regular meds IV – anti-CGRP medications for subcutaneous self-injection

self-injected anti-CGRP monoclonal antibodies (subcutaneous self-injection)

galcanezumab	**120 mg/monthly**
fremanezumab	**240 mg/monthly**
erenumab	**140 mg/monthly**

these are chronic migraine-appropriate dosing regimens – higher dose more appropriate for trigeminal pain ?
(as for galcanezumab and cluster headache (?) - 300 mg helps more than 120 mg)

[Future: classic hypodermic needles might in the future be replaced with skin patch systems (microneedles)]

Medication for Facial Pain

regular meds V – opioids

low-potency opioids — hydrocodon, oxycodon, tramadol
¶ if helpful, can be used under the appropriate guiding principles

BUT
- **when taking low-potency opioids, treatment with low-dose naltrexone becomes non-feasible**
- aim for "drug holidays" to maintain susceptibility
- aim for "opioid rotation" to maintain susceptibility

BUT ALSO
- across-the-board phobia for combined treatment of low-potency opioids with orally-dissolving clonazepam not justified

In case low-potency opioids appear essential, but also still left w significant pain
- longer-term management with
  - ¶ methadone (tablets, can also do liquid ((ultra-)low dose possible), odd doses possible; inexpensive, available)
  - ¶ butorphanole
  - ¶ levorphanole (possible difficulties in supply/coverage/$$$)

¶ fentanyl patches
opioid rotation to maintain feasibility

¶ fentanyl lozenges - for as-needed palliation

future:

BJP British Journal of Pharmacology

The multifunctional peptide DN-9 produced peripherally acting antinociception in inflammatory and neuropathic pain via μ- and κ-opioid receptors

Biao Xu, Mengna Zhang, Xuerui Shi, Run Zhang, Dan Chen, Yong Chen, Zilong Wang, Yu Qiu, Ting Zhang, Kangtai Xu, Xiaoyu Zhang, Wolfgang Liedtke, Rui Wang, Quan Fang ... See fewer authors ^ 2019

Medication for Facial Pain

regular meds VI

hypertension

migraine; other headache; TMJD

occipital/neck/vertebrogenic pain
- occipital nerve injections

MS; neuromyelitis optica
- fingolimod, S1P modulators
- rituximab (anti-CD20)

sinus disease & upper respiratory allergies
- allergic/chronic irritation (dupilumab)
- infectious

dental-oral issues
- teeth needing root canals
- RC-treated teeth w peri-apicitis
- periodontitis
- chronic recurring herpes
- oral lichen

fibromyalgia

insomnia

brain fog
- modafinil; memantine; low-dose ritalin; pitolisant

chronic inflammatory disorders
- LongNeuro-COVID
- RhA, IBD

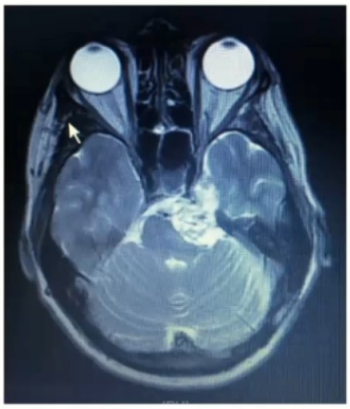
OBESITY
- semaglutide // tirzepatide // bariatric surgery
- low-dose naltrexone // other bariatrics

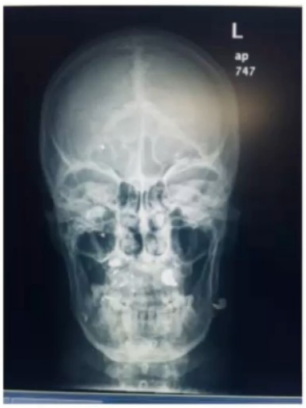
facial skin-skalp issues
- atopic dermatitis (dupilumab); rosacea; psoriasis; lupus

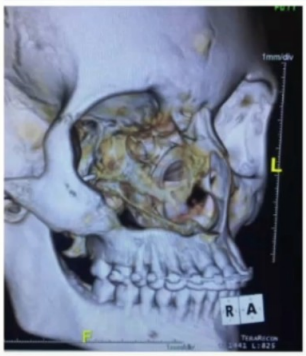
head-neck-face malignancies
- cemiplimab and other checkpoint inhibitor + co-treatments

