EVIDENCE-BASED GUIDELINES ARE NOT USEFUL IN TREATING EPILEPSY

Torbjörn Tomson
Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

Clinical guidelines are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. Clinical guidelines should be comprehensive and prioritise evidence coming from the best level of scientific evidence, preferably randomized controlled trials (RCT). At first glance, the concept appears attractive, given the multitude of available data with variable quality and the difficulty for any individual practitioner or patient to have an overview of the available evidence and to rate the quality. Guidelines generally follow a rigid and strict step-wise methodology: (1) selecting the topic, (2) formulate the clinical question, (3) find, abstract, analyse and grade the evidence, (4) develop recommendations, and (5) validate and disseminate the recommendations.

An advantage is that evidence is evaluated seemingly objectively and according to pre-set criteria. No doubt there can be benefits from guidelines provided that the methodology is sound, they are interpreted correctly and are put in context. However, although the basic principles are the same, details in methodology can differ between guidelines even when they address the same clinical question. Therefore it is perhaps not surprising that current major guidelines all of which were published in the same period (2003-2006) differ e.g. when it comes to recommending specific antiepileptic drugs (AEDs) for first-line monotherapy (1-4). How useful are evidence-based guidelines when they come to different conclusions on the same topic, and how can that be? One explanation is that they apply different criteria in their rating of the evidence. Top ratings are based on RCTs. However also the RCTs can differ in quality and many aspects are given different weights by different guidelines. As an example one systematic review of RCTs comparing efficacy and effectiveness of AEDs in newly diagnosed epilepsy concluded that there are major weaknesses in the quality of the available evidence (1). Indeed, of 33 eligible RCTs in adults with focal seizures, only 2 were rated as Class I (the highest level in terms of quality of evidence), one was rated Class II and 30 received the lowest rating (Class III). None of the trials in adults with generalized tonic-clonic or other generalized seizure types achieved Class I or II ratings. How helpful are guidelines when they conclude that evidence is lacking? Even when there are enough data to compare levels of evidence between different treatment options, this doesn't quite answer the practitioner's question: Which of the available treatment options would be the best for my patient? Differences in levels of evidence for efficacy are not the same as evidence of differences in efficacy. A further problem with guidelines' methodology is that RCTs are the gold standard. RCTs are generally carried for regulatory purposes, in order to obtain a licence. These are short term, with artificial settings and include highly selected patient groups. Hence it may be difficult to generalize from RCT results to the broader epilepsy population. RCTs focus on efficacy and effectiveness but are not suited to assess all other variables that are relevant for drug selection, e.g. idiosyncratic reactions, chronic toxicity and teratogenicity, comorbidities and much more. An additional problem with guidelines is that they rapidly become outdated.

Finally, while guidelines prioritise group data based on rigid but artificial RCTs, the objective of the prescriber is to tailor the treatment to the needs of the individual patient. In this effort, guidelines are unfortunately of limited value.

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