Alternate-Day Statin Therapy

May 10, 2013
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Every-other-day dosing, especially of statins with longer half-lives is shown to preserve lipid-lowering benefits.

In a previous article, I discussed adverse drug reactions (ADRs) attributed to statin therapy, specifically myopathies, as well as potential consequences and recommended alternatives. These ADRs are not trivial because they may lead to patient harm in severe cases and/or significant patient nonadherence in most cases. In fact, statins are frequently discontinued as a result of ADRs and for an inability to pay, leaving many statin-eligible patients at increased risk for cardiovascular morbidity and mortality.

There are several alternative dosing strategies that may improve tolerability of these drugs for patients with muscle pain while preserving therapeutic benefits. These same regimens may also help patients who cannot afford statin therapy to obtain treatment.

Results of a recent retrospective study by Zhang and colleagues suggest that patients who discontinue statin therapy because of myopathies and do not have rhabdomyolysis, should be rechallenged with the same or a lower dose of the same statin or with a different statin. In many cases, the study found, patients were able to tolerate the alternate-day regimen and were adherent at 1-year follow-up. For patients who cannot tolerate such a rechallenge, there are other options. Here I will discuss the use of alternate-day statin dosing as an option for patients unable to tolerate daily statin therapy, especially in those who have failed rechallenge with the same or similar statin. (Weekly and twice-weekly dosing have also been investigated but will not be discussed in detail here.)

Statin-related myalgias and hepatotoxicity are dose-related and so reducing systemic drug concentration may lower the incidence of ADRs and potentially increase adherence to the regimen. Every-other-day dosing, especially of the newer statins with longer half-lives (ie, rosuvastatin and atorvastatin), has also been shown to preserve lipid-lowering benefits. Every-other-day dosing has been studied in all statins with the exception of pitavastatin. It should be noted that all of these studies are limited in their external validity because of small sample sizes, and in some cases, their retrospective nature and lack of variability in the included patient population.

Most of studies reviewed demonstrated that when compared with baseline, every-other-day dosing of statins significantly lowered low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), and triglyceride (TG) levels. The size of the decrease has been shown to be similar to that seen in patients receiving daily statin therapy. The parallel is seen most consistently in patients in the alternate-day group who were taking doses double those used in the daily statin group and is most notable in statin-experienced patients. Pravastatin, however, does not appear to be as effective as other statins when used in an alternate-day schedule, nor was it as effective for LDL lowering in statin-experienced patients as decreasing the daily dose by half and maintaining the daily schedule.

Studies have also shown that alternate-day statin dosing can reduce overall drug costs by as much as half. With more statins now available in less costly generic form, this effect may be less important; however, even small decreases in cost may positively affect patient adherence. Even when doses of the alternate-day statin were doubled, cost-saving was retained.

Alternate-day statin therapy has been well tolerated in these trials, with patients experiencing very few ADRs and, overall, fewer ADRs than patients on a daily statin regimen. In particular, alternate-day rosuvastatin or atorvastatin was very well tolerated in a majority of patients who were previously statin-intolerant. Unfortunately, patient adherence was not fully addressed in all of these studies and therefore the full of effect of this dosing regimen on patients previously nonadherent
because of ADRs is unknown.²

While studies have shown that every-other-day dosing of statins can reduce lipid levels to an extent similar to that of daily therapy, it is also important to note that these studies are small and no cardiovascular outcomes have been evaluated. If this dosing regimen is considered in patients proved to be intolerant to daily dosing, it may be advisable to double the daily dose, especially in statin-experienced patients.

References:


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