

Is Gallium Nitrate a treatment or a cure for Crohn's Disease? A Case History and Hypothesis

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Abstract

Mycobacterium avium subspecies *paratuberculosis* (MAP) is the likely cause of Crohn's disease (CD) and ulcerative colitis (UC) in humans, and is believed to be the cause of the closely related Johne's disease in cattle. MAP, like all *Mycobacterium*, is an iron-dependent bacterium. Gallium ion (Ga) is bacteriostatic to all iron dependent bacteria. Ga also has anti-inflammatory properties. I hypothesized that oral-use gallium nitrate (GN), a potent source of Ga, would be beneficial in the treatment of CD, an inflammatory bowel disease. In this first instance of the use of a GN aqueous solution in the treatment Crohn's disease, efficacy was readily observed in a 50-year old woman who had been treated unsatisfactorily with a number of CD drugs over the preceding 10 years. Treatment with diluted ($\leq 1\%$) oral GN (226 mg elemental Ga) aqueous solutions resulted in complete and immediate elimination of all signs and symptoms of CD. Due to the recurring nature of CD, and the antibiotic and anti-inflammatory nature of Ga, it is unknown at this time as to whether Ga is a treatment or cure for CD. Regardless, oral Ga was highly beneficial and immediately effective. Beneficial probiotic intestinal bacteria are not iron dependent, and are not injured by Ga. No side effects were observed at the dosage used. Clinical trials of diluted GN aqueous solutions are strongly recommended to verify and extend this original observation in CD, ulcerative colitis and Johne's diseases.

Introduction

Crohn's disease (CD) is a painful, chronic, often debilitating, inflammatory disease of the intestinal tract that affects at least 500,000 Americans, about 75 out of 100,000 Europeans, and millions more worldwide. Crohn's disease (also known as Crohn-Lesniowski Disease, or "Charlotte Forditis" morbus Lesniowski-Crohn, granulomatous colitis and regional enteritis) is a chronic, inflammatory bowel disease which can affect any part of the gastrointestinal tract from the anus to the mouth. CD causes a wide variety of symptoms, including abdominal pain, diarrhea (which may contain mucous and blood), vomiting, weight loss, ulcers and fistulas. CD may also cause complications outside of the gastrointestinal tract such as skin rashes, arthritis and inflammation of the eyes. CD has been considered to be an autoimmune disease, wherein the body's immune system attacks the gastrointestinal tract, causing inflammation. CD tends to present initially in the teens and twenties, with another peak incidence in the fifties to seventies, although the disease can occur at any age.¹

There has previously been no known pharmaceutical or surgical cure for CD. Treatment options have been restricted to controlling symptoms, maintaining remission and preventing relapse, usually with anti-inflammatory agents.

The *Mycobacterium* genus includes pathogens known to cause serious diseases in mammals, including tuberculosis and leprosy. Recently, *Mycobacterium avium* subspecies *paratuberculosis* (MAP) has been suggested to be the underlying cause of CD, primarily because MAP has been shown to cause Johne's disease in cattle and sheep, a disease very similar to human CD.² MAP has been found in blood samples of sheep, and the optimization techniques used should be useful in determining the presence of MAP in humans with CD.³

GN produces a concentration-dependent growth inhibition of *Mycobacterium tuberculosis* strains and *Mycobacterium avium* complexes grown extracellularly and within human macrophages.⁴ *Mycobacterium*, including MAP, are iron-dependent bacteria, and gallium (Ga) is bacteriostatic to them.⁵ These notions suggested to this author that Ga might be beneficial in the treatment of CD – if it is caused by MAP – especially since bacteria do not develop resistance to it, and because Ga does not harm beneficial (probiotic) intestinal flora.

I hypothesized that oral GN solutions would be beneficial in the treatment of CD since it has both anti-inflammatory properties and is bactericidal to the genus that includes MAP. After explaining known side effects of oral GN treatment and receiving informed consent, GN was tested in a 50-year old woman with a long-standing case of CD that had not responded well to accepted therapies.

Methods and Procedures

Dilute GN solutions were made from a 42% GN (8.70% elemental Ga on a weight basis) product made by Recapture Metals Inc. in Blanding, Utah, USA. This GN product is a higher pH GN product, and it releases considerable free ionic Ga(III). Neither citrated GN, Ganite, nor GN with thickening agents were used.

The woman was originally diagnosed by colonoscopy to have CD in 2000, at which time she became sufficiently ill to require her to abandon her employment as a school teacher and stay at home. She daily experienced diarrhea, flatulence, mucous and abdominal pain with occasional bloody stools. Colonoscopy showed ulcers, fistulas, colitis and ileitis.

