

GYNECOLOGY

Effectiveness of app-based self-acupressure for women with menstrual pain compared to usual care: a randomized pragmatic trial



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BACKGROUND: Primary dysmenorrhea is common among women of reproductive age. Nonsteroidal anti-inflammatory drugs and oral contraceptives are effective treatments, although the failure rate is around 20% to 25%. Therefore additional evidence-based treatments are needed. In recent years, the use of smartphone applications (apps) has increased rapidly and may support individuals in self-management strategies.

OBJECTIVE: We aimed to investigate the effectiveness of app-based self-acupressure in women with menstrual pain.

MATERIALS AND METHODS: A 2-armed, randomized, pragmatic trial was conducted from December 2012 to April 2015 with recruitment until August 2014 in Berlin, Germany, among women aged 18 to 34 years with self-reported cramping pain of 6 or more on a numeric rating scale (NRS) for the worst pain intensity during the previous menstruation. After randomization, women performed either app-based self-acupressure ($n = 111$) or followed usual care only ($n = 110$) for 6 consecutive menstruation cycles. The primary outcome was the mean pain intensity (NRS 0–10) on the days with pain during the third menstruation. Secondary outcomes included worst pain intensity during menstruation, duration of pain, 50% responder rates (reduction of mean pain by at least 50%), medication intake, sick leave days, and body efficacy expectation assessed at the first, second, third, and sixth menstruation cycles.

RESULTS: We included 221 women (mean age, 24.0 years; standard deviation [SD], 3.6 years). The mean pain intensity difference during the third menstruation was statistically significant in favor of acupressure (acupressure: 4.4; 95% confidence interval [CI], 4.0–4.7; usual care 5.0; 95% CI, 4.6–5.3; mean difference -0.6 ; 95% CI, -1.2 to -0.1 ; $P = .026$). At the sixth cycle, the mean difference between the groups

(-1.4 ; 95% CI, -2.0 to -0.8 ; $P < .001$) reached clinical relevance. At the third and sixth menstruation cycles, responder rates were 37% and 58%, respectively, in the acupressure group, in contrast to 23% and 24% in the usual care group. Moreover, the worst pain intensity (group difference -0.6 ; 95% CI, -1.2 to -0.02 ; and -1.4 ; 95% CI, -2.0 to -0.7), the number of days with pain (-0.4 ; 95% CI, -0.9 to -0.01 ; and -1.2 ; 95% CI, -1.6 to -0.7) and the proportion of women with pain medication at the third and sixth menstruation cycles (odds ratio [OR], 0.5; 95% CI, 0.3–0.9] and 0.3 (95% CI, 0.2–0.5) were lower in the acupressure group. At the third cycle, hormonal contraceptive use was more common in the usual care group than in the acupressure group (OR, 0.5; 95% CI, 0.3–0.97) but not statistically significantly different at the sixth cycle (OR, 0.6; 95% CI, 0.3–1.1). The number of sick leave days and body efficacy expectation (self-efficacy scale) did not differ between groups.

On a scale of 0 to 6, mean satisfaction with the intervention at the third cycle was 3.7 (SD 1.3), recommendation of the intervention to others 4.3 (1.5), appropriateness of acupressure for menstrual pain 3.9 (1.4), and application of acupressure for other pain 4.3 (1.5). The intervention was safe, and after the sixth cycle, two-thirds of the women (67.6%) still applied acupressure on all days with pain.

CONCLUSION: Smartphone app–delivered self-acupressure resulted in a reduction of menstrual pain compared to usual care only. Effects were increasing over time, and adherence was good. Future trials should include comparisons with other active treatment options.

Key words: acupressure, dysmenorrhea, mHealth, pain

Primary dysmenorrhea¹ affects up to 81% of women of reproductive age,^{2,3} with approximately 15% experiencing severe pain.² Menstrual pain has a relevant impact on quality of life⁴ and results in a substantial economic loss.^{5,6}

Nonsteroidal anti-inflammatory drugs and oral contraceptives are effective treatments,⁷ although the failure rate is around 20% to 25%^{5,8,9} because of side effects^{7,10} and lack of effectiveness in some cases.^{10–12} Additional evidence-based treatments are needed.¹³ Of women with menstrual pain, 70% are reported to practice self-management.¹⁰ A few studies have investigated the effect of self-acupressure for dysmenorrhea, mostly as an add-on to therapist-administered acupressure.^{13–16} Although results showed a beneficial effect for self-acupressure,^{17–21} the evidence is unclear due to risk of bias (mostly due to performance and attrition bias).¹³

In recent years, the use of smartphone applications (apps)²² has increased rapidly. Mobile and electronic health solutions are already widely used in the general public and are seen as a valuable tool for various health problems^{22–25} and self-management.²⁶ Mobile health (mHealth) solutions might have improved the autonomy and participation of users already,²⁶ for example by facilitating the search for information and health services, as well as by structuring of information and data. Health data is increasingly being collected via smartphones and portable devices (so-called wearables) and can be shared with doctors and other service

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providers. Individual behavior can be positively influenced with the help of behavioral change techniques and used, for example, for smoking cessation or weight control.^{27,28} Only a few mHealth solutions have been investigated in randomized controlled trials to date, and the majority of available apps do not report any health care professional involvement in their development.^{22,25} Nevertheless, a strong increase in mHealth solutions and increasing integration into usual care is expected. App-based self-acupressure might be innovative to support women with menstrual pain; however, its effectiveness in a usual care setting remains unclear.

