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THE MEDICAL TREATMENT OF ERYTHROMELALGIA

Dr. Cohen developed severe erythromelalgia (EM) in 1995, yet he is pain free and highly active today. Dr. Cohen is an adjunct (voluntary) associate professor at the University of California, San Diego. He has published several medical journal articles on treating EM.

Erythromelalgia, with its burning, red hands and/or feet, is a painful, limiting condition, but treatment can be effective in many cases. I know because I developed EM in 1995, when little was known and the few known treatments did not work. I was bedridden for 3 years and limited for many more until, by trial and error, I found therapies that work for me. My condition today is 95% controlled, and I have little difficulty unless the temperature rises above 85 degrees. I am highly active without pain.

Because different people with EM respond to different treatments, there is no standard formula for treatment. So, it is important for you and your doctor to work with one treatment then, if necessary, another until benefit is obtained.

Be careful about allowing your doctor to try medications that are not known to benefit EM. Doctors often want to help and are tempted to try unproven treatments, but many drugs can make EM worse, so be very cautious.

With each medication, have your doctor start with the lowest dose. If no response is seen within a week or two, the dosage may be increased gradually until either benefit or worsening is seen. If your EM worsens, the drug should be stopped. If no effect is seen, the dose may be increased further. If side effects occur, discontinue. It is important to follow this method because many times, people receive a medication, see no change, and discontinue. Yet, at a higher dose, the medication might have helped. Thus, it is important to investigate each medication fully.

In EM secondary to a medical condition, the medical condition should be treated first. Sometimes the EM will disappear too. If not, the EM should then be treated.

A remarkable degree of variability is seen in people's responses to various therapies. Therapies that help some people may be ineffective or worsen symptoms in others. No one medication is reliably

effective for all EM sufferers. Combination therapy is sometimes more effective than single drug therapy.

FIRST LINE THERAPIES

Serotonin/Norepinephrine Reuptake Inhibitors (SNRIs)

SNRIs increase serotonin and norepinephrine in the nervous system and provide substantial benefit for some EM patients. Effexor (venlafaxine) has been reported many times in medical journals to help EM, but it fails sometimes too. Cymbalta (duloxetine) has also provided benefit for many.

Serotonin Reuptake Inhibitors (SSRIs)

This group increases serotonin in the nervous system. There are a handful of case reports of benefit with sertraline (Zoloft), fluoxetine (Prozac), or paroxetine (Paxil). For Tramadol (Ultram), which increases serotonin by the different mechanism, there is one report of benefit.

Gabapentin (Neurontin)

A tiny percentage of people have reported remission with gabapentin. About 50% report some pain reduction, but no change in flaring, redness or heat. Some people consider this benefit sufficient, but many others continue to seek more effective therapies.

Calcium Channel Antagonists (CCAs)

CCAs are normally vasodilators, which would make EM worse, but in some people CCAs actually improve EM, sometimes dramatically. Diltiazem helped me considerably. Nevertheless, because CCAs may worsen EM, these drugs should be used cautiously with very low doses at first (i.e., short-acting diltiazem 30 mg) and close medical supervision. My impression is that CCAs help about one-third of people with EM, worsen another third, and have no effect in the rest.

Another choice is magnesium, the body's natural CCA. Magnesium has helped me for many years. It has helped other people too, but some others have obtained no benefit or worsened, so use magnesium carefully like any CCA. Start with a small amount, 100-200 mg/day, and increase gradually. Use high quality magnesium because poor quality can cause diarrhea. My favorite magnesium product is Magnesium Plus Protein (mgplusprotein.com), but it easier to get magnesium citrate or gluconate from a health food store. Magnesium therapy requires normal kidney function and good hydration, and use in the elderly or dosing above the recommended daily allowance of 400 mg/day necessitates close medical supervision. Alternative doctors are usually more knowledgeable about using magnesium than mainstream doctors.

Other substances with mild CCA effects are chromium, alpha lipoic acid, high doses of ascorbic acid, and the herb butterbur.

SECOND LINE THERAPIES

Transdermal Therapy with Amitriptyline and Ketamine

The simplest and perhaps safest approach to treating EM is a transdermal cream containing 1% amitriptyline and 0.5% ketamine. The cream is applied over the skin affected by EM three times daily. Results are usually seen within days. Preliminary results from the Mayo Clinic suggest an improvement rate of 50% to 70%. My experience has been less positive. This therapy must be ordered by a doctor from a compounding pharmacy (www.iacprx.org).

Propranolol

There are few reports of benefit with propranolol, usually at 10 mg three-times-a-day. Higher dosages can be used. One person is using 320 mg per day with considerable benefit. Propranolol's effect may lie

in its ability to block beta2 adrenergic vasodilator nerves in the skin. Except for timolol, which has effects similar to propranolol, other beta blocker drugs do not have this effect. One of the side effects of propranolol and timolol are that they can make Raynaud's disease worse. Because Raynaud's and EM have opposite symptoms, this means these drugs may sometimes improve EM.

