

E-Diary Compliance In Acute Pain Studies

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Aims

In acute pain studies, subjects are asked to report on symptoms at specific intervals after dosing. e.g. record the time of dosing with study medication, then complete assessments at 15, 30, 45, 60, and 120 minutes post dose. One or more assessments in the series are often primary endpoints. When timed assessments are collected on paper the actual time the assessments were completed is unknown, and completion of the assessment according to the protocol cannot be enforced. Electronic patient reported outcome technologies (ePRO) allow control over the window in which a subject can complete the electronic diary (e-diary), and a time stamp is associated with diary completion. E- diaries assure the investigator of more reliable information: the 120 minute assessment was definitely completed between minute 115 and minute 125. But is there a down side? With a restricted window of time for completing an e-diary in the acute pain model, how compliant will subjects be?

Methods

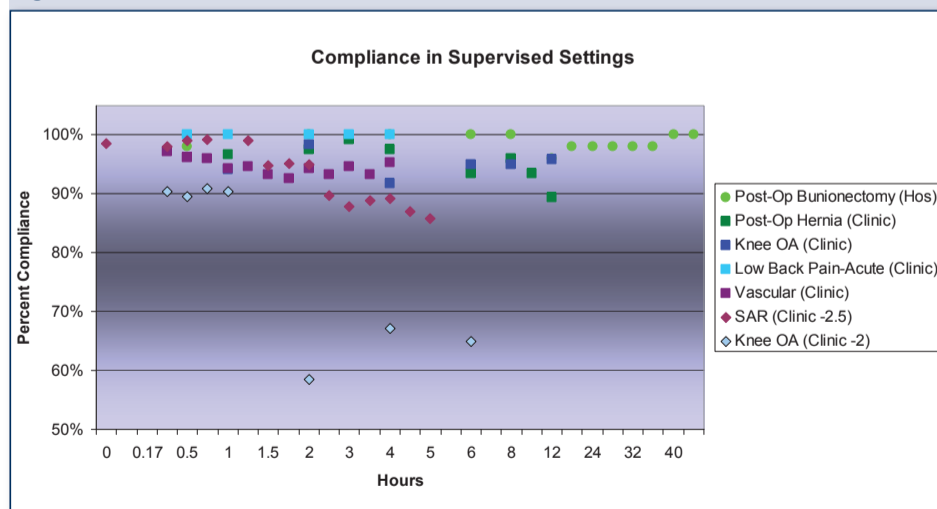
Diary completion was examined in 10 randomized clinical trials using the acute pain model. Indications were surgical pain, migraine, and break through pain. One study of seasonal allergic rhinitis also used the model of timed assessments and was included in the study. Subjects completed diaries at timed intervals after dosing with the study drug. In 2 trials, subjects completed some of the assessments in the clinic or post surgical area allowing comparison of compliance in supervised settings to compliance with e-diaries at home. The frequency of the assessments varied across the trials, allowing some description of factors which may influence compliance. Finally, design features, like a reminder alarm, were correlated with time of diary compliance to understand the usefulness of these features.

Results

Compliance in Supervised Settings

The results of 8 trials that were conducted in a clinic setting are summarized in **Figure 1**. Subjects in all 8 studies completed diaries with supervision for the first 2 hours. Subjects in 6 studies continued to complete diaries in a hospital or clinic setting, but subjects in two studies (Knee OA Clinic -2, and SAR, Clinic -2.5) went home after the first 2 hours and continued to complete diaries after discharge. Subjects who completed all their diaries in the clinic or hospital averaged 94% compliance over the length of the data collection period. Subjects who went home averaged 95% compliance prior to discharge, and 78% compliance at home.

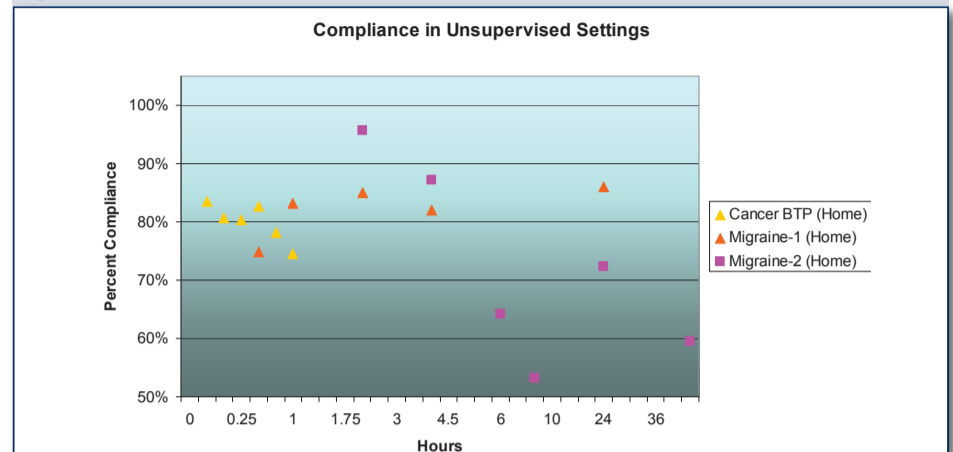
Figure 1.



