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Universitatea Transilvania din Brașov
FACULTATEA DE MEDICINĂ

LIDOCAINE FOR PAIN MANAGEMENT

Sorin Buga, MD
Clinical Professor
Department of Supportive Care
City of Hope National Medical Center

Asociația Națională de Îngrijiri Paliative
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Bună Ziua !

Mă numesc Sorin

sbuga@coh.org

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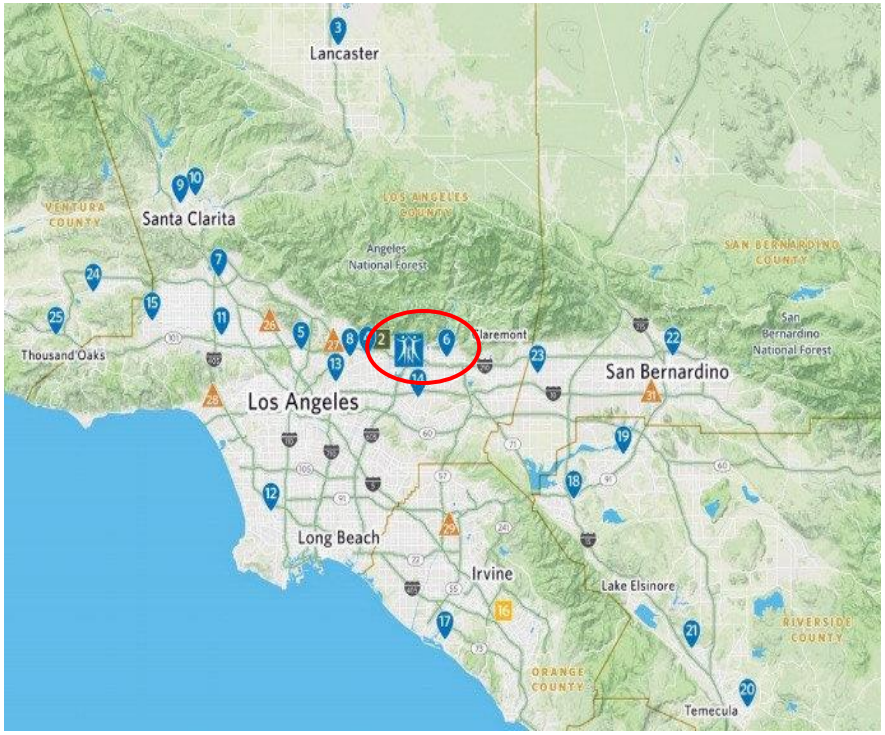

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Disclosures

- I have nothing to disclose

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Objectives

- Overview of Lidocaine for pain control
- Brief overview of Mexiletine for pain control
- Case presentation

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Case Presentation

- 28 y.o. female admitted for sacral laminectomy with decompression and kyphoplasty
- PMH:

1. MM treated with chemotx, XRT to the right hip, S/P unrelated donor stem cell transplantation on 4/19/2018 conditioning with fludarabine plus melphalan and received bortezomib, tacrolimus and methotrexate for GVHD prevention
2. GVHD skin, mouth and liver
3. Skull mass
4. Right leg DVT and Pulmonary embolism
5. Fracture of sacrum

- Allergies: Hydrocodone, Codeine, Tramadol, NSAIDs, Ketamine
- FHx: Noncontributory
- SHx: Noncontributory

Case Presentation

- Meds: Duloxetine 30 mg bid, Fentanyl patch 75 mcg q 48 hours, Fentanyl (Subsys) 400 mcg q 4-6 hours, Gabapentin 600-600-900 mg
- After Sx: fentanyl patch 75 MCG, Cymbalta 30 mg twice a day, Gabapentin 600-600-900 mg, Dilaudid IV PCA 25/15/10/40/60; could not tolerate Ketamine IV
- 12/10 pain with somatic features located in her low back related to recent surgery; quite emotional related to the pain
- Lidocaine IV bolus of 1 mg/kg body weight followed by a continuous infusion of 1.5 mg/min
- Lidocaine raised at 2 mg / hr ➔ somnolence ➔ decrease back to 1.5 mg/hr

Lidocaine Infusion for Pain and Non-Cardiac Indications

Please refer to the 'Lidocaine IV/Subcutaneous Infusion for Pain Management and other Non-Cardiac Indications' policy for more information and list of exclusions.