Serotonin Antagonists

Serotonin antagonists are logical choices for people whose EM does not respond to SNRIs or SSRIs. Cyproheptadine (Periactin) and pizotifen (Sandomigran, from Canada) are antihistamines with unique anti-serotonin effects. These drugs are commonly used for people with migraines. I believe EM and migraine have many similarities. It took many years before I got around to trying these medications. Cyproheptadine helped a little, but pizotifen was the single best medication I ever tried. Two herbs have similar although milder effects: feverfew and white willow.

Tricyclic Antidepressants

Long known to provide benefit for neuropathies, tricyclics are occasionally helpful in EM. One case of remission has been reported with amitriptyline.

Aspirin (ASA)

ASA can be rapidly effective for EM secondary to blood disorders (polycythemia, thrombocythemia, leukemia). Otherwise, it is infrequently helpful in EM. ASA dosages should be gradually increased up to 650 mg four times daily, if necessary. Side effects such as gastritis or ulcers can occur.

Prostaglandins

Reports from Europe suggest that misoprostol can often be effective, but positive reports have been few in the US.

Opiates

Codeine and similar medications sometimes provide partial pain relief, but they do not usually alter the flaring, redness or heat of EM.

Other Medications

Scattered reports have been reported of benefit with mexiletine, clonazepam, carbamazepine and others, but success is infrequent. A higher number of people seem to obtain benefit with a new drug, Lyrica (pregabalin).

PROCEDURES

Sympathetic blocks and epidurals are sometimes helpful in EM. If you improve following a sympathetic block, greater improvement might be obtained with a series of blocks. The medical literature also reports improvement with sympathectomy, but because this surgical procedure can worsen EM and is irreversible, it should be considered only if you obtain benefit from sympathetic blocks.

Morphine pumps and spinal cord stimulators have been used with some benefit in EM. These methods may help control pain but rarely alter the vascular symptoms. Intravenous lidocaine, with or without mexiletine, has been effective occasionally.

TREATMENT OF CHILDREN AND ADOLESCENTS

Many of the treatments above may also be considered for children with EM. Remissions in children or adolescents have been reported with magnesium, gabapentin, and with ketamine/amitriptyline transdermal gel. Combination therapy sometimes works better: in a 4 year old girl who developed EM after influenza vaccination, rapid improvement occurred with low-dose aspirin, carbamazepine and

propranolol. Long-term epidurals may also provide benefit in severe cases. Intravenous nitroprusside, which is contraindicated in adults, is sometimes effective in children and adolescents.

CONCLUSIONS

When I developed EM in 1995, we were still in the dark regarding treatment. Hardly any doctors had heard of EM. Only a few treatments had been reported, and they rarely worked. Today things are much better. Our understanding and methods have grown considerably, and many people can be helped. Of course, I still sleep with the covers off of my legs and avoid walking in the hot sun, but I rarely have pain and can do most of the things I want.

I believe that significant improvement is possible for most people with EM. Find a doctor who can make an accurate diagnosis and is willing to work with you, using this article as a guide. It takes patience to try one treatment after another, but don't give up. Be patient and persistent. For support, contact The Erythromelalgia Association at erythromelalgia.org. This excellent organization is run by volunteers with EM and offers extensive information you will find useful.

NOTE TO READERS: Few studies have been done on EM, so there is a lack of established scientific fact about EM and its treatment. This article reflects my knowledge and personal experience with EM, and is meant to provide information for use by you and your doctor. This information should not be considered as a substitute for the medical advice of your doctor, nor is it meant to encourage the diagnosis or treatment of any illness, disease, or other medical problem without your doctor's direction. Readers should not make any changes in drugs, doses, or any other aspects of their treatment unless directed by their doctor. Finally, after many years of disability from EM in the 1990s, Dr. Cohen is now highly active with no pain, but because people with EM vary greatly in what helps them, he makes no claim that his methods and suggestions will benefit anyone else.

Dr. Cohen is an Associate (Voluntary) Professor of Preventive Medicine and Psychiatry at the University of California, San Diego, one of the top 20 universities in America. His work in the area of preventing medication side effects has been widely published and is recognized nationally. If you would like Dr. Cohen's input on your EM, he is available for office or telephone consultations. He charges a fee for his time, just as he charges people with other medical conditions who come to his office or consult with him from around the world. For information, contact Leslie at 858-345-1760 or schle@att.net.

Dr. Cohen's Publications on Erythromelalgia:

Cohen JS. The Medical Treatment of Erythromelalgia. MedicationSense.com. January 3, 2012.

Cohen JS. Supplements and Herbs in the Treatment of Erythromelalgia. MedicationSense.com. January 3, 2012.

Cohen JS. What Is Erythromelalgia? MedicationSense.com. January 3, 2012.

Cohen, JS. Erythromelalgia: New Theories and New Therapies. Journal of the American Academy of Dermatology, November 2000; 43:841-7.

Cohen, JS. Magnesium and erythromelalgia: a clinically important vasoactive mineral and a rare disorder. Italian Journal of Pediatrics 2004;30:69-72.

Also consider joining The Erythromelalgia Association (TEA), an excellent resource for information, published articles, and support for people with EM as well as for their families, friends and health care