seizures experienced a reduction in seizures frequency of at least 50% when topiramate was used as adjunctive treatment.

In monotherapy, topiramate's half-life is approximately 24 hours, but when taken with enzyme-inducing drugs the half-life may be shortened to 12 hours. Topiramate does not alter the kinetics of carbamazepine or valproic acid but may produce a slight elevation of phenytoin level in some patients. Topiramate may reduce the effectiveness of oral contraceptives because of increased metabolism of the hormones.

Side effects of this drug tend to be mild and dose-related, with dizziness, drowsiness, and ataxia being most common. Cognitive problems are seen in some patients and may be more likely to occur with rapid dose escalation. About 1.5% of patients receiving this drug developed kidney stones, the same frequency as with acetazolamide. ■

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Beyond statistics: What is really important in medicine?

Misuse of statistics in the medical literature and unjustified faith in statistical significance have often made physicians disregard their own clinical judgment and experience. To counteract this tendency, clinicians should apply critical reasoning when interpreting the results of trials, and researchers should find better ways of measuring clinical outcomes that are considered "soft" (such as patient symptoms and quality of life), although often of paramount importance.

WHEN IS STATISTICAL SIGNIFICANCE CLINICALLY SIGNIFICANT?

Given a large enough sample size, even a trivial difference can achieve statistical significance. For example, if a hypothetical trial enrolled thousands of patients and found that 1% fewer patients died if they received an experimental treatment, such a difference might well be statistically significant. However, clinicians might question whether the difference was important.

Further, results can be expressed in ways that exaggerate their importance. Of the following statements, which sounds most impressive?

- *Treatment decreased the mortality rate by 38% compared with placebo.*
- *The mortality rates were 5% with treatment and 8% with placebo.*
- *Treatment improved the survival rate by 3% compared with placebo.*

The three statements describe the same data, but a 38% decrease in mortality sounds much more impressive.

For another example, consider three statements about the effect of exposure to an agent on the incidence of a disease:

- *The risk ratio for the disease is increased to 5 in persons exposed to the agent.*
- *The incremental risk of the disease is increased by only 4 per 10000 in persons exposed to the agent.*

• *At least 2500 persons must be exposed to the agent for the disease to appear in one person more than its usual occurrence rate.*

Here again, the statements describe the same data (the incidence of disease is 1 per 10 000 in persons not exposed to the agent, and 5 per 10 000 in exposed persons). But a risk ratio of 5 sounds much scarier.

TRIALS OFTEN ASK THE WRONG QUESTIONS

At a deeper level, "evidence-based medicine" (ie, literature-based medicine) can distort our clinical judgment by being based on clinical trials that include the wrong patients or address the wrong questions. Often, trials exclude most of the types of patients clinicians actually see in practice. In addition, by defining success or failure of treatment in arbitrary ways, trials neglect to address issues that patients and their families might care about more.

To be sure, science is based on hard data: how many people died within a time interval, what were the median results of laboratory tests (performed according to precise protocols). The trouble is that the "hard" measurements may give us objective but irrelevant statistics.

HARD THINKING NEEDED ON SOFT DATA

To assess the true value of treatment, researchers should examine factors that are difficult to count or measure: pain, symptoms, functional capacity, quality of life, satisfaction with care, and effects of illness on the family. Failure to take these factors into account dehumanizes care; we tell the patient how great the treatment is, and not about the agony it may cause.

Although many systems have been invented for measuring quality of life, they lack a unified approach, and many fail to consider the patient's own opinion. In certain situations, clinical researchers can devise their own instruments, but should keep in mind what is important to the patient. A dyspnea scale, for example, could be based on function: can the patient sit up in a chair, walk, walk up stairs, climb a mountain? Similarly, a pain scale could address what activities the pain keeps the patient from doing, such as sleeping, walking, or working. Researchers should plainly state the criteria they used, so that others can verify their findings. ■

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