The acupuncture on hot flashes among menopausal women (ACUFLASH) study: Observational follow up results at six and 12 months.

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Abstract

Objective: The previously published ACUFLASH study compared the effectiveness of individualized acupuncture treatment plus self-care versus self-care alone on hot flashes and health-related quality of life in postmenopausal women. This paper reports on the observational follow-up results at six and 12 months.

Methods: The ACUFLASH study was a pragmatic, multicenter, randomized, controlled trial with two parallel arms, conducted in 2006-2007. The 267 participants were postmenopausal women experiencing, on average, 12.6 hot flashes per 24 hours. The acupuncture group received 10 individualized acupuncture treatments during 12 weeks and advice on self-care, and the control group received advice on self-care only. Hot flash frequency and intensity (0-10 scale) and hours of sleep per night were registered in a diary. Health-related quality of life was assessed by the Women's Health Questionnaire.

Results: From baseline to six months, the mean reduction in hot flash frequency per 24 hours was 5.3 in the acupuncture group and 5.0 in the control group, a non-significant difference of 0.3. At 12 months, the mean reduction in frequency was 6.0 in the acupuncture group and 5.8 in the control group, a non-significant difference of 0.2. Differences in quality of life scores were not statistically significant at six and 12 months.

Conclusion: The statistically significant differences between the study groups found at Week 12 were no longer present at six and 12 months. Acupuncture can contribute to a more rapid reduction of vasomotor symptoms and increase in health-related quality of life in postmenopausal women, but probably has no long-term effects.

Key words: menopause, hot flash, acupuncture

Introduction

When a woman is around 50 years old, the secretion of the ovarian hormones oestrogen and progesterone decreases, and eventually the menstrual bleedings stop. This period in life is called the menopause [1].Vasomotor episodes with hot flashes and night sweating are the most prevalent complaints related to menopause. A hot flash is described as a feeling of intense heat in the face, neck and chest. It lasts, on average, four minutes, ranging from a few seconds up to 10 minutes or more. About two-thirds of all women experience hot flashes, and 10-20 percent of them find the flashes very distressing [2]. Other symptoms related to the menopause are disturbed sleep, anxiety and depression, reduced memory and concentration, urinary incontinence, and sexual problems. However, the distinction between symptoms related specifically to the menopause and symptoms related to ageing in general, and other physical and psychosocial factors, may be difficult [1]. Studies show that menopausal status is more consistently related to vasomotor symptoms than physical and psychological symptoms [3].
Reports on the duration of vasomotor symptoms vary considerably. Clinical guidelines report duration from six months to two years for most women [4 5]. In 1990, Kronenberg reported that vasomotor symptoms resolve in 85%-90% of all women within four to five years [6]. A recent longitudinal study from Australia found that the mean (SD) duration of bothersome menopausal symptoms for women who completed 13 years of follow-up and who never used hormone therapy (HT) was estimated to be 5.2 (3.8) years. If women who used HT were included, the mean (SD) duration was 5.5 (4.0) years [7].
Hormone therapy with oestrogen is considered the most effective treatment for vasomotor symptoms [8]. However, recent research shows that long-term use of oestrogen increases the risk of serious adverse effects [9 10], and women and their health care providers are looking for alternatives.
The ACUFLASH study was a pragmatic, multicenter, randomized, controlled trial with two parallel arms, conducted in 2006-2007 [11]. The objective of the study was to assess the effectiveness of a policy of use of traditional Chinese medicine (TCM) acupuncture plus self-care on hot flash frequency and intensity in postmenopausal women, compared with a policy of use of self-care alone. The effects on sleep and health-related quality of life were also assessed. Participants were defined as responders if they experienced a 50% or greater reduction in hot flash frequency.
The main findings of the ACUFLASH study was that ‘use of acupuncture in addition to self care can contribute to a clinically relevant reduction of hot flashes and increased health-

related quality of life among postmenopausal women', based on the results reported at the end of the intervention period at Week 12 [11]. The objective of this paper is to report on the results of the ACUFLASH observational study from 12 weeks to 12 months after study start. We also report on a secondary sub-group analysis to assess the effects of participant's expectations at baseline, and the effects of acupuncture use, dietary supplements, and change of living habits from 12 weeks to 12 months on change in post-menopausal vasomotor symptoms.

