

Fibromyalgia and Hypoglycemia: Their Combined Morbidity and Therapy with Guaifenesin and Diet Information For Physicians

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Abstract:

We describe fibromyalgia and its reversal using the weakly uricosuric and mucolytic drug, guaifenesin. Salicylates, topical and ingested, block benefits at the proximal renal tubular level, the active site of guaifenesin and all uricosuric drugs. Guaifenesin reverses fibromyalgia and produces the same cyclic symptoms manifested during development of the disease but with greater intensity and at an accelerated pace. Many patients simultaneously suffer from hypoglycemia as redefined and must be treated dietarily with carbohydrate restriction. There is a strong interplay between hypoglycemia and fibromyalgia, both biochemically and in symptom overlap. We propose a theory regarding the etiology of these conditions and the reason for the success of guaifenesin.

Introduction:

Malfunction by the tissues predominantly affected in fibromyalgia, determines the nature of presenting complaints. Possibilities include a preponderance of musculoskeletal symptoms (pain, stiffness and swollen areas); "brain" symptoms (fatigue, irritability, depression, apathy, nervousness, anxiety, insomnia, difficulty with memory and concentration); the irritable bowel syndrome (gas, bloating, cramps, constipation alternating with diarrhea); the genitourinary syndrome (vulvitis, vaginal spasm, dyspareunia, dysuria, pungent urinary odor, bouts of cystitis or the interstitial variety) or a dermal syndrome (itching, burning, crawling, tingling, rashes such as hives, eczema, pruritic blisters, dryness; fingernail chipping and poor hair quality). Patients who present themselves later in their illness often forget the initial symptoms of widely separated cycles.

We do not ascribe a great value in searching for tender points, but we seek out distinct, swollen lesions in their varied distributions. Involved areas are sites of total or partial tendinous, ligamentous, fascial and muscular swellings or contractions. We "map" the palpable abnormalities on a preprinted body caricature to display the degree of induration, size shape and location of each lesion. There are many more than the accepted 11 out of 18. Lesions usually correspond well with painful sites, but only objective findings are drawn, not areas of subjective complaints. Mappings are repeated each visit and are compared to determine progress during treatment.

Symptoms and mappings of patients with the so-called chronic fatigue syndrome permit us to reclassify them as fibromyalgics. These individuals complain most of fatigue and cognitive difficulties and less of pain because they possess higher pain thresholds than their other fibromyalgic cohorts. We have come to the same conclusion regarding individuals diagnosed with the myofascial pain syndrome and systemic candidiasis. We refer to each of these as fibromyalgics and treat them accordingly. Several patients with chemical sensitivities have reported resolution of the problem as fibromyalgia and hypoglycemia reverse. We do not have sufficient data to support this claim as yet.

Background:

More than 36 years ago, we found uricosuric agents reversed the symptoms of an ill-defined illness that later became known as fibromyalgia. Probenecid and sulfipyrazone, normally reserved for treating gout, proved highly effective. We required higher than usual amounts for this new entity and found that dosages must be tailored individually. We simply increased the medication until cyclic reversal of the illness began. In less responsive individuals, titration took considerably time. Some patients were allergic to sulfonamides (Benemid™) and suffered hyperacidity with sulfipyrazone (Anturane™). We knew of no alternate treatment.

A few years ago, we realized that the expectorant guaifenesin is weakly uricosuric though not sufficiently potent to treat gout.¹ Nevertheless, it has proven invaluable for reversing fibromyalgia. Our study of 264 consecutive patients has determined the variable dosages required to initiate reversal. Results are as follows: 300 mg. b.i.d. was sufficient for 20 percent of patients. At 600 mg b.i.d., another 50 percent began reversal; and at 1800 mg. per day, an additional 20 percent initiated the reduction of palpable lesions. Thus, 90 percent of our fibromyalgics began reversal of symptoms and physical findings at 1800 mg. a day or less. Obviously, 10 percent required 2400 mg. or more. Guaifenesin is distinctly more effective than our previous medications and has no listed side effects. Only rarely has a patient experience slight nausea, hyperacidity or rashes. Guaifenesin should not be prescribed in combination with other ingredients such as decongestants that do have multiple side effects. No patent remains on guaifenesin, and it is therefore inexpensive.

Benefits of uricosuric agents and guaifenesin are blocked by any source of salicylates. All plants produce this chemical as their prime weapon for defense against pests and bacteria.² The skin readily absorbs these compounds from topical preparations.^{3,4,5,6} Products that contain plant extracts such as aloe, rosemary, chamomile, barks, almond or other oil extracts etc., must not be applied to the skin. "Natural" flavors in breath savers, mouthwashes, toothpastes or chewing gums with mint, peppermint, wintergreen or spearmint must not linger in the mouth due to the rapid absorption of their salicylate content through the buccal mucosa. Herbal medications, topical or oral, will block, as will herbal supplements and teas. Many women's disposable razors have incorporated a strip of aloe on the cutting edge and deliver sufficient amounts of salicylate for blockade at the renal level. Castor and camphor oil are frequently added to lipsticks and underarm deodorants in sufficient quantities, as well. We provide our patients with a reference to check their products for these compounds.