Treatment Exclusions

**Exceptions may be made for patients with end stage disease who are suffering from refractory symptoms.

Patient should otherwise not be initiated on treatment if the following conditions exist:

1. Patients with the following EKG abnormalities:
   - Second or third degree AV block
   - Bradycardia with a rate of less than 55 beats/minute
   - Wolff-Parkinson-White (WPW) syndrome
2. If patient is receiving mexilitene, or class I or III antiarrhythmic agents, Recommendation to discontinue for a time equal to three times the medication elimination half-life prior to the administration of lidocaine infusion to provide adequate elimination time.
3. Patients receiving intraspinal, epidural or peripheral nerve catheter local anesthetics.
4. Patients who have received Exparel (liposomal bupivacaine) within the last 96 hours or who are expected to receive Exparel within 8 hours (4 half lives) after termination of lidocaine infusion.
5. Patients with amide drug hypersensitivity (lidocaine, bupivacaine, ropivacaine, mepivacaine, prilocaine)
6. Uncorrected hypoxia
7. Relevant results (EKG or Labs) not yet available

The following conditions will be considered precautions:

1. Patients with severe hepatic failure. Recommendation to dose/rate adjust in mild to moderate hepatic dysfunction, avoid in severe hepatic dysfunction.
2. Patients with indicators of heart disease, (e.g. history of myocardial infarction, congestive heart failure). For CHF, recommendation to reduce the infusion rate.
3. Avoid in patients with creatinine greater than 3. Recommendation to reduce infusion rate in mild to moderate renal dysfunction.
4. Patient is receiving Class II, IV, or V antiarrythmics. Recommendation to monitor for hypotension and bradycardia.
5. History of seizures.
6. Acute altered mental status of unknown etiology.
7. Caution in patients with uncorrected hypovolemia

Baseline EKG/Labs

1. Baseline EKG should be available in the medical record. It may be performed within 7 days of infusion, unless the patient has had recent cardiac symptoms in which case an EKG will be obtained within 48 hours of starting lidocaine.
2. BUN, serum Cr, AST, and ALT need to be documented in the previous 7 days or in a timeframe as clinically indicated.

Nursing

Vital Signs

- [x] Vital Signs
  Routine, As needed, Starting today at 1703, Until Specified
  Every hour x 4, then every 2 hours x 2, then as per standard of care (unless the patient is on continuous EKG monitoring) after initiation of therapy. Re-initiate VS as instructed with each increase in continuous dose or concentration change.

Notify Physician

- [x] Notify physician (specify) Heart rate greater than: 120; Heart rate less than: 55; Other: Hold lidocaine infusion and notify ordering service if the patient exhibits the following: heart rate greater than 120, heart rate less than 55, decrease in ...
  Routine, Until discontinued, Starting today at 1704, Until Specified
  Heart rate greater than: 120
  Heart rate less than: 55
  Other: Hold lidocaine infusion and notify ordering service if the patient exhibits the following: heart rate greater than 120, heart rate less than 55, decrease in SBP greater than 30mmHg, myoclonic twitching, or confusion.

Nursing Interventions

- [x] Nursing communication
  Routine, Until discontinued, Starting today at 1704, Until Specified
  Record pain intensity levels hourly x 8 and then as per Nursing Protocol after initiation of therapy or after any change in dose.

Labs

Chemistry Basic

Click for more

- [x] Hepatic Function Panel
  Using an existing specimen
  Weekly, First occurrence today at 1704, Until Specified
  The Hepatic Function Panel order is defaulted to a frequency of Weekly, starting today. To change the start date, change within the Starting Date field., Use existing specimen

Chemistry - Other

- [x] Lidocaine Level, Stat
  If condition(s) met - STAT, Starting today at 1703, Until Specified, For 1 occurrence
  Draw 6 hours AFTER the initiation of lidocaine infusion

- [x] Lidocaine Level, Stat
  If condition(s) met - STAT, Starting today at 1703, Until Specified
  After any change in lidocaine dose

- [x] Lidocaine Level, Stat
  If condition(s) met - STAT, Starting today at 1703, Until Specified
  24 hours after final lidocaine dose adjustment and then every week thereafter.

