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Review

Review of hot flash diaries☆

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ABSTRACT

Currently, there is only 1 published hot flash diary. This diary rates hot flash severity according to 4 categories: mild, moderate, severe, and very severe. The descriptions of these 4 severity categories are located on a separate form from the main data form. For each 24-h period, subjects record the number of hot flashes experienced for each of the 4 severity categories either by recollection or from a separate data source on which hot flashes have been tallied. This diary has been validated but does not conform to the FDA and EMEA guidance for industry. After we observed a high percentage of subjects reporting confusion when using this 4-category diary, we constructed and used a hot flash diary containing 3 severity categories that offered real-time recording of hot flashes, contained all severity definitions on the principle data form and also conformed to the FDA and EMEA guidance for industry. We compare these 2 diaries here and provide a sample of the 3-category diary, which has not been formally validated but is considered valid by the FDA and EMEA in support of drug approval. Either diary is acceptable for use in clinical trials.

Contents

1. Introduction

Hot flash clinical trials typically utilize a paper diary in order to assess subjects' hot flash frequency and severity. The most commonly used diary in academic-initiated hot flash clinical trials assesses 4-categories of hot flash severity (mild, moderate, severe, and very severe), the definitions of which were compiled from subjects' perceptions [1]. For industry-initiated hot flash trials, the Food and Drug Administration (FDA) and the European Medicines Agency (EMEA) guidelines require hot flash severity to be assessed using 3-categories (mild, moderate, and severe), the definitions of which were compiled from an FDA advisory committee [2].

After we completed an initial hot flash clinical trial that used the 4-category diary [3], the Principal Investigator for this study noted that many subjects (approximately 50% from her recollection) reported confusion regarding the hot flash severity definitions included with this diary. This prompted us to develop and use a 3-category diary that conformed to FDA and EMEA guidelines. We report here on our development and use of this 3-category hot flash diary and compare its features directly with those of the 4-category diary.

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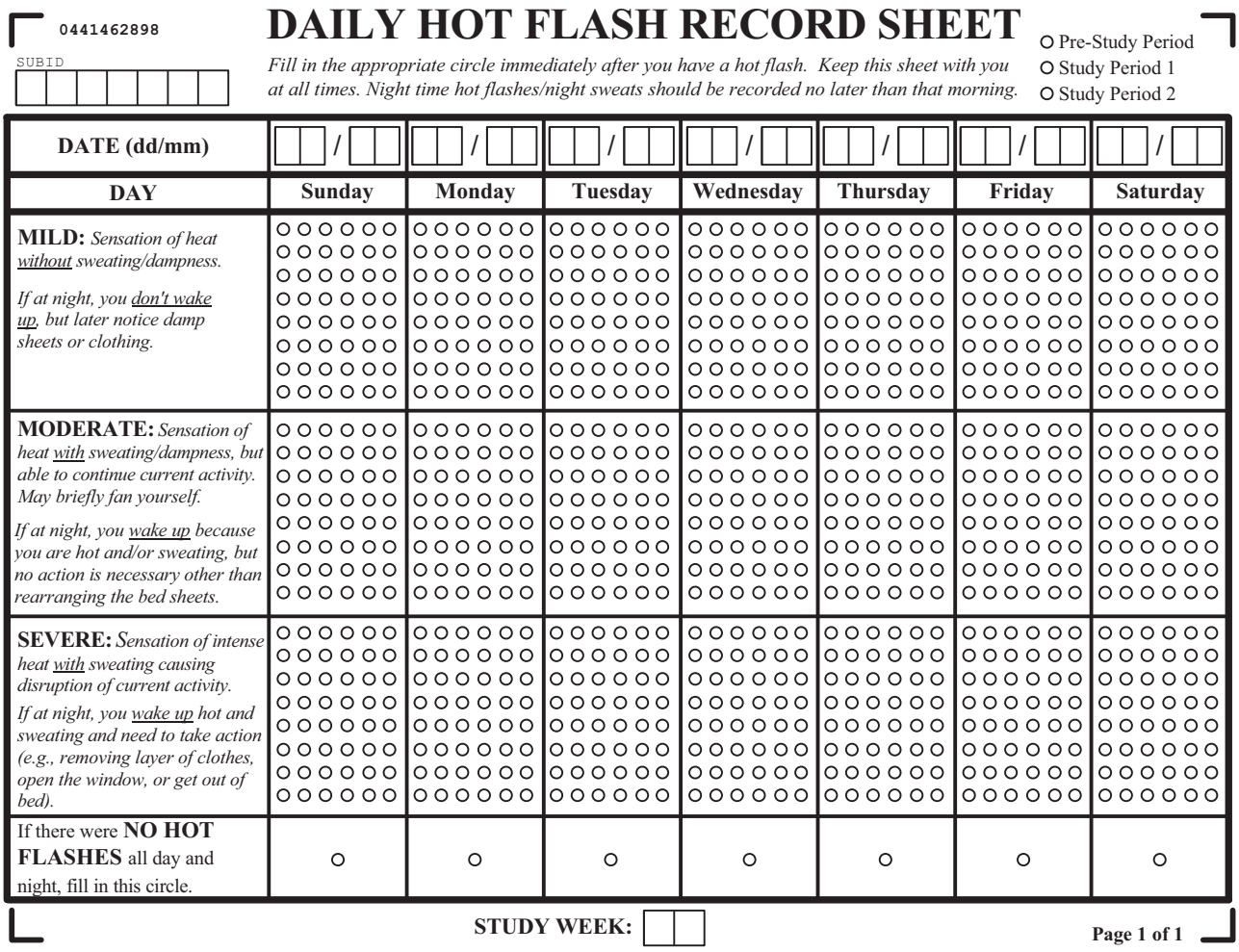
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SUBID

