Efficacy of Topical Gallium Maltolate for Neuropathic Orofacial Pain Following Surgery or Radiotherapy

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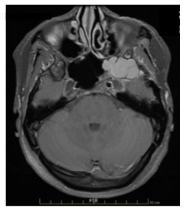
INTRODUCTION

Gallium maltolate (GaM) is reported to produce analgesic and anti-inflammatory activity when administered topically to the skin or mucous membranes. In several case studies involving neuropathic pain, topical GaM has demonstrated remarkable pain relief, even when other analgesic agents had been ineffective. GaM has also been studied as an oral agent in clinical trials, which found no significant toxicity at doses a thousand times higher than the topical doses.

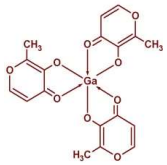
CLINICAL STUDY

This study was initiated to investigate the efficacy of topical GaM in the treatment of highly refractory orofacial pain following surgery and/or radiation therapy. The topical GaM used was the commercial product "Gallixa® skin cream", which consists of 0.5% GaM in an emulsion base of half water and half hydrophyllic petrolatum. Four subjects were studied; these were all patients who sought treatment for severe, refractory orofacial pain at the multidisciplinary clinic for the treatment of pain (CINDOR) in Curitiba, Brazil.

CASE 1 – NEUROPATHIC OROFACIAL PAIN RESULTING FROM SCHWANNOMA SURGERY AND RADIOTHERAPY IN THE CEPHALIC TRIGEMINAL REGION: A 38-year-old female patient presented with paroxysmal shock-like pain, which had been worsening for six months, in the V2 and V3 divisions of the left trigeminal nerve. MRI evaluation revealed a schwannoma in the left trigeminal region, occupying the infratemporal fossa and mastigatory space, with dimensions of 3.3 cm (lateral-lateral), 2.3 cm (antero-posterior) and 2.3 cm (cranio-caudal). The tumor was removed via pterional craniotomy at the Neurological Institute of Curitiba (INC-PR), in Curitiba, Brazil. Shortly following surgery, the patient started experiencing intense pain in the left V2 division, with burning,shock-like pain and paresthesia in divisions V2 and V3. The patient was then prescribed daily amitriptyline 150 mg, carbamazepine 600 mg and pregabalin 150 mg, which provided complete symptomatic relief. The patient then began radiotherapy sessions; shortly after their initiation, the patient started experiencing uncontrollable shock-like pain located in the V2 periorbital region, with extreme allodynia and hyperalgesia. The drug doses were increased, but no significant improvement in the symptoms resulted. Because the patient had become refractory to drug treatment, topical GaM, applied as a thin coating four times per day, was tried as a new therapy. **Results:** Remarkably strong pain relief was obtained during the first few days of using topical GaM, and complete relief of orofacial pain was achieved in 22 days. No side effects were observed from use of the therapy. Currently, the patient is under pharmacological therapy and is asymptomatic.



MRI image showing schwannoma (light gray) in 38-year-old female patient of Case 1.



Molecular structure of gallium maltolate

CASE 2 – NEUROPATHIC OROFACIAL PAIN RESULTING FROM NERVE INJURY ASSOCIATED WITH DENTAL IMPLANT INSERTION IN THE MANDIBULAR REGION: A 66-year-old female patient presented 30 days following dental implant surgery. She reported unbearably intense pain, which had started immediately after surgery, in the left mandibular region, together with dysphagia, mood swings, and difficulty sleeping. (The implant itself had been removed by the dentist 7 days after insertion.) X-rays showed that the implant had been above the left mental foramen near the nerve; the implant pin had likely caused nerve compression leading to neuropathic pain. Quantitative somatosensorial testing (QST) of the left face found extreme hyperalgesia and allodynia in the mental foramen region, associated with ongoing burning pain. The patient was prescribed 3 mg bromazepam, 25 mg nortriptiline, B vitamins, and 10 mg oxycodone daily. When the patient returned in 30 days, the pain had decreased by about 70%. The area of hyperalgesia and allodynia had become confined to the region near where the implant had been removed. Due to the patient's continued localized pain, she was prescribed 0.5% GaM topical cream as an adjuvant treatment, to be applied four times per day to the painful spot. **Results:** Thirty days later, the patient was completely asymptomatic, with no pathological facial sensations, and experienced an improved quality of life. After 60 days, the patient remained asymptomatic, which was confirmed with QST. The nortriptiline dose was reduced to 10 mg/day, the bromazepan was discontinued, the oxycodone dosing reduced to as needed, and the topical GaM dosing reduced to twice per day. After 90 days, the patient remained asymptomatic and no somatosensory abnormalities were observed. The patient reported that she had returned to a normal lifestyle, with no pain, restful sleep, and a high quality of life. All medications were discontinued.