Other Tests

Cardiac Studies

- [x] ECG 12 lead
  STAT, Once, today at 1704, For 1 occurrence
  Indication/Reason for exam: Other (Specify in comments)
  Explanatory Comment: Prior to initiation of lidocaine
  Portable: Yes

Medications

Lidocaine Infusion

Lidocaine infusion should not be administered to patients who have received Exparel within the past 96 hours or who are expected to receive Exparel within 8 hours of termination of lidocaine infusion.

- [ ] Lidocaine Loading Dose Continuous Infusion panel

Consults

Pharmacy Consults

- [x] pharmacy communication
  Not for direct medication ordering, Pharmacy Consult, other, Starting today at 1703
  Communication to Pharmacy: Other. Specify in Special Instructions
  Special Instructions: Contact Physician to discontinue antiarrhythmic medications (4 x the medication half-life) prior to the initiation of lidocaine.

- [x] pharmacy communication
  Not for direct medication ordering, Pharmacy Consult, other, Starting today at 1703
  Communication to Pharmacy: Other. Specify in Special Instructions
  Special Instructions: Lidocaine infusion should not be administered to patients who have received Exparel within the past 96 hours or who are expected to receive Exparel within 8 hours of termination of lidocaine infusion.

Additional SmartSet Orders

Search for additional order set orders

You can search for an order by typing in the header of this section.

Lidocaine

- Amide with antiarrhythmic (Class 1B), anesthetic, anti-inflammatory, antihyperalgesic properties
- Has been used to treat pain since the 1950s
- Part of opioid sparing in multimodal analgesia and early rehabilitation protocols after surgery

Seah DSE, Herschtal A, Tran H, Thakerar A, Fullerton S. Subcutaneous Lidocaine Infusion for Pain in Patients with Cancer. J Palliat Med. 2017 Jun;20(6):667-671. doi: 10.1089/jpm.2016.0298. Epub 2016 Dec 20. PMID: 27996364.
Gibbons K, DeMonbrun A, Beckman EJ, Keefer P, Wagner D, Stewart M, Saul D, Hakel S, Liu M, Niedner M. Continuous Lidocaine Infusions to Manage Opioid-Refractory Pain in a Series of Cancer Patients in a Pediatric Hospital. Pediatr Blood Cancer. 2016 Jul;63(7):1168-74. doi: 10.1002/pbc.25870. Epub 2016 Jan 19. PMID: 26784686.

Lidocaine – Mechanism of Action

- Exact mechanism of action of i.v. lidocaine still uncertain

- Blocks nerve conduction via sodium channels on sensory neurons and inhibits G protein coupled receptors and NMDA receptors
  ➔ blocks transmission of the nociceptive signal

- Anti-inflammatory effect by release of adenosine triphosphate (poly- morphonuclear granulocyte)

Wallon G, Erbacher J, Omar E, Bauer C, Axiotis G, Thevenon S, Soubirou JL, Aubrun F. Effect of intravenous lidocaine on pain after head and neck cancer surgery (ELICO trial): A randomised controlled trial. Eur J Anaesthesiol. 2022 Sep 1;39(9):735-742. doi: 10.1097/EJA.0000000000001712. Epub 2022 Jul 20. PMID: 35852564
Gibbons K, DeMonbrun A, Beckman EJ, Keefer P, Wagner D, Stewart M, Saul D, Hakel S, Liu M, Niedner M. Continuous Lidocaine Infusions to Manage Opioid-Refractory Pain in a Series of Cancer Patients in a Pediatric Hospital. Pediatr Blood Cancer. 2016 Jul;63(7):1168-74. doi: 10.1002/pbc.25870. Epub 2016 Jan 19. PMID: 26784686.