Methods

Details of the methods are published elsewhere [11]. The study was a multicenter (Oslo, Bergen and Tromsø), pragmatic, randomized, controlled trial with two parallel arms. The study was approved by the Norwegian Data Inspectorate, the Norwegian Biobank Registry, and the Regional Committee for Medical Research Ethics.

Participants

Participants were postmenopausal women experiencing, on average, seven or more hot flashes per 24 hours during seven consecutive days, recruited through newspaper advertisements and media coverage. Written informed consent was obtained, and the participants were stratified by center and thereafter, were block randomised to additional acupuncture or no additional acupuncture. A total of 267 **ethnic Norwegian** women were included in the study. Mean age at inclusion was 53.8 (*SD* = 4.4) years, and mean age at menopause was 48.9 (*SD* = 3.7) years. For further sample characteristics, see Table 1.

Intervention

All study-participants received a one-page leaflet with information about self-care strategies to relieve menopausal symptoms, and they were free to use any of these. The information included advice about sufficient sleep and rest, reduction of physical and psychological stress, regular exercise, healthy food, limited tobacco smoking, and limited alcohol intake. The acupuncture group received 10 individualized TCM acupuncture treatment sessions during 12 weeks and advice on self-care, while the control group received advice on self-care only. The acupuncturists were asked to use diagnostic methods according to the principles of TCM and diagnose TCM syndromes associated with the menopausal symptoms. After the initial diagnosis, each participant was treated with points selected according to the syndrome

diagnosis. Frequency and severity (0-10 scale) of hot flashes and hours of sleep per night were registered in a diary.

Practitioners of TCM acupuncture

All 10 acupuncturists who participated in the study had at least 2500 hours of training in TCM acupuncture, and all had a minimum of three years of clinical practice. Seven acupuncturists had previous training as physiotherapists and two as nurses. The participants received treatment in their private clinics.

Statistical analysis.

SPSS was used for all statistical analyses. Differences in change between groups were evaluated with two-sample t-tests and ANOVA, and Chi-square tests were used for categorical variables. Two-sided $p < 0.05$ was considered statistically significant. Missing data on hot flash frequency and intensity, or sleep at six and 12 months, were substituted with the mean value of the entries in the diary if at least 3 days' data had been recorded. If less than 3 days' data were recorded, the data were considered missing.

Outcomes

Primary endpoint was change in mean hot flash frequency per 24 hours from the qualifying period to the 12th week after randomization, recorded in diaries. Participants also scored the mean daily hot flash intensity on a visual analog scale of 0-10, where 0 represents no bother at all and 10 represents the worst possible intensity of flashes, and recorded hours of sleep per night. Registrations of hot flash frequency, intensity, and hours of sleep per night were performed for two weeks at baseline, and for one week at Weeks 4, 8, and 12 in the interventional study. In the observational study, identical recordings were performed at six and 12 months after study start. Baseline values were calculated using data from the last seven days of the two-week qualifying period.

Secondary endpoint was health-related quality of life, measured by the Women's Health Questionnaire (WHQ) [12 13]. Assessment of health-related quality of life was performed at baseline and at Week 12, and in the observational study, at six and 12 months after study start. When scoring the WHQ, an average score between 0 and 1 is calculated within each of the seven domains. Zero is an indicator of "good health status" and 1 is an indicator of "poor

health status". A clinically significant change within each domain of the WHQ is a difference of approximately 0.10 to 0.20 [14].

At baseline before randomization, all participants were asked this question, "Do you believe that acupuncture treatment can relieve your menopausal symptoms?" The possible answers were "yes," "no," and "do not know," and an option to give written comments.

At Months 6 and 12, all participants were asked about their use of health-care providers, medication, dietary supplements, whether they had changed their living habits (rest and sleep, physical activity, coffee drinking, alcohol intake, and tobacco smoking) and a global question addressing any changes experienced regarding menopausal symptoms (intensity and frequency of hot flashes, quality of sleep, and well-being) during the last three or six months. The participants in the acupuncture group were also asked if they would recommend acupuncture treatment to others, and whether they would want to use acupuncture another time.