In this study, we aimed to investigate whether app-based self-acupressure is more effective in reducing pain than usual care for women with menstrual pain.

Materials and Methods

Study design

We performed a 2-armed, randomized, pragmatic trial with a treatment duration and observation time of 6 menstruation cycles per woman. The design of the trial and the development of the smartphone app “AKUD” were shaped by stakeholder engagement (see previous publication²⁹). A statistician not involved in the study used “ranuni” random number generator of the SAS/STAT software version 9.2 (SAS Institute, Cary, NC) to generate the randomization list (1:1 ratio). The list was transferred into a secured database (Microsoft Office Access 2010; Microsoft Corporation, Redmond, WA) and hidden behind the interface so that it was not accessible to anyone involved in the random allocation or treatment. Eligible women were randomized by clicking a button of the database interface. The result could not be changed, which ensured allocation concealment.

This study followed the standards of the Declaration of Helsinki³⁰ and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use good clinical practice (ICH-GCP) guidelines, and were approved by the respective Ethics Committee (Charité—Universitätsmedizin Berlin EA1/027/12). All patients gave oral

and written informed consent. The trial was registered at clinicaltrials.gov (NCT01582724), and the study protocol was published.²⁹

Participants and setting

Women were recruited in Berlin, Germany, from December 2012 to August 2014, using information materials (posters, flyers, and leaflets), the intranet platforms of Charité—Universitätsmedizin Berlin, and students’ e-mail lists. In addition, the study was advertised on 2 Berlin subway lines for 5 months. Telephone interviews were used for participant prescreening. To facilitate recruitment, a financial compensation of 30 EUR was introduced after 8 months.

Participants were eligible for the trial if they fulfilled the following inclusion criteria: female sex; 18 to 25 years of age (criterion broadened to 18–34 years after 8 months of recruitment to facilitate recruitment); having dysmenorrhea, defined as self-reported cramping pain during every menstrual cycle; no prior history of a gynecologic disease that could be a reason for dysmenorrhea; having had menstruation in the last 6 weeks and a menstrual cycle duration between 3 and 6 weeks; moderate or severe pain, defined as a score equal to or greater than 6 on a numeric rating scale (NRS, 0–10) for the worst pain intensity during the last menstruation; and providing written and oral informed consent. Participants had to own a smartphone (iOS or Android) and to agree to enter study data through the app. Patients were not eligible for the trial if they fulfilled any of the following exclusion criteria: already using or planning to use acupressure, acupuncture, shiatsu, or/and tuina massage in the following 8 months; or known pregnancy or planned pregnancy in the following 8 months.

Intervention and control group

Both treatment groups received the app AKUD (Software development: Smart Mobile Factory, Berlin, Germany), which included a visualization of the menstrual cycle, questionnaires, and diaries for both groups.

Acupressure specific features were available only for the acupressure group. These included explanations of the acupressure procedure, drawings, videos, and photos of the acupressure points, as well as a timer to guide the 1-minute acupressure of each point. The acupressure intervention (points, duration, setting) resulted from a written Delphi consensus with international acupuncture experts from China, Germany, and the United States.²⁹ The acupuncture points SP6 (Sanyinjiao), LI4 (Hegu), and LR3 (Taichong) were used on both sides. In the acupressure group, a health care professional introduced the acupressure based on the instruction of the app at the baseline visit (Table 1). The women were reminded by the app every noon to apply acupressure starting 5 days before the anticipated menstruation. Users could switch off the reminders within the app. To keep the intervention standardized, the app received no major updates.

Women in the control group did not receive any study specific intervention. After the sixth menstruation cycle, that is, at the end of the study, the acupressure features were activated within the app and a personal face-to-face introduction to acupressure was offered.

The acupressure and the control groups could continue with usual care during the study, which was defined as all medical and nonmedical treatments with the exception of tuina, shiatsu, and acupuncture because of the use of similar pressure points.