CASE 3 – LOCALIZED NEUROPATHIC PAIN RESULTING FROM NERVE DAMAGE CAUSED BY INSERTION OF A DENTAL IMPLANT: A 57-year-old female patient underwent surgery to install a dental implant in the jaw near the left premolar region, but the procedure was performed without appropriate imaging studies, so the mandibular nerve was injured during placement of the implant. The patient started experiencing electric shock-like pain and burning pain immediately after surgery. The pains were associated with severe somatosensory changes, including allodynia and hyperalgesia. After 3 days, the patient returned to the dentist's office and found that the dentist had left the city without a trace. Three months later, the patient sought specialized care at CINDOR, reporting severe unremitting pain. The electric shock-like pain was paroxysmal and triggered by touching the face and speaking, while the burning pain was continuous. A quantitative somatosensory test (QST) evaluation found allodynia and hyperalgesia across the left jaw with predominance in the premolar region. Treatment was instituted using 60 mg duloxetine, 300 mg carbamazepine, and 10 mg oxycodone daily. After two months, the pain was reduced by 30%; after an additional month, a new titration of drugs had resulted in a reported 60% further decrease in pain. Burning and electric shock-like pain were still present in the premolar region, together with allodynia and hyperalgesia. When the patient returned after four months she was prescribed topical GaM cream to be used four times daily on the painful areas of the face and intra-oral region. **Results:** The topical gallium maltolate eliminated the remaining pain except for paroxysmal shocks that occur one or two times per day; the burning pain and somatosensory changes such as allodynia and hyperalgesia were eliminated. Currently the patient is continuing under the same treatment protocol.

CASE 4 – NEUROPATHIC FACIAL PAIN FOLLOWING NERVE INJURY DUE TO BONE GRAFTING IN AN ATRESIC JAW: A 54-year-old female patient received an autogenous bone graft with anchoring bolts to repair a bone defect in her right mandibular region. Immediately after surgery the patient reported burning and electric shock-like pain in the V3 dermatome, together with hyperalgesia and allodynia. The pain was originally treated by the surgeon using daily 4 mg dexamethasone and 100 mg tramadol for 5 days, which was ineffective. The patient then sought specialized care at CINDOR, 45 days after the procedure. CT imaging showed that two anchoring screws were in intimate contact with the inferior alveolar nerve. After diagnosing severe nerve damage (neurotmesis), the patient was treated with 150 mg pregabalin and 60 mg duloxetine daily; the intensity of pain remained moderate with continued hyperalgesia and allodynia. The two anchor bolts were then surgically retracted 2 mm to allow nerve decompression. The pain decreased, but the allodynia and hyperalgesia remained, together with localized burning pain near the mental foramen region. The pain remained unchanged for another month despite higher doses of pregabalin and duloxetine. At that time, adjuvant treatment was introduced consisting of topical GaM administered 4 times per day to the affected region. **Results:** In 2 days, the allodynia, hyperalgesia and burning pain began to subside. After 2 weeks of using topical GaM cream, the pain was completely gone. The patient was then weaned from all use of pregabalin and duloxetine, which had been in use for 3 months. Currently, the patient is asymptomatic, awaiting the installation of dental implants.

Conclusions

In four case studies of severe, highly refractory orofacial pain following neurosurgery and/or radiation therapy, topical gallium maltolate was highly effective at relieving, and commonly eliminating, neuropathic pain, including extreme shock-like pain, burning pain, allodynia, and hyperalgesia, with no observed side effects. Because topical gallium maltolate has already been reported effective against refractory facial postherpetic neuralgia (in case studies) and refractory trigeminal neuralgia (in a pilot clinical trial of 14 subjects), controlled clinical trials of topical gallium maltolate in orofacial pain are warranted.

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