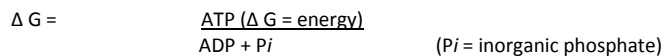
Similar to treatment in gout, in the early stages of guaifenesin response, a pronounced increase in symptoms signals the onset of disease reversal. This intensification of complaints also confirms the diagnosis since the medication, devoid of significant side effects, does not cause pain in non-fibromyalgics. This is a crucial time for ill patients who are suddenly made to feel worse by a drug that will eventually make them well. Repeat mappings on each subsequent visit serve to reassure both the patient and the physician that improvement is underway. These maps also help to determine when an adequate dosage is attained. Newly involved areas reverse sooner than older ones. The slowest rate of regression with guaifenesin is about one year for every two months of treatment. The lowest dosage patients (300 mg. b.i.d.) demonstrate their responsiveness by greatly accelerating their rate of regression and by the intensity of their reversal symptoms. Improvement begins initially with only a few better hours, later days and eventually well-being that lasts for weeks at a time. The duration of the illness and individual responsiveness determines the rate and time to recovery.

Hypothesis and mechanisms:

We believe fibromyalgia is inherited. Family members complain of similar symptoms or of osteoarthritis and, when they are mapped, display the same muscular, tendinous, and ligamentous lesions that we find in fibromyalgia. We conclude from our spectrum of patients (age range of onset from 4 to 74), that fibromyalgia today is the harbinger of osteoarthritis tomorrow. This age spread suggests multiple gene involvement. Our findings that 85 percent of our patients are women. Symptoms often develop in the pre-teens. We commonly elicit a history of growing pains. We have treated nine 4-year-old girls. One of these complained of pains beginning at age 2 and frequently awakened at night requiring hot baths and massage to resume her sleep.

We feel that fibromyalgia is a retention disease similar to gout, but one that affects many more tissues, simultaneously. Although patients respond well to uricosuric agents, urates are not involved. The multiple symptoms produced by the illness and the variety of systems affected, also make it likely that there is an excessive accumulation of an anion other than urate. This putative ion wreaks metabolic havoc throughout the body and yet evokes no inflammatory response. It is obviously perceived as a normal body constituent despite the extent of the physiologic misadventure.

For several reasons, we suspect at least a partial, pathologic role for inorganic phosphate (P_i). This is supported by some observations. Patients note cyclic chipping or peeling of their fingernails (calcium phosphate). Dental calculus (calcium phosphate) often breaks off, and sometimes no longer forms during treatment. Calcium, added to meals, allows lower dosages of medication, since it binds to phosphate allowing both to be eliminated in the stools. We have tested 24-hour urine samples of patients as they began treatment with guaifenesin, and previously with probenecid. We found a 60-percent increase in the excretion of phosphate and a rise in both, calcium as well as oxalate, each one-half of this amount. Perhaps another anion is involved, but these observations suggest a primary defect in phosphate metabolism. If so, the following formula would express the reason for the depressed ATP formation in affected mitochondria:



Bengtsson and Hendriksson biopsied trapezial lesions of fibromyalgics and reported a 20-percent decrease in ATP when compared to normals.⁷ They also noted a similar decrease in phosphocreatine, the high energy reservoir that normally regenerates ATP almost instantaneously. These aberrations were actually more extensive due to dilution from the considerable amounts of normal tissue included in their specimens. Similar changes were minimal in adjacent, unaffected muscle. Reduced ATP levels have also been documented in red blood cells of fibromyalgics.⁸ An energy deficit in affected cells would readily explain the entire syndrome as well as the chemical abnormalities of fibromyalgia.

Eighty to 90 percent of ingested phosphate is absorbed, attesting to the high bodily needs. The proximal renal tubule is the control site for either retention or excretion of the ion. We postulate that there is an inherited defect in some enzyme, receptor, carrier protein, or pump that normally provides metabolic precision for phosphate balance. This error leads to an inexorable retention that begins at birth. Initially, phosphates are adequately buffered in many tissues, particularly bone, but progressively, intracellular and mitochondrial stores increase. Excesses in any site must be similarly buffered, mainly by calcium. Calcium storage facilities are limited, and cells are primed for eventual cytosolic accumulation.

Hydrogen ions (protons) are released from enzymatic reactions within the Krebs' cycle. Inorganic phosphate (P_i) is in equilibrium with the diprotonated phosphate ($H_2PO_4^-$) that rises many fold in exercise.⁹ Since the fibromyalgic, musculoskeletal lesions are in constant contraction (exercised state), they should also accumulate hydrogen ions, P_i^- and high levels of diprotonated phosphate. These rising metabolites are closely related to ATP depletion and muscular fatigue. Higher levels of P_i^- , H^+ and $H_2PO_4^-$, are each known to block the formation of energy and therefore create a shortage of ATP required to activate the calcium pump. As a result, calcium can neither be restored to the endoplasmic reticulum nor extruded from the cell. This failure allows cytosolic calcium accumulations with pathologic consequences. Our theory of the cause of fibromyalgia is that there is defective ATP generation despite a fully operational citric acid (Krebs) cycle that produces heat instead of energy.