Outcome measurements

The primary outcome measure was the mean pain intensity on the days with pain during the third menstruation on a numerical rating scale (NRS) from 0 (no pain) to 10 (worst possible pain) assessed retrospectively after the third menstruation.³¹ The NRS and the time point were chosen based on the stakeholder process in preparation of the trial²⁹ and previous literature on acupressure on dysmenorrhea.¹⁴ The NRS is easy to apply and well suited for implementation in a smartphone app, and 3 months seemed long enough to

TABLE 1
Instructions for applying acupressure

Carrying out acupressure

Find a comfortable sitting position. The right point will feel more sensitive than the surrounding area, and you may feel a slight soreness. When you have found the point, massage the area with the thumb using medium force (strong enough, but not so strong that you injure yourself) in small circles. Pay attention that you use circular movements and do not rub back and forth. While massaging, you should notice a distinct sensation, for example, a slight soreness, tingling, hypersensitivity, or heaviness.

Method

Concentrate on the points as you are massaging them. Massage the points on both sides consecutively for 1 minute each. Start the timer.

Application

Begin 5 days before you get your period. As a function of the app, you will receive a reminder of when you should begin the acupressure. Before your menstrual period, carry out the acupressure twice a day if possible; on days when this is not possible, carry out the acupressure at least once a day. During your period, on the painful days carry out the acupressure at least twice a day. If you like, you can repeat the acupressure up to 5 times.

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allow the development of an acupressure effect without risking recruitment or study adherence because of a relatively long study duration.

Secondary outcomes were assessed during and after the first, second, third, and sixth menstruation cycle by the app in both groups. These outcomes included worst pain intensity during menstruation (NRS), duration of pain (number of days with pain), responder rates (50% reduction of mean pain intensity on the days with pain compared to the corresponding baseline value), pain medication, sick leave (days of absence from work or school due to menstrual pain), body efficacy expectation,³² adverse events, and suspected adverse reactions (intervention group only). Women in the acupressure group were also asked at the third cycle about satisfaction with the intervention. On the days on which acupressure was recommended, women were asked to record the number of acupressure sessions and the time that they spent for the acupressure.

At baseline, self-reported data were collected by paper and pencil. All other questionnaires and diaries were embedded into the app. Most outcomes were collected by questionnaires within the app at the end of the menstruation; however, data on pain medication and

time spent for acupressure were collected by the app's diary. Women were reminded by app notifications every day at noon during the menstruation to fill in the questions of the diary. In addition, they were reminded at the respective time point to complete the questionnaires at the last day of menstruation at the first, second, third, and sixth menstruations. In the acupressure group, this notification was combined with the reminder to apply acupressure.

Statistical analysis

The study was designed to detect an effect size of 0.5 for the primary outcome measure (menstrual pain), with a power of 90% and a significance level of 5% using a 2-sided *t* test. Based on previous acupuncture studies, we assumed a mean of 5.5 in the control group and 4.0 in the intervention group, with a pooled standard deviation of 3 resulting in a total of 86 participants per group. Taking a potential drop-out rate of about 20% into account, 220 participants (110 per group) were planned. The primary analysis population was the full analysis set (FAS, with available data for the respective analysis) based on the intention-to-treat (ITT) principle of including each woman into the analysis according to her randomization group regardless of her adherence to the assigned intervention.

The primary analysis of the primary endpoint was an analysis of covariance (ANCOVA) with the treatment as a fixed effect, the baseline NRS value as fixed covariate, and a 2-sided significance level of 5%. Secondary outcomes were analyzed similarly, that is, by ANCOVA or by logistic or Poisson regression (depending on the scale and distribution of the data), adjusted for the respective baseline value (if available).

As a sensitivity analysis, multiple imputation techniques were performed using Markov Chain Monte Carlo approximation and fully conditional specification (FCS) methods.³³ The imputation model included all variables for the primary and secondary outcomes and age. Furthermore, in case of relevant differences in baseline variables between the treatment groups, those unbalanced variables were used as covariates for the analysis of the primary outcome. In addition, we evaluated the subgroups of women with hormonal contraceptive use at baseline, women with a migration background, and women with age of 26 years or more versus less than 26 years. Subgroups were evaluated using the interaction term of the respective subgroup with the treatment group in the analysis model.

As further supportive analysis, mixed models for repeated measures (MMRM) were fitted to compare the treatment groups with respect to changes in the primary outcome over time. The model included terms for treatment (acupressure vs control) and time as fixed main effects, an interaction term for treatment by time, the baseline value as covariate, and the subject as a random effect.

