EDITORIAL

Safety, Not Only Efficacy Still to be Proven for Controversial New MS Treatment

Can. J. Neurol. Sci. 2011; 38: 667-668

"Science is facts; just as houses are made of stones, so is science made of facts; but a pile of stones is not a house and a collection of facts is not necessarily science." - Henri Poincaré

Scientific evidence is gathered through observation and repetition. The evidence and the ways of making it are closely scrutinized. One must always remember that the burden of proof is on the person making a contentious claim (i.e., presenters of a paper), in which the presenters argue for their specific findings. In an attempt to avoid the bias inherent to anecdotal data, scientific evidence must be collected through a system, such as the hypothetico-deductive scientific method: induction (formulating a hypothesis based on existing data), deduction (making specific predictions based on the hypothesis), observation (gathering data, driven by the hypothesis) and verification (testing the predictions against further observations to confirm or falsify the initial hypothesis).

While in clinical practice, formulating a benefit/risk hypothesis is an intuitive and implicit process based on expert judgment, the Hippocratic Oath includes the promise "to abstain from doing harm" or that "given an existing problem, it may be better not to do something, or even to do nothing, than to risk causing more harm than good"[1]. Good clinical practice and the best interests of the patient require that physicians use legally available therapies according to their best knowledge and judgement, to base its use on firm scientific evidence, and to maintain records of its use and effects.

The possibility of loss, injury, or other adverse or unwelcome circumstance is known a risk (Oxford English Dictionary). Unsurprisingly, there are no uniform definitions or unvarying concepts for benefit and risk in medical practice, or accurate and precise guidance on the process of their balancing. Most notably, complications or just the uncertainty of realizing a benefit from the use of a pharmaceutical product or medical/surgical procedure are frequently mentioned as a risk. Perhaps one of the most challenging situations is that in which the effects, positive or negative, of a given treatment are mostly unproven or simply unknown. There is a great variance of opinion amongst stakeholders, and in particular people living with multiple sclerosis (MS) and their physicians not always share the same view on the meaning of benefits and risks, and on their weighing[2].

In this issue of CJNS, Burton and colleagues from the University of Calgary raise a very important and timely issue for people living with MS and their physicians[3]. They report on a range of moderate to severe complications associated with endovascular vein dilation procedures and stent placement in internal jugular and azygous veins performed on people with MS who have sought treatment abroad. Local follow-up by the treating physician is not typically provided and complications may go under-reported or misclassified, so the risk/benefit profile of endovascular procedures for presumed venous stenosis in MS patients remains unknown. Interestingly, as Burton et al point out, Zamboni et al[4] reported that no operative or postoperative complications occurred in their trial, however bleeding from vascular access sites happened "occasionally" while the acute post-procedure monitoring time was only four hours. Fatal consequences, albeit rare, have also been reported[5]. A review of 344 endovascular interventions in Poland reported minor complications with virtually no clinical consequences, while there were in fact two thrombosed stents, five hospitalizations including one gastrointestinal hemorrhage, two cases of atrial fibrillation, four cases of stent migration requiring additional stenting, pseudoaneurysm development and surgical intervention to remove an angioplastic balloon[6]. Another review of 495 endovascular procedures in Bulgaria concluded "there were no major adverse events during the hospital stay". However, complications included four groin hematomas, one AV malformation ruptured, six cardiac arrhythmias (1 ventricular tachycardia associated with ST elevation), 2 azygos veins ruptured, 15 vein wall dissections, 8 acute thrombosis, recanalized by selective fibrinolysis, mechanical thrombo-aspiration, and additional balloon angioplasty[7]. Remarkably, some of these events would meet widely accepted international definitions for reportable Serious Adverse Events[8].

Amidst controversy and without independent confirmation or scientific evidence, it has been hypothesized, but not proven, that abnormal venous drainage of the brain is strongly associated to MS, and also that dilation or stenting of the abnormal veins can improve symptoms of MS. Such procedures are not approved for the treatment of MS in Canada, but principles for the management of complications in patients with MS who have had endovascular procedures in other countries are being developed by experts consensus opinion. Can medical decisions be wisely made without supportive data? Can experimental procedures with unknown risk/benefit profiles be systematically offered to patients? Is it justifiable to seek benefits despite the risks involved, and when the benefits should be foregone because of the risks? Can pressure from vulnerable patients with unmet needs and their opportunistic advocates lead science in the absence of convincing scientific evidence? While the debate continues, and science runs its course, Burton et al[3] remind us that these procedures are not without risk, and that follow-up care should focus on identification of potential complications, as it is the duty of the treating physician to identify, investigate, and mitigate such risks while maximizing benefits. As Aldous Huxley famously said "facts do not cease to exist because they are ignored."

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Disclosure

The author or the named institutions have received operating and research funds, or consulting fees from various sources including the MS Society of Canada, the endMS foundation, the Canadian Institute of Health Research, Bayer, Biogen, Genzyme, Novartis, Sanofi-Aventis, EMD Serono and Teva.

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https://doi.org/10.1017/S0317167100118578 Published online by Cambridge University Press