Treating *Herpes Zoster* with Vitamin C: Two Case Reports

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ABSTRACT

Two cases of *Herpes zoster*, of one day's and one week's duration, were treated with injections of intravenous vitamin C with good results.

If the outcome of this treatment is as good as previously claimed, efficacy could be proved in a double-blind crossover study with as few as 20 subjects. In the absence of such a study, it is still reasonable for clinicians to use this modality.

Although there are no randomized controlled trials to investigate the use of parenteral ascorbic acid in the treatment of *Herpes zoster* (shingles) in the manner described by Joel Kauffman,[1] it is reasonable for clinicians to use ascorbic acid for this purpose. The possibility of adverse effects of treatment is remote. The condition is not only painful acutely, but may be followed by refractory postherpetic neuralgia. Cases involving the geniculate ganglion may produce the Ramsay Hunt syndrome.

In the case series referred to by Kauffman, "success" was achieved in 14 of 14 cases in one, and 7 of 8 cases in the other.

Case Reports

Case 1. An 84-year-old man presented with pain over the left side of his scalp in the temporoparietal area. Within a few hours, he developed tiny blisters that evolved into a typical *H. zoster* rash. There were no lesions in the ear canal. He was advised to take 3 g of vitamin C orally and 1 g every two hours while awake.

Within about 24 hours, having been informed of the potential usefulness of injected vitamin C, he asked for an injection. Using a winged injection set, 3 g (6 cc) of "ascorbic acid" was injected slowly into an antecubital vein. The preparation used was "ascorbic acid" 50 mg/cc in sterile water with 0.025% edetate disodium, buffered to pH 5.5 to 7.0 with sodium bicarbonate, from Bioniche Pharma (Canada) Ltd.

Two to three hours later, the patient's pain was much diminished. By the next day, it was possible to touch his scalp without causing discomfort; at first merely touching the hair had been very painful. A total of six injections at approximately 12-hour intervals were administered, and the patient was instructed to take 1 g of vitamin C orally every two hours while awake.

After injections had been stopped for about nine days, pain worsened, and an additional IV injection was given. Because venous access was difficult, this was followed by injection of 2.5 cc of ascorbic acid plus 0.5 cc of 1% lidocaine IM in each buttock, 24 and 48 hours later. The injections appeared to cause minimal discomfort. The total dose of ascorbic acid in each set of two injections was 2.5 g.

Four days later, after talking to his sister-in-law about a brother's recent death, the patient developed a painful flare, with marked erythema and tenderness. New blisters appeared. Within one hour of IM injections, the erythema, pain, and tenderness were much diminished. Three more sets of IM injections were given at approximately 12-hour intervals. By this time, the patient's discomfort was minimal, and his activity level had increased. He walked more around the house, even venturing outdoors for the first time in some weeks.

Because of the possibility of provoking hypoglycemia in a diabetic,[2] a sugar-containing drink was kept available. However, the patient's blood sugar, monitored with Accu-Chek strips, ran unusually high during the course of the illness. Ascorbic acid is not an interfering substance for Accu-Chek, according to the manufacturer's customer support service.

The patient had mild residual discomfort 6 weeks after the onset of the outbreak. At no time did he take pain medication other than two acetaminophen tablets two to three times daily. Application of warm wet washcloths provided substantial relief.

Case 2. A 40-year-old white woman had experienced severe pain ("not as bad as a kidney stone") for about a week, and a typical rash on the right side of her chest extending just beneath her breast. She was unable to wear a bra because of pain. After reading Kauffman's article, she requested an injection, although informed that treatment might be less effective given the duration of symptoms. After the first IV injection of 3 g of vitamin C, she had only slight relief, but decided to continue the treatment. After four injections at approximately 12-hour intervals, plus 1 g of vitamin C orally every two hours while awake, she was virtually pain free and the rash had resolved. No postherpetic neuralgia occurred.

In both cases, patients experienced a burning sensation along the course of the vein after the injection when a hand or wrist vein was used, lasting a few minutes, but no significant discomfort when an antecubital vein was used. Patient 2 felt weak and faint on two occasions after the injections, but these symptoms resolved within a few minutes. Dilution with sterile water or 5% dextrose would probably diminish the discomfort associated with IV infusion.

Discussion

Very high doses of intravenous vitamin C, up to 150 g, have been used, particularly by Frederick Klenner, M.D., a family physician, to treat a variety of conditions, including viral infections, snake bite, and black widow spider bites (latrodectism). Klenner claimed "cures" of polio, but his diagnosis was based on clinical findings alone, without lumbar puncture.[3]

The mechanism of action is unknown; a nonspecific stimulus to the immune system is often posited. However, under aerobic conditions in vitro, vitamin C causes degradation of proteins by breaking peptide bonds, generating a shower of peroxides and free radicals. This remarkable though generally unremarked discovery was made by Steve Richheimer, a graduate student working in the laboratory of Arthur Robinson.[4] A similar effect had been previously described with DNA[5] by C.W. Orr, who also demonstrated that the degradation of catalase by vitamin C was enhanced by metal ions,[6,7] and that vitamin C killed viruses in culture (A.B. Robinson, personal communication, 1994).

Linus Pauling, Richheimer's official adviser, suppressed dissemination of knowledge about this important effect of vitamin C in a creative way. Pauling told Richheimer that his beautiful discovery merited an early Ph.D., without any further work, and forced its approval over the objections of the rest of the thesis committee. Then Pauling refused to coauthor a paper or recommend Richheimer for a postdoctoral position.[7]

Because the work lacked the necessary quantitative, confirmatory studies, publication was restricted to an obscure journal,[8] and the findings were generally ignored (A.B. Robinson, personal communication, 2005). One may surmise that Pauling wanted vitamin C to be regarded as a benign "antioxidant" rather than a destroyer of macromolecules, and was willing to ruin a scientist's career to protect the reputation of a supposed panacea and its most prestigious promoter.

