Successful Treatment of Refractory Trigeminal Neuralgia with Topical Gallium Maltolate
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INTRODUCTION

Gallium maltolate has produced analgesic activity when administered topically to the skin or mucous membranes. In several previous case studies involving neuropathic, trigeminal pain, topical gallium maltolate has demonstrated remarkable efficacy, even when other analgesic agents had been ineffective.

Gallium

Gallium is a semi-metallic element that has no known essential physiological role, but displays therapeutic biological activities. The element is chemically similar to ferric iron (Fe³⁺), unlike Fe, it cannot be reduced to the divalent state under physiological conditions. This difference is crucial physiologically; it means that, unlike Fe, (1) Ga cannot participate in Fenton-type reactions that produce oxygen free radicals, and so is less toxic than Fe; (2) if Ga competes with or substitutes for Fe in enzymes, the enzymes become non-functional; and (3) Ga does not become incorporated in heme, reducing its toxicity. Ga also shares some chemical similarities with Zn.

Numerous animal studies have demonstrated potent anti-inflammatory activity for gallium, including in models of inflammatory arthritis, lupus, and multiple sclerosis. 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 [1].

Gallium has displayed apparent analgesic activity in human clinical cases of multiple myeloma, metastatic prostate cancer, and hepatocellular carcinoma. We previously reported efficacy of topically applied gallium maltolate (GaM) in cases of postherpetic neuralgia (PHN) and other types of neuropathic pain [2]. The efficacy is hypothesized to be due in part to anti-inflammatory activity, plus possible interference with substance P, certain matrix metalloproteinases, and NMDA receptors [2]. In this pilot study, the aim was to explore the efficacy of topical GaM in the treatment of perhaps the most severe form of neuropathic pain, trigeminal neuralgia (TN).

Gallium Maltolate

Gallium maltolate (GaM) is a coordination complex of gallium and maltol. Maltol is naturally present in many plants; it also ready penetration of skin and cell membranes, including neuronal membranes.

Molecular structure of gallium maltolate

Gallium maltolate molecule from x-ray crystallography

Anti-inflammatory activity of Ga has been shown in rat models of rheumatoid arthritis, in which orally administered GaM significantly inhibited ankle swelling, joint inflammation, bone degradation, and enlargement of spleen and liver [4].

In human cancer clinical trials, GaM has been well tolerated, with no dose-limiting or other serious toxicities observed at oral doses of up to 3500 mg/day for repeated 28-day cycles [3]. In these trials, dramatic pain reduction has often been noted, though it has not been clear if this is strictly an analgesic effect or is primarily related to GaM’s anticancer activities.

CLINICAL STUDY

Methods: An open-label pilot study was conducted on a series of 14 TN cases (11 women, 3 men, ages 43-105). Subjects were administered topically to the skin or mucous membranes. In this pilot study, the aim was to explore the efficacy of topical GaM in the treatment of perhaps the most severe form of neuropathic pain, trigeminal neuralgia (TN).

Table 1: Successful Treatment of Refractory Trigeminal Neuralgia

<table>
<thead>
<tr>
<th>Subject Gender/ Age</th>
<th>Years with TN</th>
<th>Prior medications</th>
<th>Pain Level (0 to 10 scale)</th>
<th>Years using Topical GaM</th>
<th>Contact</th>
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<tbody>
<tr>
<td>1. L/F 56</td>
<td>10</td>
<td>0-3</td>
<td>10</td>
<td>0-3</td>
<td>Lawrence R. Bernstein, PhD Gallixa LLC 285 Willow Road, Menlo Park, CA 94025 US Tel.: +1-650-324-3344 or +1-650-799-5561 Email: <a href="mailto:LawrenceRBernstein@gmail.com">LawrenceRBernstein@gmail.com</a></td>
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