Lidocaine – Mechanism of Action

- Increased acetylcholine concentrations in the cerebrospinal fluid with associated inhibition of descending pain pathways
- Release of endogenous opioids
- Significantly increase beta-endorphin within 1 hour after infusion in patients with diabetic neuropathy and in normal volunteers

Buchanan, D.D., J. MacIvor, F. A role for intravenous lidocaine in severe cancer-related neuropathic pain at the end-of-life. Support Care Cancer 18, 899–901 (2010). https://doi.org/10.1007/s00520-010-0864-3

Bruera E, Ripamonti C, Brenneis C, Macmillan K, Hanson J. A randomized double-blind crossover trial of intravenous lidocaine in the treatment of neuropathic cancer pain. J Pain Symptom Manage. 1992 Apr;7(3):138-40. doi: 10.1016/s0885-3924(06)80004-7. PMID: 16967580.

Lidocaine - Metabolism

- Processed in the liver to active metabolites:
  monoethylglycinexylidide
  glycinexylidide

- Major substrate of CYP1A2, CYP3A4
- Minor substrate of CYP2A6, CYP2B6, CYP2C9

- Dose reduction with potent CYP3A4 and CYP1A2 inhibitors

Buchanan, D.D., J. MacIvor, F. A role for intravenous lidocaine in severe cancer-related neuropathic pain at the end-of-life. Support Care Cancer 18, 899–901 (2010). https://doi.org/10.1007/s00520-010-0864-3

Atayee RS, Naidu D, Geiger-Hayes J, Saphire ML, Hausdorff J, Edmonds KP. A Multi-Centered Case Series Highlighting the Clinical Use and Dosing of Lidocaine and Mexiletine for Refractory Cancer Pain. J Pain Palliat Care Pharmacother. 2020 Jun;34(2):90-98. doi: 10.1080/15360288.2019.1704339. Epub 2020 Feb 24. PMID: 32091938.

Lidocaine - Indications

- Diabetic neuropathy
- Postsurgical pain
- Postherpetic neuralgia
- Headache
- Refractory cancer pain

Ferrini R, Paice JA. How to initiate and monitor infusional lidocaine for severe and/or neuropathic pain. J Support Oncol. 2004 Jan-Feb;2(1):90-4. PMID: 15330376.
Kintzel PE, Knol JD, Roe G. Intravenous Lidocaine Administered as Twice Daily Bolus and Continuous Infusion for Intractable Cancer Pain and Wound Care Pain. J Palliat Med. 2019 Mar;22(3):343-347. doi: 10.1089/jpm.2018.0243. Epub 2018 Dec 1. PMID: 30508406.

Lidocaine – Contraindications / Precautions

Treatment Exclusions

**Exceptions may be made for patients with end stage disease who are suffering from refractory symptoms.

Patient should otherwise not be initiated on treatment if the following conditions exist:

1. Patients with the following EKG abnormalities:
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   - Bradycardia with a rate of less than 55 beats/minute
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The following conditions will be considered precautions:

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2. Patients with indicators of heart disease, (e.g. history of myocardial infarction, congestive heart failure). For CHF, recommendation to reduce the infusion rate.
3. Avoid in patients with creatinine greater than 3. Recommendation to reduce infusion rate in mild to moderate renal dysfunction.
4. Patient is receiving Class II, IV, or V antiarrythmics. Recommendation to monitor for hypotension and bradycardia.
5. History of seizures.
6. Acute altered mental status of unknown etiology.
7. Caution in patients with uncorrected hypovolemia

Lidocaine – Contraindications / Precautions

- *Contraindications:*
  - ❖ Hypersensitivity to another local anesthetic of the amide type
  - ❖ Severe degrees of SA, AV, or intraventricular heart block (except in patients with a functioning artificial pacemaker)

- *Precautions:*
  - ❖ Glucose-6-phosphate dehydrogenase deficiency
  - ❖ Congenital or idiopathic methemoglobinemia
  - ❖ Pseudocholinesterase deficiency
  - ❖ Hypokalemia / hypomagnesemia

Lidocaine Precautions

ELICO Trial:

- 118 patients (lidocaine 57; placebo 61, excluded 26)
- Conclusions:

  no significant difference in morphine consumption in the first 48 postoperative hours

  no significant difference in pain scores or consumption of analgesics 3 - 6 months after surgery

Wallon G, Erbacher J, Omar E, Bauer C, Axiotis G, Thevenon S, Soubirou JL, Aubrun F. Effect of intravenous lidocaine on pain after head and neck cancer surgery (ELICO trial): A randomised controlled trial. Eur J Anaesthesiol. 2022 Sep 1;39(9):735-742. doi: 10.1097/EJA.0000000000001712. Epub 2022 Jul 20. PMID: 35852564.

