Epilepsy and nonadherence

Did you take your medicine?

“I think so.” Sound familiar? In this issue of Neurology®, Gollwitzer et al. report that even in Germany, many persons with epilepsy do not take their medications very regularly. So the equivalent call and response, “Hast du deine Medizin?” “Ich denke schon,” must be heard often. Failure to take one’s medication as prescribed is termed nonadherence. The authors assessed demographic and medication-related factors predicting nonadherence using a representative national database of 31,317 adults treated for epilepsy (2010–2013). The disturbing result was that over one third of persons failed to take their prescribed antiepileptic drug (AED) at least 80% of the time. Their adherence measure was the medication possession ratio (MPR), a commonly used metric that is simply actual time between prescription refills divided by time prescribed for refills. Nonadherence to AED regimens is especially ominous since it has been associated with high rates of morbidity and mortality.

Predictors of good adherence were residence in West Germany (possibly a surrogate for socioeconomic status) and learning disability (possibly a surrogate for caregiver-supervised dosing). Age, sex, insurance status, and treatment by neurologists were not predictive. Among drug-related factors, the largest difference was between old AEDs (those available before about 1990) and new AEDs: 55.6% MPR >80% vs 70.0%. Taking one daily dose vs 3 improved adherence from 57.1% to 64.8%. Adherence varied by drug: valproate was taken least reliably (55.1% MPR); levetiracetam was taken most reliably (78.8% MPR). Since this was unrelated to presumed drug efficacy, perhaps side effects were a factor.

Results from this large study corroborate those found in smaller, less generalizable cohorts. Nonadherence is widespread and certain groups are at higher risk. These are useful data, but each of the variations between subgroups in this study is smaller than the magnitude of the overall problem. The reported rate of nonadherence of 35.3% exceeded the subgroup differences, which varied from 1% to 33%, and were mostly less than 15%. This suggests that we are still missing some large factor. Gollwitzer et al. describe which patients are nonadherent, but not why.

So why don’t patients take their medication? Physicians may be disdainful of such patients, but that attitude is not helpful. Surely the problem is not one of simple contrariness. If patients are asked, by far the most common excuse is forgetting—not side effects, not hopelessness, not overconfidence.

Those reasons may be disguised by self-reporting, but maybe we should take patients at their word. In fact, there is evidence from studies of some diseases that intensive educational efforts are of limited value. Memory aids may be more effective. These can take the form of associating doses with daily routines (toothbrushing, morning coffee), filling weekly pill boxes, strengthening associations (intention implementation intervention: having patients write down and repeat their planned routine), and electronic pill bottle recording. Setting timed alarms on smartphones can be helpful. A time-consuming but feasible strategy would be for pharmacies or providers to contact patients when refills are due. Considering the potential cost savings, maybe insurers should do this.

There are limitations to the Gollwitzer et al. study. Others have identified entirely different factors predictive of nonadherence, including age, comorbidities, disparities between doctor and patient beliefs, and membership in certain ethnic groups. Depression was not identified as a factor in this cohort using coded diagnoses, but was significant in another study when a scale designed for measuring depression in epilepsy was used. Germany, with near-universal drug insurance, may not be representative of places with serious financial and educational problems. In general, claims-based studies such as this one benefit from huge numbers, but are limited in granularity, and thus can rarely pinpoint clear cause-and-effect links. And although 80% MPR is often selected as the threshold for good adherence in studies of many diseases, this is arbitrary and may have little to do with the biology of epilepsy or what an individual patient needs for seizure control.

The problem of drug nonadherence is not unique to epilepsy therapy. It hampers treatment of many conditions. After all, we are asking people to take
medications day after day, year after year. How can physicians help? Gentle assessment with nonpejorative questioning is essential. Do not ask, “Do you take your medications every day?” No one does, so acknowledge that, thereby giving permission for a more honest answer to the better question, “How often do you think you miss doses?” Then the critical follow-up: “Do you know what to do when you miss a dose?” This right answer depends upon the pharmacokinetics of a particular drug. Education concerning the serious risks of nonadherence, including death, has its place, but simple suggestions for jogging the memory may be most effective.

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REFERENCES