Results

Observational study

Study participants

Between February 2006 and March 2007, a total of 535 women contacted the study coordinators, and 267 were included, 134 in the acupuncture group and 133 in the control group. The study groups were well-balanced with respect to background characteristics at baseline (see Table 1). **During the interventional study, altogether, 19 women (7%) dropped out; 16 in the control group and 3 in the acupuncture group. No cross-over's occurred during the interventional study. The dropouts were asked but were not willing to provide hot flash data after the termination of their study participation; hence, an intention to treat analysis could not be performed.** The numbers providing data for each outcome at six and 12 months are given in Tables 2 and 3. At six months, missing values for one day were substituted with the mean of the reported data in five diaries. At 12 months, missing values for one day were substituted with the mean of the reported data in one diary, and for two days in one diary.

Hot flash frequency and intensity

Mean frequency of hot flashes per 24 hours among all participants was 12.6 (range, 4.7–31.0) at baseline. From baseline to six months, the mean reduction in hot flash frequency per 24 hours was 5.3 in the acupuncture group and 5.0 in the control group, a difference of 0.3 (95% CI, -1.6 to 1.1) (Figure 1 and Table 2). At 12 months, the mean reduction in frequency was 6.0 in the acupuncture group and 5.8 in the control group, a difference of 0.2 (95% CI, -1.7 to 1.3).

Mean hot flash intensity at baseline was 6.9 (range, 2.1–10 on the 0–10 scale), among all participants. At six months, mean reduction in hot flash intensity was 2.9 units in the acupuncture group, and 2.6 units in the control group, a difference of 0.3 (95% CI, -1.0 to 0.4). At 12 months, the mean reduction in intensity was 3.4 in both groups (see Table 2).

Baseline mean hours of sleep per night was 6.1 (range, 2.9-8.3) among all participants. At six months, mean hours of sleep increased by 0.37 hours in the acupuncture group and 0.14 hours in the control group, a difference of 0.23 hours (95% CI, -0.01 to 0.48). At 12 months, mean hours of sleep had increased by 0.33 hours in the acupuncture group and 0.10 hours in the control group, a difference of 0.23 hours (95% CI, -0.10 to 0.56).

There were no statistically significant differences between the study centers regarding changes in hot flash frequency and intensity and duration of sleep at 12 weeks, six months and 12 months.

Health-related quality of life

The baseline scores and the changes in scores for the seven domains of the WHQ are shown in Table 3. The differences in WHQ score changes between the groups were not statistically significant at six and 12 months. In the acupuncture group, the scores in the vasomotor symptoms subscale did not change from 12 weeks to six and 12 months, whereas in the control group the scores decreased to the level of the acupuncture group at six and 12 months.

Sub-group analyses

Treatment for menopausal symptoms after the end of the interventional period

At six months, 35 participants in the acupuncture group and 20 participants in the control group had used alternative treatment for menopausal symptoms during the last three months (p=0.07), and at 12 months, 36 participants in the acupuncture group and 23 participants in

the control group had used alternative treatment for menopausal symptoms during the last six months (p=0.14). Of these, a large proportion had used acupuncture treatment (see Table 2). Participants using acupuncture treatment in the period from 12 weeks to 6 months, and in the period from 6 months to twelve months, experienced a larger reduction in hot flash frequency and intensity than the participants not using acupuncture during this period, although the differences were not statistically significant (Table 2).

Seven participants had used hormone treatment (HT) for menopausal symptoms during the period from Week 12 to six months; three in the acupuncture group and four in the control group. Ten participants had used HT for menopausal symptoms during Months 6 to 12, five in the acupuncture group and five in the control group. Excluding HT users from the analyses did not change the results.

The number of participants that had used dietary supplements or changed their living habits during the observational period and the corresponding change in vasomotor symptoms are listed in Table 2.

Responders and expectation

Participants achieving 50% or more reduction in hot flash frequency were regarded as responders. At Week 12, 50% of the participants in the acupuncture group and 16% in the control group had experienced a ≥50% reduction in hot flash frequency (Figure 2). At six months, 48% of the participants in the acupuncture group and 34% in the control group were responders, a statistically significant difference (p=0.02). At 12 months, these percentages were 58% and 42%, respectively, (p=0.03).

In the acupuncture group, 16% of the participants who were responders at 12 weeks were non-responders at six months and 5% of the responders at six months were non-responders at 12 months. The corresponding percentages in the control group were 8% at both six and 12 months.