Snake venom and other peptide toxins that are injected once in a limited dose would be prime candidates for treatment with a peptide destroyer. The organism receiving the vitamin C may also suffer some damage but is able to repair itself.

During infections, the leukocyte ascorbic acid content decreases.[9] It is possible that vitamin C is sequestered for safe transport in leukocytes, from which it is released to generate peroxides and free radicals when needed to destroy invading microorganisms (A.B. Robinson, personal communication, 2005).

Another possibility is that the burst of antigens released in the breakdown of macromolecules serves as a stimulus to the immune system.

In the internet era, physicians may encounter patient demands for a trial of Klenner's protocols,[10] especially in the event of life-threatening infections for which no effective treatment exists, including viral encephalitis and pandemic influenza.

Suggested Research Design

As successes are far more likely to be reported than failures, a controlled trial would be highly desirable. But if patients are fully informed, it seems likely that many will not want to give consent to possible receipt of a placebo when they have a painful condition with a high likelihood of months—or even a lifetime—of pain requiring opioids for adequate relief. This is especially true with a treatment that is low in cost and apparently without significant adverse effects. Therefore, a crossover design is needed.

Patients could be randomly assigned to receive solution A or solution B, with both patient and investigator blinded to which is active, along with vitamin C capsules or placebo capsules matched to the solution. The vitamin C solution should be sufficiently dilute, or mixed with a local anesthetic, to prevent burning on injection.

Three hours later, patients who do not have resolution or marked diminution of pain could receive the other solution and the other type of capsule. Three hours after that, the patient could decide which of the two solutions should be continued for a total of six injections. If the patient detects no difference, then the first substance would be used for the course. Patients should be evaluated soon after the last injection and at 1, 3, and 6 months for occurrence of postherpetic neuralgia. Outcome measures should include duration of rash, duration and severity of pain, and severity of constitutional symptoms.

If treatment is as effective as Kauffman's sources claim, a very small number of cases would be adequate to demonstrate the effect with a high degree of confidence. Using tools made available on the internet by DSS Research (www.dssresearch.com), one can determine the sample size that would be required under various assumptions about treatment and placebo effect and the desired confidence interval:

If vitamin C gives rapid pain relief in 80% of cases, and placebo in 10%, only about 10 subjects would be needed in each group to show a statistically significant difference with $P<0.01$. If vitamin C is 50% effective and placebo 10% effective, about 30 subjects would be needed in each group. If the placebo effect is 30% and vitamin C is 50% effective, about 130 subjects in each sample would be required. In each of these cases, the power of the test would be 80%; in other words, the risk of inappropriately failing to reject the null hypothesis would be 20%.

Note should be made of duration of symptoms. Patients who have had symptoms longer than 72 hours might not respond as quickly. Although it might well be worthwhile to offer treatment, as case 2 illustrates, one might wish to exclude such patients from the study, or place them in a separate group. Age, concurrent treatment, and comorbidities should be noted.

Inclusion of patients taking antiviral drugs and/or predisone would contaminate the results. Because drugs such as acyclovir have been accepted as standard therapy, some may have an ethical objection to a placebo-controlled trial. Intravenous acyclovir is not generally used for shingles except in patients who are severely immunocompromised. Conceivably, oral acyclovir could be used in the control group, but significant side effects may occur.

The window of time for starting acyclovir is up to 72 hours after onset of symptoms.[11] Thus, patients who enter the trial very early in their course would still have the option of taking standard therapy if they got no relief from the injections. Those who had already had symptoms longer than 72 hours are generally not offered antivirals, so pressure to use "standard" treatment should not impede their participation in a placebo-controlled trial. The effect of ascorbate on the drug, which is a nucleoside analogue, should be determined before combination therapy is considered.

In a randomized, controlled trial done in the UK, the prevalence of postherpetic pain in patients over age 60 in the placebo arm was 61% at 1 month, 24% at 3 months, and 13% at 6 months. The rate at 6 months for such patients was 35% in another trial.[12] Overall, the rate of postherpetic neuralgia is said to be 20%.[11] If vitamin C reduces the rate from 20% to 10%, a sample size of nearly 200 in each group would be needed to demonstrate a difference with a $P<0.05$ and a power of 80%. If vitamin C reduces the rate nearly to 0, say to 1%, a much smaller sample size of around 30 should be adequate.

In the event that the vast majority of patients in the trial choose the preparation containing vitamin C, there might not be a control group sufficiently large to compare incidence of postherpetic neuralgia, so that comparisons with placebo groups in other trials may be the best that can be done, given the design outlined here.

Conclusions

Vitamin C treatment of the first two patients who came to my attention after the publication of Kauffman's article[1] had gratifying results. A facility with a pharmacy capable of supplying the required solutions and capsules, personnel to administer intravenous therapy, and a sufficiently high patient volume should perform a double-blind crossover study.

Even in the absence of such a study, clinicians should consider using this therapy. Because the effect seems to be substantial, a small series of cases should enable the clinician to judge whether the effort and expense is worthwhile. If a clinician keeps a running tabulation of patient outcomes, future patients can be told what percentage of patients can expect relief, and make their decisions accordingly.

Safe, low-cost therapies such as vitamin C are probably underutilized, owing to the absence of randomized controlled trials, the current disinclination of medical journals to publish case reports, and increasing pressures on clinicians to follow the "standard of care." A methodical evaluation of the effectiveness of such therapy and of its physiologic actions is long overdue.

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