Liberation therapy for multiple sclerosis: the intersection of science, policy and the public

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It would be difficult to be a Canadian and be unaware of the controversy regarding "liberation therapy" for multiple sclerosis (MS). Dr. Zamboni, an Italian physician, has hypothesized that multiple sclerosis is caused by a newly discovered abnormality of venous drainage from the brain that he has called chronic cerebrospinal venous insufficiency (CCSVI), and that treatment of CCSVI with angioplasty can markedly improve the symptoms of MS(1,2). The intervention has been called the liberation procedure, after the Italian word for freedom. The overwhelming majority of MS researchers dismiss Dr. Zamboni's findings because they fly in the face of what we know about the etiology of MS, and because of the poor scientific quality of Dr. Zamboni's work. His studies of the association between CCSVI and MS have not been consistently replicated, and his trials addressing the effectiveness of angioplasty were not randomized. These are important and valid criticisms.

The public profile of CCSVI in Canada was raised in the fall of 2009 by a relatively uncritical Globe and Mail article and an even more uncritical W5 television programme (3,4). Both focused relatively little on the criticisms of Dr. Zamboni's studies, and portrayed him as a pioneer whose theories were discounted by conventional medicine. Many Canadians with MS, eager for an effective treatment for their miserable disease, have been convinced by Dr. Zamboni's research and the testimonials of patients who have travelled to other countries to receive the procedure. They accuse many in the MS scientific community of being narrow minded, obsessed with irrelevant scientific niceties, and in the clutches of the pharmaceutical industry(5). They demand that the liberation therapy be made available in Canada, or at the very least that a randomized trial of the procedure be started immediately.

Into this perfect storm have marched the Canadian Institutes for Health Research (CIHR) and the Multiple Sclerosis Society of Canada. In September of this year they released a summary of the deliberations of a "Joint Invitational Meeting" of clinical and scientific experts who examined the scientific literature relating CCSVI and MS (6). The experts decided that the evidence linking CCSVI and MS was so unconvincing that it would be inappropriate at this time to perform a clinical trial examining the benefits and risks of angioplasty as a treatment for MS.

At first glance, for those of us who are proponents of evidence-based health care and evidence-informed policy making, what the CIHR and MS Society have done seems sensible. Interpreting the scientific literature is a specialized task – leave that to unbiased experts. The politicians and policy makers can then use the experts' findings to make decisions about whether and how angioplasty should be funded. However, it hasn't been that simple. Concerns have been raised about the membership of the expert panel and how it reviewed the literature, whether science is the only factor that should be considered when deciding whether to conduct a clinical trial, and how the public has been engaged in the interpretation of the panel's findings. No proponents of the liberation procedure participated in the Invitational Meeting, raising questions about potential biases among panel members.

The panel recommended that no clinical trials of CSSVI should be conducted until the association between MS and CCSVI has been firmly established. The rationale for this recommendation is based upon a sensible paradigm – one should not expose patients to the risks of angioplasty, which although rare can be fatal, if there is no rational scientific reason to think that CCSVI causes MS. However, it is possible that the paradigm the panel used to decide that a randomized trial is not warranted at this time was too narrow. A number of Canadians are now spending large amounts of their own money to travel to other countries to undergo the procedure, performed by surgical teams whose quality standards are not always clear. Is it really true, as the panel strongly states, that it is inappropriate to conduct a randomized trial under these circumstances? Wouldn't these patients be better off, and policy makers and the public better informed, if a randomized trial is conducted now? If patients are fully informed about current doubts about the association of CCSVI and MS, the limitations of Zamboni's non-randomized trial of angioplasty, and the side-effects of angioplasty, shouldn't they be given the opportunity of participating in a trial now? Of course, surgeons and interventional radiologists should not participate in the trial if they feel that the current evidence suggests they are likely to do more harm than good to their patients. However, we know of reputable Canadian vascular surgeons who would currently operate on MS patients as part of a randomized trial.

A clinical trial of angioplasty funded by the CIHR or provincial governments would consume public resources, which are clearly limited. Given the controversy, and given the way this issue has galvanized the public, the decision about whether or not to conduct a clinical trial should be informed by the public. There are a number of ways this goal could be implemented. For example, it is possible to included members of the public on review committees such as the one convened by the CIHR and the MS Society. By "members of the public", we do not mean patients with multiple sclerosis, but thoughtful citizens who can consider all points of view, deliberate about them, and make informed recommendations. If half a dozen or so such individuals had participated on the CIHR panel, they might have asked questions about why proponents of the liberation procedure were not members of the panel, and they could have contributed greatly to the discussion about the appropriateness of a clinical trial in the face of poor scientific evidence supporting the CCSVI hypothesis. Even had their involvement not changed the report at all, the very fact that they were on the committee would likely have increased the legitimacy of the report in the eyes of the public (although not everyone).

The public pays for research funded by the CIHR and MS Society, are impacted by the findings, and are more likely to be supportive of research in general if they feel that researchers are more in touch with the community. In the future, members of the public should be more actively involved in such scientifically-based but patient-relevant, and emotionally charged issues.

Disclosures

AL is reimbursed by Novartis for his membership on a Data Monitoring Committee which is monitoring studies conducted in patients with multiple sclerosis of two drugs: fingolomid and a drug that has not yet been licensed. ASS chairs an Advisory Committee for Rx&D and is compensated for this. Both AL and ASS are, or have been, members of CIHR committees and receive funding from the CIHR for their research (none of which is related to multiple sclerosis). No funding for this commentary was required.

Contributions

AL wrote the first draft, and AS and AL revised the manuscript together thereafter. AL is the guarantor of the article.

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