When asked at baseline if they believed acupuncture treatment would relieve their menopausal vasomotor symptoms, 80 participants in the acupuncture group answered “yes” and 53 answered “do not know,” whereas nobody answered “no” and one was missing. At six months, 41 of the participants within the sub-group with higher expectancies were responders, compared with 19 in the lower-expectancy group (p = 0.08). At 12 months, 47 and 21 participants, respectively, were responders (p=0.11).

In the control group, 68 participants expected that acupuncture would relieve hot flashes, and 61 answered "do not know," four were missing. At six months, 18 participants within the higher-expectancy group and 19 within the lower-expectancy group were responders. At 12 months, 33 participants within the higher-expectancy group and 15 within the lower-expectancy group were responders, a statistically significant difference ($p < 0.01$).

In both study groups, the higher expectation sub-group experienced a larger reduction in hot flash frequency and intensity than the lower expectation sub-group at all points of time. In the acupuncture group, the differences between these sub-groups were statistically significant at six and 12 months regarding frequency and at 12 months regarding intensity (Table 2). In the control group, the differences between these sub-groups were statistically significant at 12 months regarding frequency and intensity.

Changes in climacteric complaints

At six months, 98 participants in the acupuncture group answered "yes" on the global question addressing if they had experienced any changes regarding their climacteric complaints, compared with 69 participants in the control group. This difference was statistically significant ($p = 0.005$). At 12 months, the corresponding numbers were 95 and 83; the difference was not statistically significant.

Discussion

As far as we know, this is the first study that observed the long-term effects of acupuncture treatment for menopausal vasomotor symptoms. Six and 12 months after study start, the statistically significant differences between the study groups that were seen at the end of the intervention period were no longer present. The participants in the control group experienced a continuous decrease in hot flash frequency from baseline to 12 months. The participants in the acupuncture group experienced a corresponding decrease during the 12-weeks intervention period, and subsequently, a steady state to 12 months (Table 2 and Figure 1). The number of responders was still significantly larger in the acupuncture group at six and 12 months. The WHQ scores in the control group had decreased to the level of the acupuncture group at six and 12 months (Table 3), hence, no statistically significant differences between the study groups regarding health-related quality of life were present at these points of time.

A reason for the reduction of vasomotor symptoms might have been the use of HT after Week 12. However, only a small number of participants and similar numbers in each group used HT during the follow up period. Thus, HT use probably had a comparable influence on vasomotor

symptoms in both groups and it had a negligible influence on the general improvements of the vasomotor symptoms.

An equal number in both groups had used other medications and dietary supplements for menopausal symptoms and an equivalent number in both groups had changed their living habits during the observational period. We did not find any statistically significant differences in reduction of hot flash frequency and intensity between the sub-groups.

A sub-group of participants in both study groups used acupuncture treatment in the period from Week 12 to six and 12 months (Table 2). The subgroups using acupuncture treatment after Week 12 experienced a larger reduction in hot flash frequency and intensity and a larger increase in duration of sleep from Week 12 to six and twelve months. Although the observed differences were not statistically significant, the findings support practitioners' observations that follow-up treatments may be desirable after the initial series of treatments for optimal long-term effects.

The participants in the control group did not receive acupuncture treatment during the intervention period. However, participation in clinical studies alone can have therapeutic effects. Factors that may affect the placebo response in clinical studies include the consent process, increased therapeutic attention and surveillance, and increased self-surveillance [15 16]. Hence, these are factors that may have contributed to the clinical effects in both study groups. Other factors contributing to the reduction of symptoms and increase in quality of life may be regression to the mean and spontaneous improvement of the symptoms. Menopausal vasomotor symptoms are self-terminating, and the mean duration of vasomotor symptoms in a study of Australian women was 5.5 years. [7] In the ACUFLASH study, the mean time period from menopause to inclusion in the study was 4.2 years in the acupuncture group and 5.5 years in the control group. A spontaneous reduction in symptoms within both groups had to be expected.

