Gallium Maltolate: A New Topical Analgesic Agent

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INTRODUCTION

Gallium maltolate, an experimental anticancer compound, has been discovered to have analgesic effects when administered topically to the skin or mucous membranes. In several case studies involving neuropathic pain, topical gallium maltolate demonstrated remarkable efficacy, even when other analgesic agents had been ineffective.

Gallium

The semimetallic element gallium has repeatedly shown anti-inflammatory and anti-analgesic activity in preclinical and clinical studies [1]. These biological activities stem largely from the chemical similarities between Gar- and Fe(III) complexes, which allow gallium to enter many of the biochemical pathways of ferric iron. Unlike ferric iron, however, gallium is unable to be reduced to the divalent state under physiological conditions, and it cannot participate in redox reactions. These factors make gallium an irreducible, and therefore non-functional, biochemical mimic of ferric iron.

For example, the iron transport protein transferrin can bind Ga3+, which can then be taken up by rapidly multiplying cells that overexpress transferrin receptor—in particular, many types of cancer cells. Such cells require iron to synthesize DNA, because Ga(III) is an excellent substitute for ferric iron in its active site. Gallium, by acting as a non-functional competitive mimic of ferric iron, can act to inhibit DNA synthesis and thus cellular proliferation [1].

The potent anti-inflammatory activity of gallium is due in part to its ability to selectively inhibit the activation and multiplication of T helper type 1 (pro-inflammatory) cells, and also the secretion of pro-inflammatory cytokines from activated macrophages. Small molecules containing iron tend to be highly pro-inflammatory; it is likely that gallium enters these inflammatory pathways but, due to its lack of redox activity, suppresses inflammation [1].

CASE STUDIES

Topical Analgesic Agent

Neuropathic Pain Following Hand Injury

A 32-year-old male physician developed squamous cell carcinoma of the tongue, as well as more than 20 therapies that had been tried with no success. The patient continued to experience severe pain in his mouth due to the effects of the cancer and the surgery. To relieve the pain, the patient received continuous transdermal fentanyl (150 µg/h) and one-daily oral diclofenac (25 mg). Even with these medications, the patient continued to experience severe pain, at a self-reported level of 4 to 6 on a 10-point scale (where 0 is no pain and 10 is the worst pain imaginable).

A 23-year-old female medical student accidentally cut her left hand at the lateral edge of her left nostril, and eye, with severe allodynia, accompanied by left side facial edema. She reported a 50%-75% reduction of pain throughout the affected area within ten minutes, with further pain reduction over the next few hours. After two days of using the GaM cream, pain was relieved within a few minutes, and the pain was only present on the left side of her face and forehead. The patient used this treatment two to three times per day, her facial and jaw edema were nearly eliminated, and her quality of life was improved. Her severe pain was nearly eliminated by the cream, which was followed by highly refractory postherpetic neuralgia (affecting the mandibular branch of her left trigeminal nerve). For four years, numerous therapies were tried to relieve the severe pain. These therapies included systemic anticonvulsants, tricyclic antidepressants, and opioid analgesics, as well as topical lidocaine and capsaicin, all with unsatisfactory results. The pain was frequently so severe that the patient required hospitalization, and she had become highly depressed.

The topical application of gallium maltolate at a concentration of 0.5% in an emulsion of water and hydrophilic petrolatum, was found to relieve the severe pain in about ten minutes, with the relief lasting for about six to eight hours [4]. The patient used this treatment two to four times per day for most of five years, with no adverse effects and a highly significant improvement in her quality of life. Her severe pain was nearly eliminated by the cream, though mild alodinia sensations still remained. The patient noted that the GaM cream also rapidly relieved pain from insect bites, spider bites, abrasions, and minor burns. A placebo effect is considered very unlikely in this case.

A 43-year-old woman had a 15-year history of worsening trigeminal neuralgia, affecting the left ophthalmic (V1) and maxillary (V2) nerves. She experienced left side facial pain in the cheeks, trigeminal nerve, rostral, and eye, with severe alodinia, accompanied by left side edema around the jaw and cheek, which interfered with eating and talking. Numerous therapies, including a variety of topical and systemic drugs, as well as chiroptiatric and acupuncture, produced moderate, temporary relief at most. A topical solution containing 5% ketamine produced moderate relief of alodinia. The patient applied 0.5% GaM in an emulsion base to the left side of her face, and reported a 50-75% reduction of pain throughout the affected area within ten minutes, with further pain reduction over the next few hours. After two days of using the GaM cream, pain was relieved within a few minutes, and the patient continued to use the GaM emulsion to relieve post-surgical pain as well as remaining neuropathic pain.

A 50-year-old developed vaginal inflammation of unknown etiology, accompanied by severe burning and pain. A commercial vaginal cream containing 5% benzocaine and 2% resorcinol was tried, but this had no effect on pain reduction has often been noted, though it has not been clear if this was simply an analgesic effect or was primarily related to GaM’s anticancer activity.

REFERENCES