Lidocaine - Infusion

- Bolus 1-3 mg/kg IV in 20-30 minutes or 1.5 mg / kg in 4 min (lidocaine challenge)
- Careful observation every 30 min (EKG, VS)
- Assess therapy daily; D/C if ineffective
- Infusion 0.5 – 2 mg/kg /hr; rarely > 2 mg/kg/ hr
- Reduce opioids if signs of toxicity (sedation)

Ferrini R, Paice JA. How to initiate and monitor infusional lidocaine for severe and/or neuropathic pain. J Support Oncol. 2004 Jan-Feb;2(1):90-4. PMID: 15330376.

N Eipe, MBBS MD, S Gupta, MD FRCPC, J Penning, MD FRCPC, Intravenous lidocaine for acute pain: an evidence-based clinical update, *BJA Education*, Volume 16, Issue 9, September 2016, Pages 292–298, https://doi.org/10.1093/bjaed/mkw008

Lidocaine - Infusion

- 1–7.5 mg/kg infused over 30 min, 60 min, 4 hrs, or 6 hrs as a single dose or repeated every 4 weeks

- Serum lidocaine concentrations were not reliably correlated with infusion rates

Kintzel PE, Knol JD, Roe G. Intravenous Lidocaine Administered as Twice Daily Bolus and Continuous Infusion for Intractable Cancer Pain and Wound Care Pain. J Palliat Med. 2019 Mar;22(3):343-347. doi: 10.1089/jpm.2018.0243. Epub 2018 Dec 1. PMID: 30508406.
Gibbons K, DeMonbrun A, Beckman EJ, Keefer P, Wagner D, Stewart M, Saul D, Hakel S, Liu M, Niedner M. Continuous Lidocaine Infusions to Manage Opioid-Refractory Pain in a Series of Cancer Patients in a Pediatric Hospital. Pediatr Blood Cancer. 2016 Jul;63(7):1168-74. doi: 10.1002/pbc.25870. Epub 2016 Jan 19. PMID: 26784686.

Lidocaine - Infusion

- Loading dose of 1 mg/kg in 15 minutes
- Continuous infusions 1mg/kg/hr
- Adjust dose based on patient's response and lidocaine levels
- STAT lidocaine levels 5-8 hours after the initiation of therapy or after any change in dose, and every week thereafter

Lidocaine – Home Infusion

If unable to/do not want to taper off Lidocaine; hospice; end of life care

Determine whether to use IV or SQ, bolus vs. continuous infusion vs. both
Patient must have a stable caregiver with 24-hours supervision
Visiting nurse 2-7 times / week
Local side effects (redness) ➔ switch to a different site
Patient should agree to frequent adjustments of lidocaine dosage to determine the minimum dose at which the patient is comfortable
Patient / caregiver should be able to see signs of toxicity and turn off the infusion
Patient / caregiver should be provided with a lidocaine patient information sheet
Benzodiazepines at home for SL or SQ administration in the event of seizures

Ferrini R, Paice JA. How to initiate and monitor infusional lidocaine for severe and/or neuropathic pain. J Support Oncol. 2004 Jan-Feb;2(1):90-4. PMID: 15330376.

Lidocaine - Toxicity

- 3 mcg/ml: rarely
- 4 - 6 mcg/ml: lightheadedness, perioral numbness, dizziness, metallic taste, high BP
- 8 mcg/ml: visual / auditory disturbances, twitching, low BP
- 12 mcg/ml: convulsions
- 16 mcg/ml: coma
- 20 mcg/ml: respiratory arrest and cardiovascular collapse

Ferrini R, Paice JA. How to initiate and monitor infusional lidocaine for severe and/or neuropathic pain. J Support Oncol. 2004 Jan-Feb;2(1):90-4. PMID: 15330376.