We found a larger, although not statistically significant, proportion of responders among the participants in the acupuncture group assuming that acupuncture treatment would relieve their vasomotor symptoms than among those that "did not know" at six and 12 months. In the control group, we found a significant majority of responders in the higher expectation sub-group at 12 months. Participants with higher expectations experienced a larger reduction in hot flash frequency and intensity than those with lower expectations. In a systematic review on expectancy of therapeutic gain, 15 of 16 studies reported that positive patient expectations were associated with better health outcomes[17]. Other studies of acupuncture have shown that

patient expectations can have a large impact on clinical outcomes [18-20]. Our results support these findings. It is interesting to note that expectations of acupuncture effect also were of importance among participants in the self-care group. It is generally believed that cognitive factors such as expectancies can trigger physiological mechanisms such as the release of endogenous opioids and dopamine and the modulation of endogenous cholecystokininergic systems, but we do not yet know details about this phenomenon [21].

Conclusion

The reduction of postmenopausal vasomotor symptoms and increase in health-related quality of life observed after 10 TCM acupuncture treatments over 12 weeks persisted up to six and 12 months after study start, and the proportion of responders were still larger in the acupuncture group at these points of time. However, in the control group, frequency and intensity of vasomotor symptoms decreased and health-related quality of life increased to the level of the acupuncture group at six and 12 months. Expectancies of a positive effect of acupuncture treatment were associated with a greater reduction of vasomotor symptoms. A policy of use of TCM acupuncture in addition to self-care can contribute to a faster reduction of vasomotor symptoms and increase in health-related quality of life in highly bothered postmenopausal women, but probably has no long term effects.

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Summary sentence:

Acupuncture can contribute to a more rapid reduction of vasomotor symptoms and increase in health-related quality of life in highly bothered postmenopausal women, but probably has no long-term effects.

Table 1. Baseline characteristics of the study participants in the ACUFLASH study [a]

Characteristics	Acupuncture group (n = 134)	Self care group (n= 133)
Age at randomisation – year	53.5 ± 4.4	54.1 ± 3.7
Age at menopause – year	49.3 ± 4.0	48.6 ± 4.9
Self-reported weight – kg	71 ± 12	70 ± 12
Self-reported height – cm	167 ± 6	168 ± 6
Years of education		
≤ 10	60 (44.8)	64 (48.1)
11 – 13	12 (9.0)	13 (9.8)
14 – 17	31 (23.1)	18 (13.5)
> 17	31 (23.1)	36 (27.1)
Missing	0	2 (1.5)
Previous use of hormone treatment (HT)	71 (53.0)	61 (45.9)
Previous use of acupuncture	86 (64.2)	85 (63.9)
Sleep problems affecting work last year		
Yes	63 (47.0)	63 (48.8)
No	70 (52.2)	66 (49.6)
Missing	1 (0.7)	4 (3.0)

[a] Data are either means (SD) or n (%)

Table 2

Table 2. Change in hot flash frequency and intensity at week 12 in the study groups and at 6 and 12 months in the study groups and in selected sub-groups in the ACUFLASH study [a]