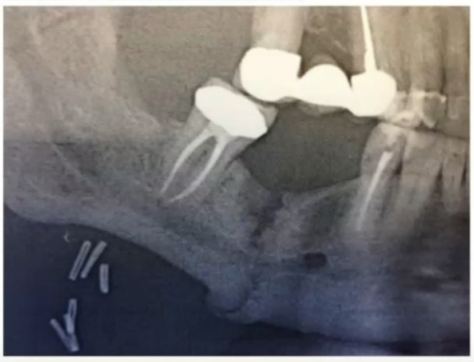
orbital/ eye disease

exemplary case from my clinics – **CO-MORBIDITIES ! FIX THEM !!!**



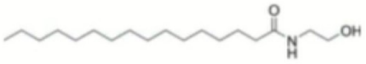






Medication for Facial Pain – Addendum: Naturals

natural product: palmitoylethanolamide



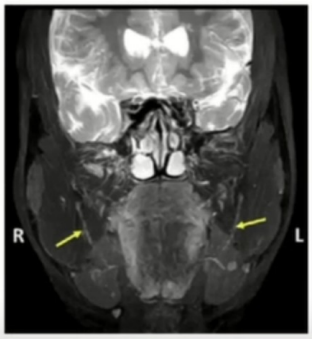
Palmitoylethanolamide (**PEA**) is an endogenous fatty acid amide, and a known lipid modulator of inflammation.

In a recent randomized, double-blinded placebo-controlled clinical study, PEA (600 mg 2x/d) showed effectiveness in post-molar tooth-extraction trigeminal neuropathic pain. It also showed unswelling of the inflamed branches of the trigeminal nerve, displaying a protracted course of action (weeks), and a moderate-strong benefit on pain when using PEA in conjunction with established anti-neuropathic medications pregabalin (Lyrica; 75mg) plus nortriptyline (10mg). Effect size was apparent using a small-scale study with n=20 patients per arm. No safety issues were noted.

The Comparative Efficacy of Palmitoylethanolamide (PEA) With the Combination of Pregabalin and Nortriptyline on Post-extraction Trigeminal Neuropathy by Using Magnetic Resonance (MR) Neurography: A Randomized Clinical Trial

Amlendu Shekhar [1], Adit Srivastava [1], Nimisha Verma [2], Ashish Verma [3], T P Chaturvedi [4]
Banaras Hindu University, Varanasi, India

Cureus Feb 24, 2024: 16(2): e54843. DOI 10.7759/cureus.54843



Parameters	Groups	Mean	P-value
NRS at baseline	Group I	5.40	0.692*
	Group II	5.60	
	Group III	5.30	
NRS after one month	Group I	3.72	0.001**
	Group II	4.07	
	Group III	2.80	
NRS after three months	Group I	1.90	0.001**
	Group II	2.35	
	Group III	1.50	

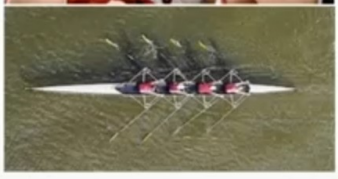
n=20 pt/arm

I: nor + Ly
II: PEA
III: PEA + nor + Ly

NRS: pain 1-10

Care needs to build teams with colleagues **who are open to working across disciplinary boundaries** with dedicated focus on a challenging clinical entity:

- orofacial pain-dentistry
- dentistry: endodontics
- dentistry: oral surgery, maxillofacial surgery
- physical therapy – head/neck/face focused
- pain-nursing
- alternative medicine providers / acupuncturists
- anesthesiology/pain
- neurology/headache – trigeminal pain
- neurosurgery – pain neurosurgery
- plastic/facial surgery
- pain clinical immunologists/ allergologists
- pharmacists
- pain-psychiatry
- pain-geronto
- ENT
- opthalmology
- ob-gyn
- oncology
- pain-admin; pain-lawyer; pain-PR



NOBODY owns trigeminally-mediated pain
she/he who suffers should NEVER land between the chairs