She was first treated with Asacol (mesalamine) daily for two years, then had a severe flare-up and the drug failed. She was then treated with Azulfidine (sulfasalazine) but became allergic to it. She was then given Entocort EC (budesonide) but it was ineffective. She developed severe diarrhea, mucus, and bleeding and required a 2-week hospitalization late in 2006, where she was given IV prednisone and her stools again normalized. Three weeks after release, diarrhea returned with bleeding and mucus, and she was given oral prednisone. Azasan (azathioprine) was given next and it caused her to vomit and resulted in elevated liver enzymes. She was then given oral Colozal (balsalazide disodium) in combination with Mesalazine (5-aminosalicylic acid) rectal suppositories for about 6-weeks, which was terminated upon starting Remicade. Remicade (infliximab) infusions were given starting in January of 2007. Remicade was stopped in July of 2009 due to peripheral arthritis-like symptoms in wrist, finger joints, shoulder joints, ankle joints and neck. She was retreated with oral prednisone. At no time did she have surgery.

One drug treatment or another for CD was required daily for her to maintain a degree of normalcy. At diagnosis in 2000 she weighed 56.7 KG (125 pounds) and after 10 years of treatment with anti-inflammatory drugs, her weight had dropped to 45.4 KG (100 pounds) and her health remained poor. She had become physically weak and had difficulty lifting objects heavier than 4.5 KG (10 pounds).

On August 20, 2009, while on prednisone, she started GN. Daily dosage of the 42% GN solution was 2 ml (226 mg elemental Ga), which was further diluted with 400 ml water. She took the GN solution in split doses daily throughout the days and evenings. She tapered off of prednisone, taking her last dose on Oct. 1, 2009. She had taken prednisone with GN for 43 days. She continued with GN alone without any other treatment or medicine for CD for an additional two months, terminating treatment on November 30, 2009, having taken GN for 104 days. Several minor mouth ulcers were treated by holding the same GN solution in the mouth for 5 minutes.

Results

All CD symptoms terminated within a few days after starting GN with prednisone, with her stools rapidly becoming normal. After three months of GN treatment, her Dec. 1, 2009 colonoscopy

appeared normal in all regards without any evidence of ulcers, fistulas, colitis and ileitis, although one internal hemorrhoid was found. Since the colonoscopy, she has been off of GN and off of all other treatments and medications for CD, and has not had any symptoms of CD return as of this writing, January 17, 2010, which is 47 days. Since starting GN, she has been free of CD symptoms for at least 153 days. She no longer has the daily diarrhea, flatulence, bloody stool, or any other indication of CD that previously plagued her life. Both the intestinal symptoms and the mouth ulcers responded to Ga treatment and have not returned. Her arthritis-like symptoms have also disappeared, which is consistent with the improvements previously shown for treating human arthritis with GN.⁶ After starting GN treatment, her weight increased by 7.3 kg (16 pounds) within 5 months. She reported that she felt better, and was more energetic and stronger than she had felt at any time in the previous 10 years. She was sufficiently well to resume her career as a school teacher. She did not experience any side effects to GN treatment, except for noting that its taste was quite astringent and drying.

Discussion

CD is known for its flare-ups and remissions, consequently this observation must remain hypothetical of gallium's role as an effective treatment for CD until more research is conducted. A much longer off-treatment period (several years) will be needed without relapse and without further treatment to be convincing of the nature of Ga in curing CD. The mechanisms of action appear to be both anti-inflammatory and antibacterial in nature. Consequently, the main question remains: "Is gallium nitrate a treatment or a cure for Crohn's disease?"

The incidence of CD in industrialized parts of the world is increasing, and an effective, side effect-free treatment or cure is greatly needed. This is the first known test of Ga as a treatment for CD, and it tentatively appears both highly successful and without side effects.

Since ulcerative colitis (UC) and Johne's disease are also believed to be caused by MAP, Ga treatment of those diseases should produce similar benefits. The dosage should be adjusted for use in other subjects on a body weight basis. The dosage for cattle with Johne's disease is hypothesized to be similar or identical to the dosages used to treat horses with navicular disease.⁷ GN is sufficiently inexpensive that it is likely to be economically feasible to treat or cure Johne's disease in domestic livestock, which should reduce exposure of humans to MAP.