	Acupuncture group (n = 134)	Control group (n = 133)	p [b]
Hot flash frequency/24 hours			
Baseline	12.0 (4.3)	13.1 (4.9)	
Difference from baseline at:			
12 weeks (n=131/117)	- 5.8 (4.6)	- 3.7 (3.7)	< 0.001
6 months (n = 124/112)	- 5.3 (4.9)	- 5.0 (5.5)	0.736
Acupuncture use 3-6 Mo (n=32/10)	- 6.0 (4.8)	- 6.2 (9.7)	
No acupuncture use 3-6 Mo	- 5.0 (4.9)	- 4.9 (5.0)	
Higher expectation baseline (n = 75/58)	- 6.0 (4.9)*	- 5.3 (6.7)	
Lower expectation baseline	- 4.0 (4.6)*	- 4.7 (4.1)	
Dietary supplem/medic 3-6 Mo – yes (n = 95/89)	- 4.9 (5.1)	- 5.0 (5.8)	
Dietary supplem/medic 3-6 Mo - no	- 6.3 (4.3)	- 5.4 (4.4)	
Change living habits 3-6 Mo – yes (n = 34/35))	- 5.6 (4.3)	- 5.3 (4.8)	
Change living habits 3-6 Mo – no	- 5.1 (5.1)	- 4.9 (5.9)	
12 months (n = 119/114)	- 6.0 (5.2)	- 5.8 (6.3)	0.810
Acupuncture use 6 -12 Mo (n=29/16)	- 6.7 (4.4)	- 6.1 (6.9)	
No acupuncture use 6 -12 Mo	- 5.8 (5.5)	- 5.7 (6.2)	
Higher expectation baseline (n = 75/59)	- 7.0 (5.2)*	- 7.1 (7.6)*	
Lower expectation baseline	- 4.3 (4.9)*	- 4.3 (3.9)*	
Dietary suppl/medic. 6-12 Mo – yes (n = 95/87)	- 6.2 (5.3)	- 5.5 (6.5)	
Dietary suppl/medic. 6-12 Mo - no	- 5.9 (5.3)	- 7.0 (5.5)	
Change living habits 6 -12 Mo – yes (n = 27/32)	- 5.9 (4.9)	- 5.9 (5.5)	
Change living habits – no	- 6.1 (5.3)	- 5.8 (6.6)	
Hot flash intensity (0-10)			
Baseline	6.7 (2.0)	7.1 (1.7)	
Difference from baseline at:			
12 weeks (n = 111/107)	- 3.2 (2.5)	- 1.9 (2.2)	< 0.001
6 months (n = 107/101)	- 2.9 (2.6)	- 2.6 (2.7)	0.410
Acupuncture use 3-6 Mo (n=25/9)	*-3.3 (2.2)*	*-4.3 (3.5)*	
No acupuncture use 3-6 Mo	*-2.8 (2.7)*	*-2.5 (2.6)*	
Higher expectation baseline (n = 75/59)	*-3.3 (2.4)*	*-3.0 (2.9)*	
Lower expectation baseline	*-2.4 (2.9)*	*-2.2 (2.4)*	
Dietary supplem/medic 3-6 Mo – yes (n = 81/81)	*-2.8 (2.7)*	*-2.6 (2.8)*	
Dietary supplem/medic 3-6 Mo - no	*-3.5 (2.5)*	*-2.8 (2.2)*	
Change living habits 3-6 Mo – yes (n = 34/35))	*-3.0 (2.5)*	*-2.3 (2.6)*	
Change living habits 3-6 Mo – no	*-2.9 (2.7)*	*-2.7 (2.8)*	
12 months (n = 102/102)	- 3.4 (2.9)	- 3.4 (2.8)	0.924
Acupuncture use 6 -12 Mo (n=26/16)	*-3.7 (2.7)*	*-2.9 (2.2)*	
No acupuncture use 6 -12 Mo	*-3.3 (2.9)*	*-3.4 (2.9)*	

Higher expectation baseline (n = 61/53)	*-4.0 (2.8)**	*-4.2 (2.7)**
Lower expectation basline	*-2.6 (2.7)**	*-2.3 (2.6)**
Dietary suppl/medic. 6-12 Mo – yes (n = 79/79)	*-3.3 (2.8)*	*-3.2 (2.8)*
Dietary suppl/medic. 6-12 Mo - no	*-3.7 (3.0)*	*-3.8 (2.7)*
Change living habits 6 -12 Mo – yes (n = 22/29)	*-3.5 (2.2)*	*-3.0 (2.8)*
Change living habits 6 -12 Mo– no	*-3.4 (3.0)*	*-3.5 (2.8)*

[a] Data are means (SD) [b] Results from t-tests, acupuncture group versus control group
* Difference between sub-groups is statistically significant

Table 3. WHQ scores at baseline and mean change in scores at 12 weeks and at 6 and 12 months in the ACUFLASH study [a]