Compliance in Unsupervised Settings

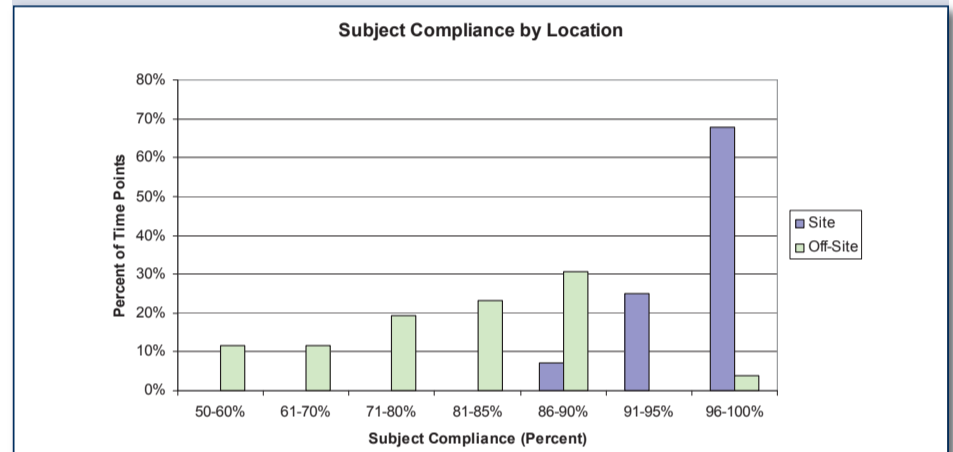
Three studies in our sample completed diaries only at home. (**Figure 2**) Both migraine studies were of subjects with moderate to severe pain. Compliance is typically 80% with this sample, although frequent assessments correspond with decreased compliance. The subjects with break through pain completed diaries at 5, 10, 15, 30, 45 and 60 minutes post dose. Diary compliance was at 80% or better in the first 4 assessments but dropped below 80% for the last 2 assessments. One study of pain related to migraines required frequent assessments, and e-diary compliance was 75% - 85% and increased over time. The other migraine study shows a rapid drop in diary compliance after the first 2 assessments. In this study the diary was extensive, taking an estimated 15 minutes to complete. eDiary compliance in unsupervised settings is varied, and this sample may be influenced more by the demand on the subjects than on the diagnosis.

Figure 2.



Pooling compliance data from all 10 trials, we found is a statistically significant difference between diary compliance at home and diary compliance in supervised settings (**Figure 3**)

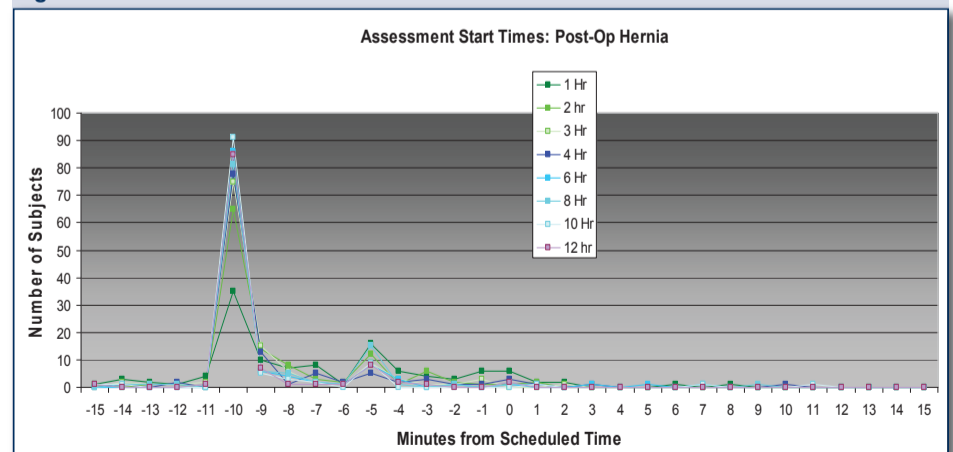
Figure 3.



Alarms: Do They Work?

An inherent part of all these designs was an alarm that sounded to remind subjects that an assessment was due to be completed. The alarm typically sounded a few minutes before the exact time point, at the time point and after the time point. Once the diary was completed, the alarm would no longer sound for that diary. For example, the alarm may sound at 55 minutes, 60 minutes and 65 minutes post-dose for a diary to be completed 60 minutes after the dose. In **Figure 4**, assessments for a study of pain after hernia repair are represented by a line for each assessment. Assessments were completed 8 times post dose: at 1, 2, 3, 4, 6, 8, 10 and 12 hours post dose. Each diary was alarmed 10 minutes and 5 minutes before the exact time the diary was to be completed. In each time point, there is increased activity at the time of the alarms (-10 and -5 minutes), and subjects responded to the first alarm more often as they gained experience with the system.

Figure 4.



Conclusions

Factors that correspond with e-diary compliance are supervision, frequency and overall demand on subjects. Diary alarms are closely associated with the time of diary completion. High levels of diary compliance can be achieved in acute pain studies when the data are collected in supervised and in unsupervised settings. In our sample, overall demand on subjects is inversely correlated with diary compliance in unsupervised settings. However, the number of studies in this category was small so further research is warranted.