Viable MAP is found in human and cow milk and is not reliably killed by standard pasteurization.⁸ MAP is ubiquitous in the environment including in potable water,² consequently its disease-causing potential in humans is related to environmental, food quality and immune system integrity. It is common throughout nature and many species can be infected and diseased by it.²

CD increases the risk of cancer in the area of inflammation, and Ga has anti-cancer properties that have been used to treat colon cancer.⁹

Ga is also known to have immunosuppressive capability,¹⁰ and it has strong beneficial effects generally on inflammation and edema. Unlike steroids, it does not injure the immune system. Injectable GN solutions, approved in the United States for the treatment of hypercalcemia of malignancy, have been known for more than 2 decades to have immunosuppressive properties.¹⁰ At therapeutic doses, Ga has few adverse effects, although high-dose IV infusions may result in severe anemia and severe nephrotoxicity, particularly in patients who are not adequately hydrated.¹⁰ To prevent these side effects, GN is suggested to always be given highly diluted and given with large amounts of water.

In animal models - and in humans to some extent - Ga has been shown to have efficacy in the treatment of arthritis, type 1 diabetes, experimental autoimmune encephalomyelitis, pulmonary inflammation, cardiac allograft rejection, autoimmune uveitis, endotoxic shock, and systemic lupus erythematosus.¹⁰ Clinical trials have demonstrated efficacy of Ga in Paget's disease of bone.¹⁰ Other

clinical trials underway include studies of Ga for sarcoidosis and rheumatoid arthritis.¹⁰ Based upon its pharmacological properties, Ga may be found to have benefits not only in other autoimmune diseases, such as multiple sclerosis, but also in graft-versus-host disease, leprosy, and acquired immunodeficiency syndrome (AIDS).¹⁰ Ga has been found to have strong anti-HIV properties.¹¹

Ga has been used to treat other bacterial infections. For example, delivered subcutaneously it produced 100% survival in the lethal *P. aeruginosa*-infected thermally injured mouse model.¹² Ga works in part by decreasing bacterial Fe uptake and by interfering with Fe signaling by the transcriptional regulator *pvdS*.¹² Ga inhibited *Pseudomonas aeruginosa* growth and biofilm formation and killed planktonic and biofilm bacteria in vitro.¹³ Ga was also shown effective in 2 murine lung infection models.¹³ Ga is being investigated to determine its efficacy in suppressing *Rhodococcus equi*, the cause of foal pneumonia.¹⁴ The antibacterial effects of Ga appear extremely broad, since they terminate the growth of all iron dependent bacteria, fungi and parasites. Since Ga does not kill bacteria outright, they do not become resistant to it.

Iron-dependent pathogenic microorganisms treatable with Ga comprise: *Streptococcus*, *Staphylococcus*, *Yersinia*, *Salmonella*, *Chlamydia*, *Coxiella*, *Ehrlichia*, *Francisella*, *Legionella*, *Pasteurella*, *Brucella*, *Proteus*, *Hilicobacter*, *Klebsiella*, *Enterobacter*, *Escherichia*, *Tropheryma*, *Acinetobacter*, *Aeromonas*, *Alcaligenes*, *Campylobacter*, *Capnocytophaga*, *Bacillus*, *Clostridium*, *Corynebacterium*, *Erysipelothrix*, *Listeria*, *Mycobacterium*, *Pseudomonas*, *Streptococcus mutans*, *Streptococcus sanguis*, *Streptococcus gordonii*, *Atopobium parvulum*, *Porphyromonas gingivalis*, *Eubacterium sulci*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, β -hemolytic streptococci, *Corynebacterium minutissimum*, *Microsporum audouinii*, *Microsporum canis*, *Microsporum gypseum*, *Microsporum canis*, *Sporothrix schenckii*, *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Pityriasis versicolor*, *Exophiala werneckii*, *Trichosporon beigeli*, *Malassezia furfur*, *Fusarium* spp. and *Aspergillus* spp.; including the microorganisms that are known to have become resistant to first-line antibiotics. Such resistant microorganisms include *Escherichia coli* O157 (a causative organism for gastroenteritis, haemorrhagic colitis or urinary and genital tract infections), vancomycin-resistant *Enterococcus faecalis* (a causative organism for endocarditis, urinary tract infections, and wound infections), methicillin-resistant *Staphylococcus aureus* (MRSA; a causative organism for various skin infections, eye infection, wound, oral and other infections), *Salmonella* LO typhi (the causative organism for typhoid fever), and fungi, such as *Candida albicans*, *Microsporum canis*, *Sporothrix schenckii*, *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Malassezia furfur*, *Pityriasis versicolor*, *Exophiala werneckii*, *Trichosporon beigeli*, *Coccidioides immitis*, *Histoplasma capsulatum*, *Blastomyces dermatitidis*, *Aspergillus fumigatus*, *Epidermophyton* spp., *Fusarium* spp., *Zygomycetes* spp., *Rhizopus* spp. and *Mucor* spp.⁵

