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EDITORIAL

Guidelines for Status Epilepticus: Are We There Yet?

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Guidelines are a curate's egg. They are to be welcomed for the obvious reason that clinicians need advice, and especially so in emergency settings, and the simple fact that in status epilepticus, for instance, the adoption of a protocol improves outcome. Also, it is important to take a scientific approach to the evaluation of evidence, and guidelines offer this potential. Herein, however, lie their drawbacks. Hard evidence is scarce on the ground in many clinical situations and where strictly evidence-based recommendations only are made in a guideline, the guidelines tend to be bland and self-evident. Conversely, where the guideline strays from the evidence-based path, there is an inevitable adoption of subjective and selective opinion. The therapy of status epilepticus presents a classic example of this problem.

In this issue, 'Guidelines for the evaluation and management of status epilepticus' are published [1]. The authors, who were appointed by the Neurocritical Care Society, recognised the lack of controlled data and have opted for a less stringent approach than is often taken—categorising their recommendations according to the GRADE system [2], rather than the more testing schema usually chosen. This is a good decision allowing the recommendations to be wider than would otherwise be the case. However, there is much that is opinion and whether this article would best be considered a 'consensus statement' is a moot point. All other guidelines in the field of status epilepticus, of which there are a large number, have similar limitations.

A definition of status epilepticus as a seizure prolonged beyond 5 min is a formulation increasingly adopted, in place of the traditional definition requiring 30 min. Whatever the definition, all are agreed that the therapy of status should be 'staged' and this is confirmed in these guidelines. These guidelines rather unnecessarily change the commonly used terminology used in staging, referring to first-stage therapy as 'emergent' (quite what is meant by this term is not clear; if it means urgent—then surely this applies to therapy at all stages) and the second stage as 'Urgent Control Therapy' (therapy at all stages aims at urgent control).

The stage of initial therapy has been the subject of the most definitive investigation. On the basis of a number of major studies almost all authorities agree that parenteral benzodiazepines are the preferred choice. However, which drug should be used, in what dose and by what route of administration are all less certain. Much depends on whether the patient is in hospital or outside and this distinction is not given emphasis in these guidelines. Where out-of-hospital therapy is given (i.e where facilities for resuscitation are not present), non-IV benzodiazepine is recommended. The recent publication of the RAMPART study, a landmark in the field shows how effective IM midazolam is as out-of-hospital therapy can be. There is also no mention of intranasal or buccal use of midazolam which is certainly the treatment of first choice in out-of-hospital settings in Europe, and indeed is supported by large-scale controlled studies. It seems likely that all IV benzodiazepines are equally effective, any differences in the studies due to differences in doses—but the therapeutic effects of lorazepam are longer-lasting and lorazepam has kinetic advantages which give it the edge as in-hospital IV therapy. Another point which certainly would not be agreed by all is the recommendation that after control with benzodiazepines, IV antiepileptics should always be given. There surely are many seizures, lasting 5 min or more and

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terminated with benzodiazepine which do not require further emergency treatment.

The recommendation of second line therapy, where benzodiazepines have failed to control seizures, is for IV phenytoin/fosphenytoin, valproate, phenobarbital, levetiracetam or continuous infusion of midazolam. It must be pointed out that levetiracetam is not licenced as a therapy for 'status epilepticus' and although widely used, the evidence for effectiveness and safety is based only on open studies, and in many countries too valproate is not licenced for status epilepticus. Special caution therefore is advisable in the use of these drugs. It is slightly surprising to find infusions of midazolam mentioned at this stage as midazolam is usually reserved either as a single dose for initial therapy or for refractory status epilepticus.

The refractory stage of status, that when benzodiazepine and IV antiepileptic drugs have failed to control the seizures is a totally 'evidence-free' zone. It is common to refer to the use of anaesthetic drugs at this stage, but here the guidelines recommend 'continuous infusions of antiepileptic drugs'. As the drugs recommended (thiopental/pentobarbital, midazolam, propofol) are the same, the terminology may not matter, but the guidelines also imply that sometimes these drugs can be used without assisted ventilation—this would be a practice surely to be avoided. There is only brief mention of other therapies at this stage such as steroids, IVIg, ketogenic diet, hypothermia, in spite of the fact that these are quite widely used. This is a pity as advice on their value is urgently needed. In passing, it should be noted that the use of steroids is not restricted to autoimmune encephalopathy and Hashimoto disease, nor ketogenic diet to Landau–Kleffner Syndrome as is implied in the table.

Other points are worth noting. Etiology needs emphasis in the treatment of status epilepticus, and successful therapy of an underlying cause is crucial to the outcome of status epilepticus. Non-convulsive status too is given only brief mention, and the division into two categories does not do justice to the wide range of types and the widely differing treatment approaches that are adopted and the different range of antiepileptic drugs. The term subtle status too is used here in a way which some would disagree with. The staging of therapy in non-convulsive forms of status epilepticus is not necessarily appropriate, and it might have been better to exclude non-convulsive forms of status epilepticus entirely from these guidelines.

There is much that is good in these guidelines, and they should be celebrated. However, as will be clear, there are other points which are controversial. If one thing is clear from these guidelines and all the others, it is that the optimal therapy of status epilepticus, especially in the established or refractory stages requires much more study. Our current treatment is based on inadequate evidence, and this is a deficit which, as the authors of these guidelines emphasise, should be urgently addressed.

References

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