WHQ dimensions	Acupuncture Mean (SD)	Control Mean (SD)	p [b]	Reference values [c] Mean (SD)
Depressed mood, baseline (n=265)	0.19 (0.21)	0.23 (0.22)		0.30 (0.26), n=4484
Mean change from baseline to 12 weeks (n=247)	-0.09 (0.18)	-0.04 (0.24)	0.083	
to 6 months (n=246)	-0.06 (0.19)	-0.04 (0.21)		
to 12 months (n=241)	-0.06 (0.18)	-0.05 (0.24)		
Somatic symptoms, baseline (n=265)	0.48 (0.26)	0.55 (0.24)		0.38 (0.28), n=4468
Mean change from baseline to 12 weeks (n=247)	-0.12 (0.24)	-0.05 (0.21)	0.011	
to 6 months (n=246)	-0.08 (0.22)	-0.09 (0.26)		
to 12 months (n=241)	-0.09 (0.23)	-0.10 (0.24)		
Memory/concentration, baseline (n=265)	0.49 (0.38)	0.54 (0.38)		0.37 (0.37), n=4461
Mean change from baseline to 12 weeks (n=247)	-0.09 (0.29)	-0.03 (0.30)	0.108	
to 6 months (n=246)	-0.03 (0.30)	-0.08 (0.34)		
to 12 months (n=241)	-0.10 (0.35)	-0.11(0.33)		
Vasomotor symptoms, baseline (n=263)	0.98 (0.09)	0.98 (0.10)		0.47 (0.45), n=4429
Mean change from baseline to 12 weeks (n=243)	-0.28 (0.39)	-0.04 (0.20)	<0.001	
to 6 months (n=244)	-0.23 (0.39)	-0.19 (0.37)		
to 12 months (n=239)	-0.29 (0.42)	-0.25 (0.40)		
Anxiety/fears, baseline (n=264)	0.22 (0.26)	0.29 (0.26)		0.30 (0.32), n=4502
Mean change from baseline to 12 weeks (n=246)	-0.09 (0.20)	-0.05 (0.27)	0.101	
to 6 months (n=245)	-0.05 (0.20)	-0.06 (0.26)		
to 12 months (n=240)	-0.07 (0.22)	-0.08 (0.27)		
Sleep problems, baseline (n=265)	0.57 (0.33)	0.61 (0.32)		0.46 (0.37), n=4549
Mean change from baseline to 12 weeks (n=247)	-0.17 (0.36)	-0.04 (0.27)	0.002	
to 6 months (n=246)	-0.11 (0.33)	-0.11 (0.34)		
to 12 months (n=241)	-0.13 (0.34)	-0.13 (0.32)		
Attractiveness, baseline (n=263)	0.35 (0.39)	0.31 (0.39)		0.58 (0.38), n=4193
Mean change from baseline to 12 weeks (n=240)	-0.14 (0.35)	-0.09 (0.34)	0.194	
to 6 months (n=246)	-0.07 (0.35)	-0.01 (0.38)		
to 12 months (n=239)	-0.10 (0.35)	-0.03 (0.37)		

[a] The values of the scores vary between 0 and 1, where 0 is an indicator of "good health status" and 1 is an indicator of "poor health status"
[b] Results from t-tests, acupuncture group versus control group
[c] Reference values are taken from the IQOD WHQ Database, postmenopausal women

