

Recent Experience Using Immunoglobulin to Treat Post-Polio Syndrome

Lauro Halstead, MD, Post-Polio Program, National Rehabilitation Hospital, Washington, DC, and Julie K. Silver, MD, International Rehabilitation Center for Polio, Framingham, Massachusetts

Over the past 20 years there has been a growing body of evidence that suggests an inflammatory process may be causing most, if not all, of the symptoms of post-polio syndrome (PPS). In 2002, Henrik Gonzalez and colleagues, working in Stockholm, Sweden, reported finding an elevated level of cytokines—a marker of inflammation—in the cerebral spinal fluid (CSF) of a group of polio survivors with PPS. Elevated levels of proinflammatory cytokines (as opposed to anti-inflammatory cytokines) are found in a number of neurological disorders with an inflammatory component such as multiple sclerosis. Other researchers have also found elevated proinflammatory cytokines in individuals with PPS but normal levels in polio survivors without PPS.

These findings strongly suggested that anti-inflammatory medications might be an effective way of treating PPS symptoms. One of the most potent anti-inflammatory medications is immunoglobulin. Immunoglobulin is a group of protein molecules that is part of the body's immune system. These molecules play an important role in defending the body from bacteria and viruses and are used to reduce inflammation in a variety of neurological disorders. When immunoglobulin is given intravenously it is called IVIG.

With this in mind, researchers began administering IVIG to polio survivors with PPS and discovered they were able to reduce proinflammatory cytokines to normal levels and improve some of the symptoms of PPS. As these were small preliminary investigations, they lacked the rigor of larger, more definitive studies using a randomized, placebo-controlled design.

In the most recent study, published by Gonzalez and co-workers in *Lancet Neurology* (Vol. 5, Issue 6, pp. 493-500) in June 2006, the researchers studied 142 polio survivors at four university clinics who were randomly assigned to either an infusion group or a placebo group. This was a double-blind study, so neither the polio survivors nor the investigators knew whether they were getting the study drug or not.

All subjects were carefully screened to ensure a diagnosis of PPS; exclusion criteria included obesity, unstable chronic diseases or the presence of musculoskeletal disorders with symptoms that mimicked PPS symptoms. The researchers evaluated a number of outcomes including a selected study muscle with 25–75% of expected strength for age and gender, a quality of life measurement, an assessment of vitality, overall muscle strength, level of physical activity, fatigue and pain.

The results showed that the study muscle strength improved, on average, 8.6% in participants who received the immunoglobulin compared with those who received the placebo.

Although 8.6% difference was statistically significant and seems impressive, it reflects a mean improvement of 2.3% in the treatment group combined with an average decline of 6.3% in the placebo group. (This is in contrast to the average decline in muscle strength reported in the literature of 1–2.5% per year.) The authors discuss several explanations for the marked decline in strength in the placebo group but the reasons for this finding and the discrepancy with other reports are not clear. Other significant findings in the study group included an improvement in vitality, an increase in physical activity and a reduction in pain (in one subgroup). Overall, the study drug was well tolerated.

Is this good research?

The research design and implementation are excellent. However, future studies done in different geographic locations by independent researchers are needed to verify the results.

Which polio survivors will benefit?

It is not entirely clear at this time who will benefit the most from this medication. Because the diagnosis of PPS is still imprecise, perhaps the only way to be certain if you would be a good candidate or not for IVIG treatment, is to have your cytokine levels checked. This involves having a spinal tap to obtain a sample of CSF and access to a lab that performs these tests on a regular basis. It is important to keep in mind that an average muscle strength increase of 2.3% in the IVIG group may translate into more significant gains in one's ability to function.

What are the side effects?

IVIG is given intravenously, therefore usually in a hospital setting or in a physician's office. A typical course would be an infusion once a day for 3–5 days. The rate of the infusion can affect the side effects which may include fever, headache, nausea, vomiting, fatigue, backache, leg cramps, itching, flushing and elevated blood pressure. (This is not a complete list.) Polio survivors should also be aware that more serious side effects, including renal failure, have occurred rarely over the years.

What does IVIG treatment cost and will my insurance cover it?

Cost may vary depending on the pharmaceutical company. Even the cheapest might cost as much as \$10,000 per course of therapy. Because insurance companies vary in what they cover, check with your individual carrier or Medicare. Unfortunately, there are only two randomized, placebo-controlled, double-blind studies in the literature describing the use of IVIG in individuals with PPS. One, published by researchers in Norway in a Norwegian language medical journal, involved 20 subjects but did demonstrate positive benefits for the treatment group. The other study by the Swedish group was published in June 2006 and discussed briefly above.

Is this enough data to justify coverage by an insurance company in the US? We doubt it, especially as there have been no similar studies published in the US. Despite this, the authors know of two individuals in this country who have been treated with IVIG and obtained reimbursement from their insurance companies. The use of IVIG in people with PPS shows some promise but further research is required to prove its value and determine who will likely have the greatest benefit.

Sidebar:

Is it Ivlg or IVlg
or IVIG or ??

All of these abbreviations are in use today. The National Institutes of Health (NIH) uses IVIG. The brand name used in the Gonzalez study mentioned in this article was Xepol, manufactured by Instituto Grifols, Spain.

About the Authors

Lauro Halstead, MD, is the Director of the Post-Polio Program at the National Rehabilitation Hospital (www.nrhhealthtown.com/healthtown/network/network.aspx) and Professor of Rehabilitation Medicine, Georgetown University Medical Center, Washington, DC. He is the editor of the forthcoming second edition of *Managing Post-Polio: A Guide to Living and Aging Well with Post-Polio Syndrome*.

Julie K. Silver, MD, is the Director of the International Rehabilitation Center for Polio (www.polioclinic.org) at Spaulding Rehabilitation Hospital in Framingham, Massachusetts, and an Assistant Professor at Harvard Medical School. She is the author of *Post-Polio Syndrome: A Guide for Polio Survivors and Their Families*.

“It is not unreasonable in the meantime for polio survivors to share the information about the current studies with their physicians and begin a dialogue about the possible use of IVIG in the future.”