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SUCCESSFUL MANAGEMENT OF ERYTHROMELALGIA SYMPTOMS WITH TOPICAL KETAMINE AND CLONIDINE: A CASE REPORT

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Background and Importance

Erythromelalgia (EM) is a rare neurovascular disorder characterized by episodic **redness, heat and intense pain** in the extremities (feet and hands). Its pathogenesis remains poorly understood, making **pharmacological management** particularly **challenging**. Despite efforts to avoid known triggers, patients frequently experience **recurrent flare-ups** that significantly impact their **quality of life**.

Interesting facts about EM

Epidemiology: Incidence < 2 per 100,000 people/year, in **adult women,** rare in children.

Causes: **Primary EM** abnormal sodium channel function in sensory nerves, mutations in *SCN9A* gene).

Secondary EM myeloproliferative disorders: e.g. polycythemia vera, essential thrombocythemia, autoimunne diseases, neurologická disorders.

Diagnosis: Five criteria **1.** burning pain in extremities, **2.** pain aggravated by heat, **3.** pain relieved by cooling, **4.** skin erythema, **5.** skin temperature increased.

Skin biopsy and serological tests may assist in ruling out other conditions but do not confirm EM.

Prognosis: EM typically remains **intermittent**, some patients experience **progressive worsening**.

Aims and Objectives

This study aims to review the published evidence on management with a focus on topical treatments for EM and present our single-center experience through a case report.

Figure 1: A case report of a patient with erythromelalgia on topical treatment

Patient: 54-year-old female, problems with adherence.

Medical history: trombocythemia dg. 2003 on treatment with anagrelide, refusing venesection –> myeloproliferative disorder (JAK2-negative, normal karyotype) dg. 2022, arterial hypertension, chronic back pain (road traffic accident in 2015).

Current treatment: omeprazole 20 mg OD, aspirin 100 mg OD, anagrelide 0.5 mg QDS, perindopril arginine 10 mg/indapamide 2,5 mg/amlodipine 10 mg OD, bisoprolol 5 mg OD, moxonidine 0.3 mg ON, tramadol 37.5 mg/paracetamol 325 mg 2 tablets QDS PRN.

Current complaint: erythromelalgia (EM) symptoms first noted in **12/2019, recurrent flare-up 04/2024** - predominanly left foot, warmth, redness, burning sensation, tenderness, **previously relieved with compound amitriptyline 1% + ketamine 0.5% ointment** –> currently stock shortage of amitryptiline (04/2024) –> calling clinical pharmacist.

Clinical pharmaceutical plan:

- Modify ointment composition (adapted from *Cline and Turrentine, 2016*)[3]: **ketamine 2% + clonidine 0.1% in SydoFarm® ointment** TDS locally. Alternate with **ketoprofen 5% cream** BD PRN for pain relief.
- **Cooling strategies** (fan use, cool water immersion, damp cloths), limb elevation to reduce swelling and improve circulation, avoidance of triggers (heat, prolonged standing, tight footwear).
- **Medical check-up after 6 months:** After an **initial excellent response, EM symptoms recurred**. Patient adherence to non-pharmacological measures needs improvement. Local treatment could be further optimized and systemic treatment added for better symptom control.

Materials and Methods

- **Literature Review:** A systematic search was conducted in PubMed, Google Scholar and UpToDate for EM treatments.
- **A Case Report:** The patient's medical records were reviewed using the electronic prescribing system. Treatment plan by a clinical pharmacist was developed in collaboration with a haematologist.

Results

- EM is a difficult condition to manage, with limited evidence in the published literature regarding effective treatments and no definitive cure (Tab.1).
- The treatment goal is to manage symptoms and prevent flare-ups. All patients should initially have **counselling** on **non-pharmacological options +/- aspirin + topical treatment**. Additional systemic therapies are second-line options.
- A case report of a **54-year-old female** with EM is presented (Fig. 1). Due to amitriptyline shortage, an alternative **extemporaneously compounded ointment (ketamine 2% + clonidine 0.1% in SydoFarm®)** was prescribed 3× daily providing good symptom relief.

Conclusion

Topical agents provide a **safe and effective first-line treatment** for EM, particularly when combined with **non-pharmacological measures**. As therapy must be **individualized**, further studies are needed to **standardize protocols**. A **multidisciplinary approach**, including pharmacist involvement, is essential for optimal care.

Table 1: Erythromelalgia management (adapted from 1, 2)

Management strategy	Recommendation
Non-Pharmacological – all patients	
Maintaining a normal lifestyle	Minimize triggers in daily activities. Adequate hydration.
Pain management and psychosocial adaptation	Patient counselling, stress reduction techniques, use topical/systemic treatment as needed, support group.
Cooling measures	Avoid prolonged ice/water immersion (≤10 min, max. 4× daily), use alternative cooling methods like damp cloths and cool air (fan) to help sleep. Showering instead of bathing.
Physical activity modification	Avoiding prolonged standing, excessive walking, or intense physical exertion. Planning outdoor activities around the cooler temperatures of early morning or late evening. Swimming instead of running. Yoga, pilates. Limb elevation during symptom episodes. Pain rehabilitation.
Pharmacological (anecdotal experience, case reports)	
Systemic	Aspirin (especially in myeloproliferative disease)-a trial for all patients without contraindication.
	Gabapentin or pregabalin, venlafaxine, sertraline, amitriptyline, duloxetine, mexiletine, carbamazepine, misoprostol, systemic glucocorticoids, beta blockers (metoprolol, atenolol, propranolol), diltiazem, sodium nitroprusside, high-dose oral/intravenous magnesium (2 g every 2-3 weeks), cetirizin, cyproheptadine, intravenous lidocaine, epidural bupivacaine hydrochloride.
Topical	Mainly ointments/creams/patches are used: non-steroidal anti-inflammatory agents, menthol-methylsalicylate cream, lidocaine (4-5%), capsaicin, gabapentin 6% and combination of amitriptyline 2% with ketamine 0.5-5% to alleviate pain. Topical midodrine 0.2%, oxymetazoline 0.05%, brimonidine tartrate 0.33% or timolol maleate 0.5% are used to reduce redness.

References

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