Figure 1

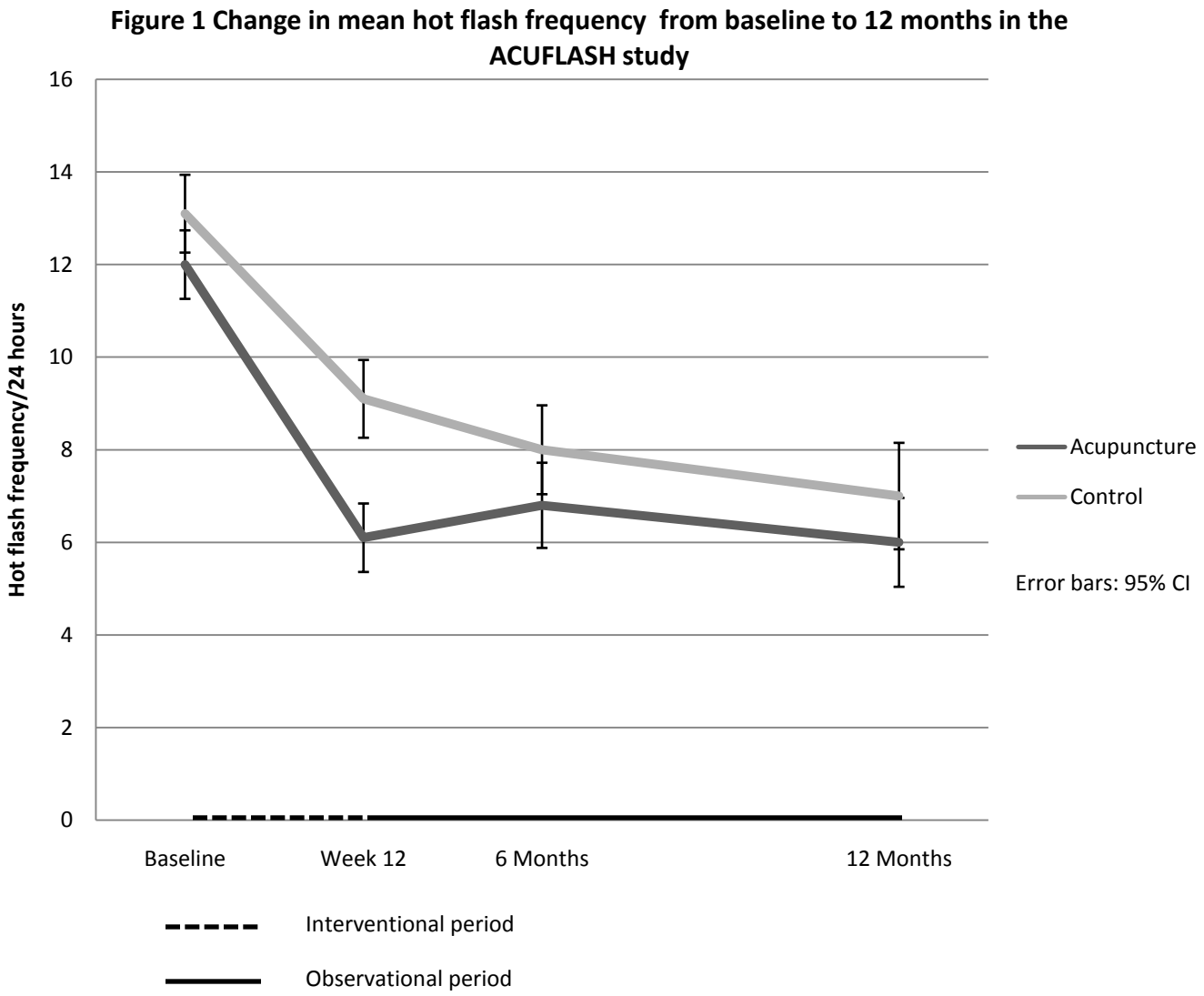
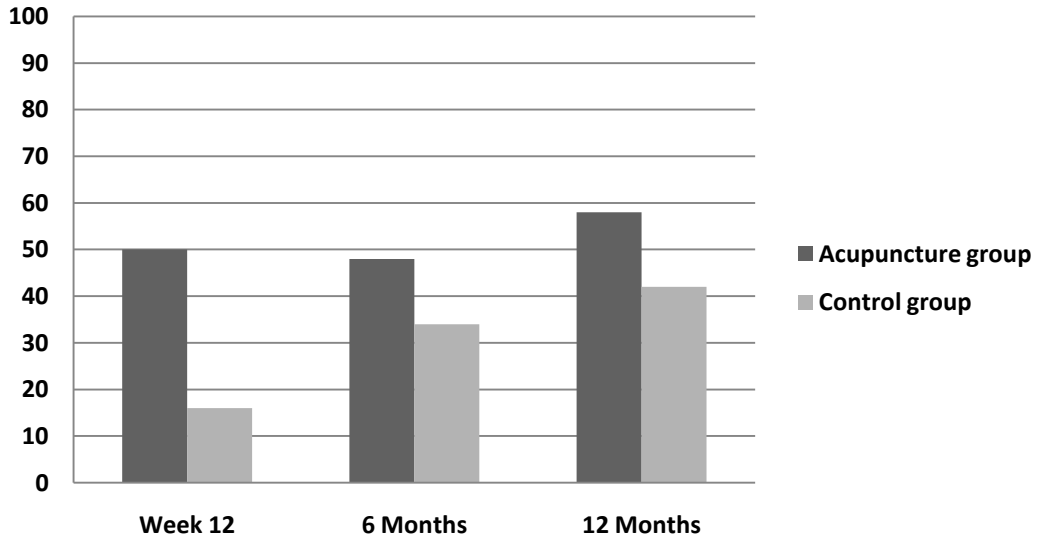


Figure 1 Change in mean hot flash frequency from baseline to 12 months in the ACUFLASH study
Hot flash frequency/24 hours
16
14
12
10
8
6
4
2
0
Baseline
Week 12
6 Months
12 Months
Acupuncture
Control
Error bars: 95% CI
Interventional period
Observational period

Figure 2

Figure 2 Percentage of responders* at different points of time in the ACUFLASH study



*Responder: participant achieving ≥50 % reduction in hot flash frequency