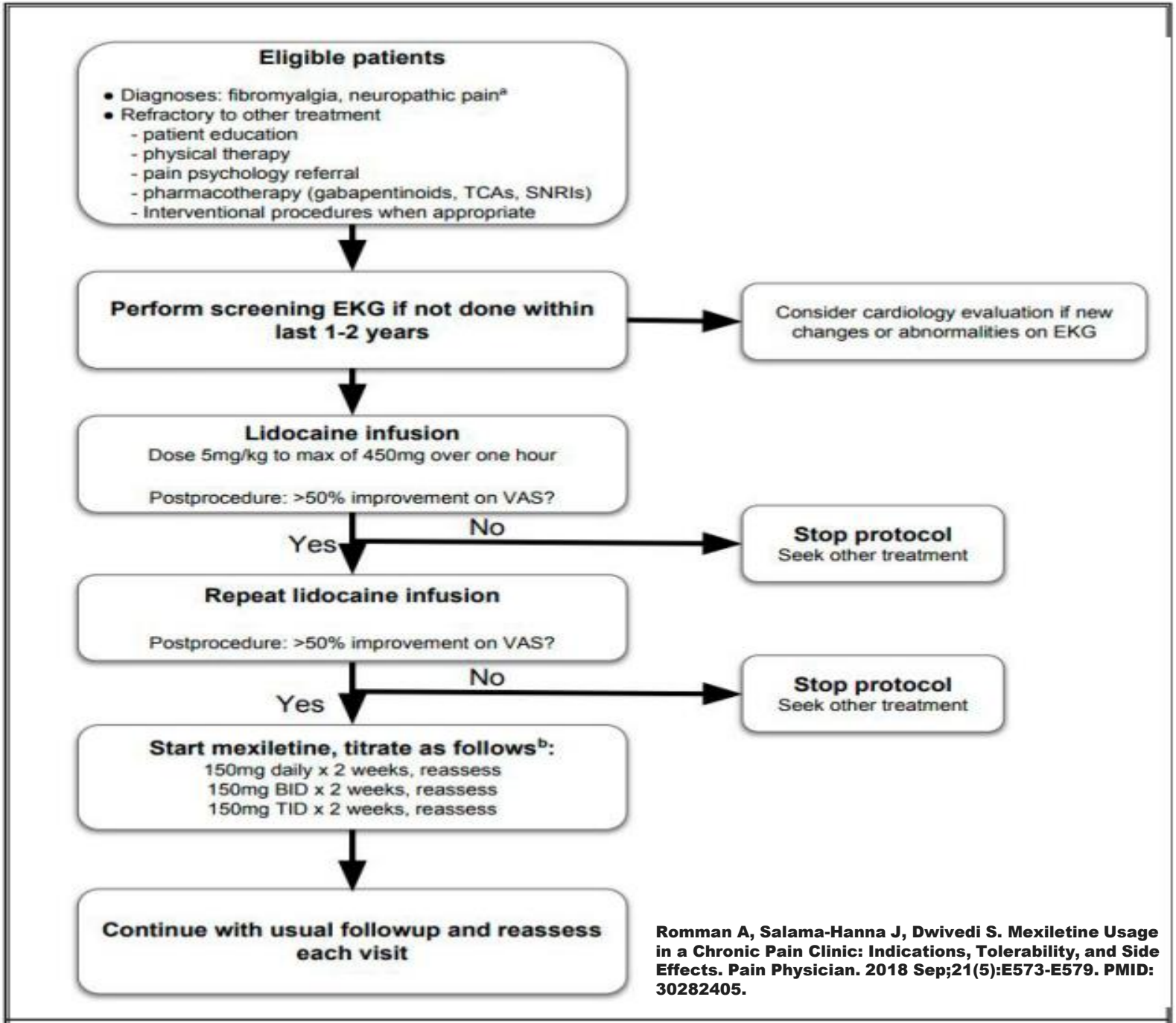
Case Presentation

- Continue with fentanyl patch 150 MCG every 48 hours
- Continue Fentora 600–800 MCG q4 hrs PRN for moderate–severe pain
- NSAIDs (ketorolac IV) 15 mg IV every 6 hours; renal function and platelet count within normal limits
- Continue with Gabapentin, Cymbalta, Lidoderm patches the same
- Transition lidocaine IV to mexiletine 150 mg bid with the option of raising the mexiletine to 150 mg tid (off label indications for pain)