Miscellaneous applications of mild, soluble Ga compounds may be utilized in many different applications. For example, Ga compounds may be applied topically or directly to a body area, including an open wound and an internal organ or tissue exposed to an outer environment during surgery in addition to an external area that needs to be protected from or is afflicted with various infections caused by pathogenic organisms. GN solutions of up to 42% have been used to treat some skin infections, although there may be discomfort. Such infections include acne, cellulites, folliculitis, boils, carbuncles, erysipelas, impetigo, erythrasma, paronychia, staphylococcal scalded skin syndrome, candidiasis (e.g., oral thrush), ring worm, tinea versicolor and methicillin-resistant *Staphylococcus aureus* (MRSA). Eye infections, such as blepharitis, hordeola and conjunctivitis, must be treated with a $\leq 1\%$ solution and not stronger solutions to prevent eye pain. Causative organisms for skin infections include species of *Staphylococcus*, such as *S. aureus* and *S. epidermidis*; Group A streptococci, such as *Streptococcus pyogenes* and *Pseudomonas aeruginosa*. Typical yeasts or fungi that cause skin infections include *Candida albicans*, species of genus *Microsporum*, such as *M. audouinii* and *M. canis*; species of *Trichophyton*, such as *T. mentagrophytes* and *T. tonsurans*. Causative organisms for eye infections include *Staphylococcus aureus*, *Streptococcus pyogenes*, *Haemophilus influenzae*, *Chlamydia trachomatis*,

Neisseria gonorrhoeae, *Propionibacterium*, *Nocardia*.spp, *Bacteroides* spp and *Fusarium* spp. Nasal infections caused by *Streptococcus pneumoniae* may lead to ear infection, sinusitis, bronchitis, and pneumonia. Heavy metals, such as zinc, nickel and cadmium, have been shown to cause persistent to permanent anosmia when directly applied to the olfactory organ,¹⁵ and caution is advised when applying Ga, a heavy metal, to the nose. The infections caused by these organisms have become more and more common because of the development of drug-resistant microorganisms, such as MRSA, as well as due to the increased number of immune-compromised individuals due to HIV infection or AIDS, organ transplants and treatments for autoimmune diseases. Thus, the applications of Ga compounds for human uses as well as veterinarian uses appear highly beneficial especially in view of their low toxicity, absence of side effects and very low risks for generating resistant microorganisms.⁵

Even nanobacteria appear treatable with Ga, resulting in removal of pathological calcium from kidneys, uterus, arteries and eyes.^{16,17}

Probiotic (beneficial) intestinal microorganisms including species of the genera *Lactobacillus*, *Lactococcus* and *Bifidobacterium* are not affected by Ga because they are not iron-dependent.⁵ In practice Ga appears harmless to beneficial intestinal bacteria in humans and horses and most likely other species, and oral GN has been used to treat navicular disease in tens of thousands of horses since 1996 without producing colic or other side effects,^{7,18} and it appears harmless in the treatment of human and equine arthritis.⁶

Oral GN solutions must be $\leq 1\%$ to prevent mouth discomfort and pain. Severe overdose of Ga may result in displacement of other minerals in tissues and blood, with toxic or even fatal consequences. Modest overdose of GN may cause dizziness, nausea, anorexia, allergy-like symptoms, abdominal cramps, vomiting, itching, bone marrow depression leading to anemia, bloody diarrhea, blood damage with subsequent renal damage, weakness, convulsions, gastrointestinal tract injury and collapse.¹⁹ Severe overdose of nitrates may lead to weakness, depression, headache, and mental impairment.¹⁹ GN must not be given with drugs that have kidney injuring potential such as aminoglycosides and amphotericin B, other drugs that lower blood pressure (BP) (since the nitrate in GN may lower BP), and drugs such as Viagra and Cialis and other drugs that are not to be taken with nitrates.

Use of low-doses of Ga to safely treat CD appears to be a landmark departure from the use of side-effect prone, anti-inflammatory drugs previously used. Perhaps safely killing the bacteria that cause the digestive tract inflammation without side effects is a desired means of treating CD. Clinical trials of oral Ga in treating CD and other diseases, especially inflammatory bowel diseases such as UC and John's disease are strongly recommended.

Possible conflict of interest

The author sells 42% GN solutions for the treatment of navicular bone and joint disorders in horses at <http://galliumnitrate.com>.

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