New terminology should be coined to properly reflect the perturbed biochemistry of this illness. Fibromyalgia means pain in muscles and fibers and therefore describes only a few of the patient's symptoms. Findings, such as decreased growth hormone, IGF-1, neuropeptide Y, TSH response to TRH, serotonin, free ionic calcium (Ca^{2+}), free urinary cortisol, certain amino acids; increased serum prolactin, substance P, and angiotensin converting enzyme, make it obvious that this is a widespread, fundamental disease that affects many organs and systems. At times, the cycling fibromyalgic almost meets full energy demands; at other times, barely, or not at all. Periodic availability of energy permits some bursts of effort but, expenditures by any activated system, readily deplete the marginal energy bank. Thus, an accident, emotional stress, infection or surgery may greatly exacerbate or precipitate the first attack of fibromyalgia.

"Amorphous crystals" are frequently found on urinalysis. We suspect that these are precipitates of our putative calcium phosphate abnormality. In concentration, they can denude the bladder trigone and urethra, causing abrasions with consequent dysuria and repeated bouts of cystitis, either local or interstitial. Vaginitis, vulvitis and pelvic floor muscular spasms, which cause dyspareunia and the syndrome of vulvodinia, are included in the "genitourinary syndrome." These and other symptoms such as eye irritation, scalded or metallic tastes, pruritus, various rashes, faulty hair texture and growth, and fingernail chipping attest to the involvement of the integument and various mucosae. Disintegrating mast cells have been reported in the epidermis and bladder wall releasing histamines and the myriad of their other contents. Immunoglobulin G was found in high concentration in the same dermatology report. The biochemical abnormalities of fibromyalgia affect not only the dermis, brain, musculoskeleton, intestinal and genitourinary tracts but also most other bodily structures and functions.

The multiple, over-stimulated areas of fibromyalgia burn fuel steadily. This results in sugar-craving in a futile attempt to create energy. Increasing carbohydrate intake yields little due to the impediment to ATP formation. Sugars and starches induce repetitive insulin surges that, in susceptible individuals, initiate the "hypoglycemia" syndrome. Some 40 percent of fibromyalgic females and 20 percent of males are affected. Most dramatic are the acute symptoms: frontal headaches, tremors, sweats, heart pounding or tachycardia and the sudden feeling of anxiety. Symptoms occur a few hours postprandially and often nocturnally. Episodes last approximately 20 to 30 minutes.

Genter and Ipp studied the release of counter-regulatory hormones during glucose tolerance tests performed on normal individuals.¹⁰ Blood was sampled every 10 minutes and showed a rise of epinephrine beginning 10 minutes before and peaking with the nadir of the blood sugar. One-half of these young, healthy subjects exhibited the symptoms as epinephrine neared its peak. None of the samples fell to the accepted hypoglycemic level of 50 milligrams per deciliter. Seemingly, each person has an individual brain set-point for glucose below which glucopenia is signaled. Well-defined corrective measures are induced. Epinephrine is the fail-safe hormone that corrects hypoglycemia within one or two minutes but also causes symptoms, which, when most intense, are labeled "panic attacks." We no longer perform glucose tolerance tests since the "epinephrine-symptoms" suffice for a diagnosis of the carbohydrate intolerance usually referred to as hypoglycemia.

The chronic symptoms of hypoglycemia overlap strikingly with fibromyalgia. Both conditions produce similar brain symptoms such as fatigue, irritability, nervousness, depression, insomnia, impaired memory and concentration, as well as anxieties and diarrhea. The diseases are readily distinguished from one another by the musculoskeletal complaints of one and those due to epinephrine bursts of the other. Symptoms of hypoglycemia do not improve without the proper dietary restrictions. Patients must eliminate caffeine, simple sugars and complex carbohydrates (potatoes, pasta, rice, etc.) The diet prevents wide swings in blood glucose and thereby prevents insulin surges and the need for epinephrine counter-regulation. Failure to comply with these dietary recommendations would not delay the reversal of fibromyalgia, but the symptoms of carbohydrate intolerance would persist.

Summary:

We have discussed certain facts and added theoretical considerations to help understand fibromyalgia. Guaifenesin is our most effective medication to date. Any source of salicylate will block its benefits by interference at the proximal tubular level. All plants make varying amounts of this compound. Salicylates are readily absorbed through the skin or mucous membranes. Even the small amounts contained in cosmetics and other topicals will prevent success in treatment. Body maps made during treatment illustrate reversal of previously noted progress if salicylates are used unwittingly. Many fibromyalgic patient, especially women, are carbohydrate intolerant ("hypoglycemic") and must restrict their intake of sugar and starches. These overlapping syndromes have distinguishing symptoms that must both be recognized and treated for successful therapy.

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