ARE PATIENT REPORTS ACCURATE?

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The problem of having patients determine their own dosing during clinical trials is widely recognized. If data obtained in clinical trials where patients take medication once or twice a day are known to be inaccurate, it follows that data from patients taking medication intermittently over longer intervals will be even less accurate. Such studies generally rely on the patient recording the date and time they self medicate in a diary.

One area of clinical trials where patient adherence is especially problematic is in studies of medications designed to be taken when patients experience signs or symptoms of disorders such as:

- Chronic pain
- Angina pectoris
- Asthma / COPD
- Environmental allergies
- GERD/dyspepsia
- Gout
- Headache
- Side effects from other medications

Trials in which patients determine their own dosing commonly use blister-packaged medication with a place to record the date and time of dosing beside each blister. The package might be 6in x 9in (23cm x15cm) or larger and does not come with a pen attached. Is it likely that a patient will carry around a large blister package and pen for several months when only the occasional tablet will be required? It is more likely the patient will take one or two tablets out of the package and put them away in a purse or pocket. In one Med-ic®-monitored clinical trial it was found that 40 percent of patients deblistered (took their medications out of the blister package at one time) at least once. The reason was the extra-large package (designed by the sponsor to cut costs). Redesigning the package to pocket size reduced subsequent deblistering to a more typical 3 to 4 percent. Are patients likely to remember to record the date and time they took the tablet?

It should come as no surprise that very little is known about how patients self-administer *prn* (as required) medications, and that at least two such medication categories - opiate analgesics and hypnotic sedatives - are subject to abuse and have high dependence liability. Unfortunately, the methodology for obtaining accurate medication adherence data has fallen behind clinical research methodologies, research ethics, and the ability of pharmaceutical companies to develop new drugs. Adherence data is currently the weakest link in the chain and   information about how such patients administer *prn* medications is extremely limited.

In clinical pharmacy applications, the situation is complicated by the fact that two categories of medication that are widely prescribed (in many cases inappropriately) in this way are also the largest sources of prescription drug abuse and dependence. Hypnotic sedatives, especially benzodiazepines, are often prescribed to be taken *prn* for the management of anxiety or to induce sleep. It is well known that a significant number of such patients abuse benzodiazepines by taking more than is prescribed, taking them more often than prescribed, using them to cope with other uncomfortable psychological states, or combining them with alcohol to augment their effect. Abusers who are genetically predisposed to addiction and/or anxiety disorders are at high risk to progress to benzodiazepine dependence.

Opioids are subject to similar dynamics, especially shortening of the intervals between uses. This can lead quickly to both psychological and physical dependence.

At the abuse stage, before the patient becomes psychologically dependent, the problem can be corrected relatively easily with targeted education guided by non-adherence data. Unfortunately, abusive patterns of *prn*benzodiazepine and opioid use are often difficult to detect until the problem has progressed in severity because adherence data are rarely available. Monitoring the adherence of patients prescribed such medications to be taken on a *prn* basis can reduce the likelihood of progression to dependence by indicating to the prescribing physician or pharmacist early in the process that a problem may be developing. Problematic use patterns can then be addressed using non-adherence data to target those behaviours that need to be changed.

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