DAILY HOT FLASH RECORD SHEET

Fill in the appropriate circle immediately after you have a hot flash. Keep this sheet with you at all times. Night time hot flashes/night sweats should be recorded no later than that morning.

○ Pre-Study Period
○ Study Period 1
○ Study Period 2

DATE (dd/mm)	/	/	/	/	/	/	/
DAY	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
MILD: *Sensation of heat without sweating/dampness.* *If at night, you don't wake up, but later notice damp sheets or clothing.*							
MODERATE: *Sensation of heat with sweating/dampness, but able to continue current activity. May briefly fan yourself.* *If at night, you wake up because you are hot and/or sweating, but no action is necessary other than rearranging the bed sheets.*							
SEVERE: *Sensation of intense heat with sweating causing disruption of current activity.* *If at night, you wake up hot and sweating and need to take action (e.g., removing layer of clothes, open the window, or get out of bed).*							
If there were **NO HOT FLASHES** all day and night, fill in this circle.	○	○	○	○	○	○	○

STUDY WEEK: ☐☐

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Fig. 1. 3-Category hot flash diary.

2. Methods

In development of the 3-category diary, the definitions for mild, moderate, and severe hot flashes and night sweats were taken from the FDA guidance for industry [2] and the NIH hot flash workshop [4], respectively, and included on each diary (Fig. 1). The EMEA guidelines [5] are identical to the FDA guidelines.

In order to support real-time subject recording of hot flashes, 48 empty circles were placed in each hot flash severity category for each calendar day. Each circle represented the occurrence of a distinct hot flash event when filled in by the subject. Subjects were instructed to keep the diary with their person at all times possible and to record each hot flash immediately after it occurred in order to reduce errors secondary to memory recall. Night sweats were to be recorded no later than that morning upon awakening to start a new day. If no hot flashes occurred for a full 24 h, a separate circle would need to be filled in. It was explained to subjects that this was the only way for the research team to distinguish between the absence of hot flashes and a subject's failure to record hot flashes over a full day.

The diameter and spacing of the circles were chosen to interface with digital scanning software employing optical mark recognition (OMR) to identify positively indicated hot flash episodes by the research participant [6]. In the circumstance where a subject mistakenly recorded a hot flash using an ink pen, the subject was instructed to place an X through the marked circle. During the data validation step of the scanned diaries, such events were easily detected and discounted from the record.

This 3-category diary was then used in 2 randomized controlled trials (RCTs) enrolling 151 subjects in total [7,8]. The 3-category diary (Fig. 1) interfaced well with OMR scanning software. There was never an occasion when all 48 circles were filled in over a single day for any severity category among all of the diaries. Thus, there was no potential for hot flashes not being recorded due to lack of space on the diary. The Principal Investigator for these RCTs did not recall any subjects reporting confusion when using this 3-category diary.

The 4-category diary (Fig. 2) and its hot flash severity definitions (Fig. 3) are provided for direct comparison to the 3-category diary (Fig. 1) and discussed.

3. Discussion

The 3-category diary provided in Fig. 1 is the first published hot flash diary that conforms to the FDA and EMEA guidelines. Besides this important feature, this diary also has several other unique qualities (such as supporting the real-time recording of hot flashes, requiring subjects to confirm that a day is free of hot flashes, including the severity category definitions on the same form as where hot flashes are recorded, and being designed to interface well with OMR scanning software) that should help with the accuracy of subjects' hot flash recording and the accuracy of the digitalized hot flash record. This diary has not been formally validated. Nevertheless,