Alberta Health Services

February 16, 2010

Alberta Health Services Statement on Venous Imaging and Venous Angioplasty in Multiple Sclerosis (MS)

Two recent studies by an Italian vascular surgeon, Dr. Paolo Zamboni, describing a potential new approach to treating Multiple Sclerosis (MS), have generated significant interest. The studies by Dr. Zamboni suggest that there *may* be an association between chronic cerebrospinal venous abnormalities and MS. However, this possible association requires confirmation by independent investigators conducting larger, "controlled" research trials. In fact, preliminary results from the University of Buffalo suggest the association is much weaker than that reported by Dr. Zamboni. Funding for further studies is currently being expedited by MS Societies in several countries including Canada.

On the basis of Dr. Zamboni's studies, many MS patients have sought diagnostic imaging services, neurological and vascular surgery consultations, and venous angioplasty.

Synopsis of Dr. Zamboni's Studies

Dr. Zamboni's first study reported the coexistence of MS and venous abnormalities which have been called "chronic cerebrospinal venous insufficiency" or CCSVI.

In his second study, Dr. Zamboni performed venous angioplasty on MS patients with coexistent CCSVI (as defined in his first study). Although the percentage of patients who were symptom-free was reported to have increased after venous angioplasty, the actual annualized relapse rate for the entire group remained unchanged. These findings, which appear somewhat contradictory, are likely explained by a small number of people having more relapses after intervention and / or by differences in the period of observation before and after the procedure. Nonetheless, the relapse outcomes do not clearly support a clinical benefit of venous angioplasty.

Dr. Zamboni also described improved neurological status and reduced inflammatory activity, as detected by Magnetic Resonance Imaging (MRI), in patients with the "Relapsing – Remitting" form of MS. However, this study did not have an untreated comparison ("control") group of patients, and outcomes were not measured according to accepted research standards (below).

Why must there be further research to determine if Dr. Zamboni's results are truly related to venous angioplasty?

Neurological Function

Improvement in the main study measure of neurological function, the "Multiple Sclerosis Functional Composite" (MSFC), is often seen due to "practice effects." Performance on the walking, hand function, and cognitive tasks that make up this scale improves initially because of practice and increasing familiarity with the tasks by the patients being tested. Therefore, in research studies, the scale must be repeated by study participants at least three or four times before a baseline (pre-treatment) assessment is recorded. No such practice trials were undertaken in Dr. Zamboni's study. Thus, improvement may have been due to "practice."

Quality of Life Measurement

Quality of life typically improves after many research-related interventions and it is well recognized that results after interventions cannot be interpreted without a randomly determined "control" group; i.e. a group of similar patients who are tested and followed in the same fashion but who did not receive the intervention being studied.

MRI

As reported by the study authors, the MRI scans in Dr. Zamboni's trials were undertaken at different intervals before and after the intervention, on different MRI scanners, and using different MRI protocols. Therefore, the results of the scans cannot be reliably compared or interpreted.

Relapse Frequency
In other MS treatment trials, relapse frequency decreases even in untreated (control or placebo-treated) patients. The reported increase in the number of people who were relapse-free after treatment in Dr. Zamboni's study is therefore expected. However, without an untreated comparison group, this possible benefit cannot be interpreted as being due to venous angioplasty itself. In addition, the occurrence and number of relapses in Dr. Zamboni's study were determined only by recall of the patients, rather than through assessment by their healthcare providers. Thus, the relapse numbers can only be considered estimates that require confirmation in well designed clinical trials.

Cerebrospinal venous occlusion
Jugular venous occlusions occur in other situations and do not cause MS or brain injury

Preliminary Results from the University of Buffalo

Dr. Zivadinov has reported preliminary results of venous ultrasounds completed on 500 people. In his study CCSVI was found in 56.4% of people with MS and in 22.4% of people without MS. This supports a possible *association* between MS and CCSVI but suggests that CCSVI does not *cause* MS.

Venous Angioplasty – Surgical Intervention

Angioplasty of veins is not a standard intervention for any condition and the risks of venous angioplasty in otherwise healthy people are unknown. Furthermore, venous stenting has led to serious complications, including death, in some MS patients treated for CCSVI in the United States.

Alberta Health Services Position

1. **At this time, it is only a hypothesis that CCSVI contributes to, or causes, Multiple Sclerosis, and that venous angioplasty is clinically beneficial.**
2. **Further, independent and controlled studies are required to prove, discount, or better understand Dr. Zamboni's study results.**
3. **The nature and frequency of the risks on venous angioplasty are not yet fully understood. Without a clear indication that venous angioplasty carries a clinical benefit that outweighs the risks, it cannot yet be supported as standard practice.**
4. **At present, there is no proven indication for venous imaging or venous angioplasty in patients with Multiple Sclerosis. Therefore, unless part of an approved research protocol, these procedures will *not* be provided by AHS to persons with MS.**
5. **If, and when, there is independent scientific validation of Dr Zamboni's results, Alberta Health Services will seek approval from Alberta Health and Wellness, under the province's health technology assessment process (described at http://www.health.alberta.ca/initiatives/AHTDP.html), to introduce the new procedure into practice in Alberta.**

Background: MS in Alberta

Alberta's network of MS clinicians and researchers are world leaders. Proposals to study CCSVI are being submitted to the MS Society of Canada by researchers in both Calgary and Edmonton. Alberta's team of experts will keep AHS, government agencies, MS patients, and the public informed of developments in understanding CCSV, and other new potential therapies, as they evolve.

Patients or members of the public with further questions or concerns may contact Alberta Health Service Patient Concerns at 1-877-753-2170 (for Red Deer and Northern Alberta residents) or 1-877-957-9771 (for Southern Alberta residents).