Lidocaine / Mexiletine

- Lidocaine dose: 1.5 mg/kg bolus in 20 min followed by 1 mg/kg/hour
- After 10 hours when lidocaine infusion reaches steady state, may consider increasing to 1.5 mg/kg/hour if patient tolerating
- Prior to starting lidocaine: Consider decreasing MEDD by 20–25% especially if most of the opioid usage is from long-acting meds
- Trial mexiletine prior to hospital discharge
- Cross titration to mexiletine: initiate mexiletine at 150 mg PO q8h; consider going to 200 mg PO q8h if indicated

Atayee RS, Naidu D, Geiger-Hayes J, Saphire ML, Hausdorff J, Edmonds KP. A Multi-Centered Case Series Highlighting the Clinical Use and Dosing of Lidocaine and Mexiletine for Refractory Cancer Pain. J Pain Palliat Care Pharmacother. 2020 Jun;34(2):90-98. doi: 10.1080/15360288.2019.1704339. Epub 2020 Feb 24. PMID: 32091938.



Romman A, Salama-Hanna J, Dwivedi S. Mexiletine Usage in a Chronic Pain Clinic: Indications, Tolerability, and Side Effects. Pain Physician. 2018 Sep;21(5):E573-E579. PMID: 30282405.

Fig. 3. *Flow chart of our revised clinic protocol for mexiletine initiation.*

Mexiletine

- Antiarrhythmic Agent, Class Ib
- Indication: Mixed nociceptive and neuropathic pain, diabetic neuropathy, RSD, Amyotrophic lateral sclerosis, Myotonic dystrophy
- Mechanism of action: inhibits the fast sodium channels
- Contraindications: Cardiogenic shock; 2nd or 3rd degree AV block (except artificial pacemaker)
- Precautions: Blood dyscrasias, hepatotoxicity, heart failure, hypokalemia or hypomagnesemia, seizures, use of antiarrhythmics

Atayee RS, Naidu D, Geiger-Hayes J, Saphire ML, Hausdorff J, Edmonds KP. A Multi-Centered Case Series Highlighting the Clinical Use and Dosing of Lidocaine and Mexiletine for Refractory Cancer Pain. J Pain Palliat Care Pharmacother. 2020 Jun;34(2):90-98. doi: 10.1080/15360288.2019.1704339. Epub 2020 Feb 24. PMID: 32091938.

Mexiletine

- Major substrate of CYP1A2, CYP2D6 cytochromes
- Dose reduction with potent CYP1A2 and CYP2D6 inhibitors
- Common adverse effects: nausea, vomiting, dizziness, tremor, ataxia
- It does not prolong the corrected QT interval (QTc)
- Median time to discontinuation of mexiletine for neuropathic pain at 43 days with fewer than 20% continuing at 1 year

Atayee RS, Naidu D, Geiger-Hayes J, Saphire ML, Hausdorff J, Edmonds KP. A Multi-Centered Case Series Highlighting the Clinical Use and Dosing of Lidocaine and Mexiletine for Refractory Cancer Pain. J Pain Palliat Care Pharmacother. 2020 Jun;34(2):90-98. doi: 10.1080/15360288.2019.1704339. Epub 2020 Feb 24. PMID: 32091938.
Romman A, Salama-Hanna J, Dwivedi S. Mexiletine Usage in a Chronic Pain Clinic: Indications, Tolerability, and Side Effects. Pain Physician. 2018 Sep;21(5):E573-E579. PMID: 30282405.

Case Presentation

- Mexiletine was D/C about 1 month later

- Currently pain managed with Fentanyl patch 75 mcg q 48 hours, Duloxetine 60 mg bid, Fentanyl (Fentora) 400 mcg q 6 hours, Gabapentin 600-600-600 mg, Lidoderm patch

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Întrebări?
Mulțumesc mult pentru atenție !