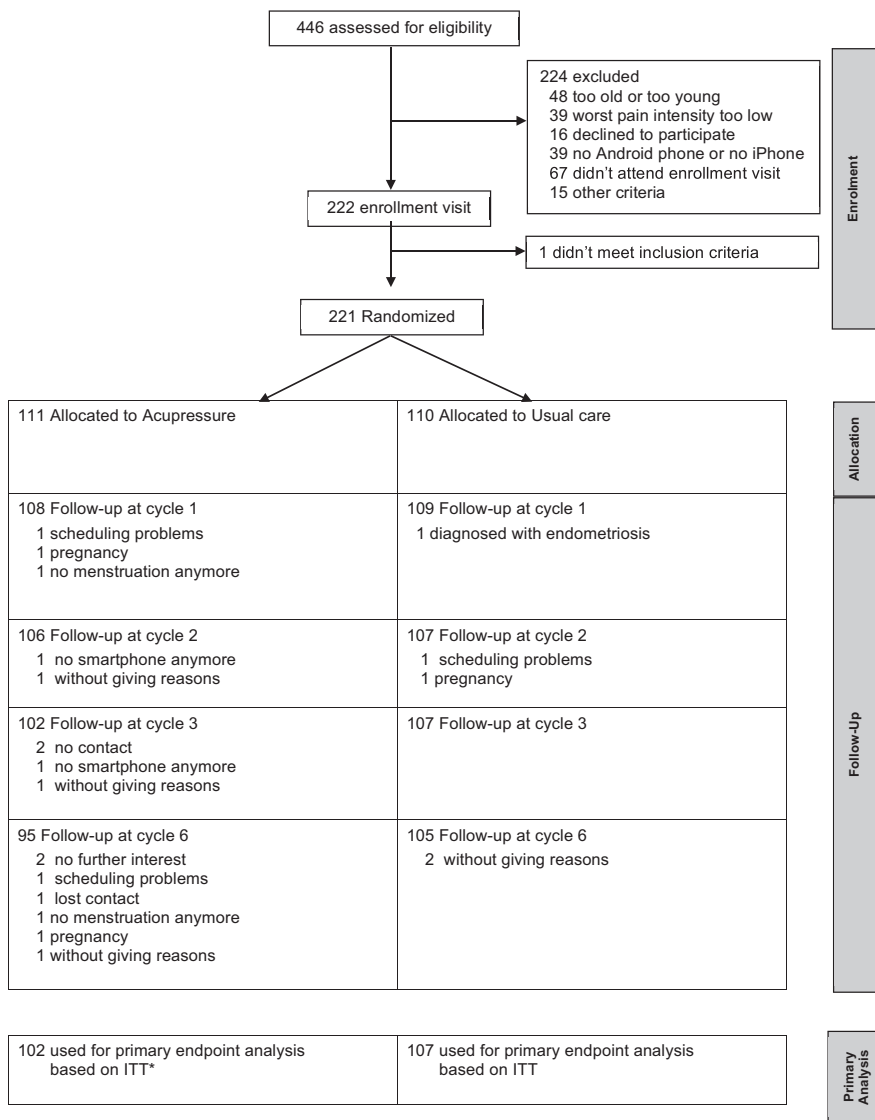
Analysis was done using SPSS 21.0 (SPSS Inc, Chicago, IL) and SAS 9.4 (SAS Institute, Cary, NC).

Results

Participants

The study was conducted between December 2012 and April 2015, with recruitment from December 2012 until August 2014.

Of 446 screened women, 221 were eligible for the study, gave consent, and were randomized either to

FIGURE 1
Trial flow chart.

*ITT = Intention to treat

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self-acupressure (n=111) or to usual care (n=110)(Figure 1).

The women had a mean age of 24.0 years (standard deviation [SD], 3.6 years) and were highly educated, with 89.6% having 12 or more years of school education (Table 2). A total of 37 women (16.7%) had a migration background. At baseline, the mean pain intensity on the days with pain on the NRS was 6.2 (SD, 1.6) and most women (81.0%) had taken medication during their last menstruation. The following group

differences with possible relevance were seen at baseline: fewer women in the usual care group (65.1%) had a partner (acupressure group 78.4%), and more women in the usual care group used oral contraceptives (36.4% vs 23.4%).

Outcomes

Both groups showed a reduction in pain at the third and sixth menstruation cycle. The primary outcome measurement (mean pain intensity on the days of pain during the third cycle after therapy start)

showed a statistically significant difference in favor of the acupressure group (acupressure: 4.4; 95% CI, 4.0–4.7; usual care: 5.0; 95% CI, 4.6–5.3; mean difference, –0.6; 95% CI, –1.2 to –0.1; $P = .026$ (Table 3 and Figure 2). At the sixth menstruation cycle, the mean difference between the groups increased (–1.4; 95% CI, –2.0 to –0.8; $P < .001$) and was considered clinically relevant.³⁴ The effect size (Cohen's *d*) for the mean pain intensity was 0.24 at the third cycle and 0.63 at the sixth cycle. Moreover, the chance to be a responder was higher for women in the acupressure group after the first, the third, and the sixth cycle with odds ratios of 2.3 (95% CI, 1.0–5.2), 2.0 (1.1–3.6), and 4.4 (2.5–7.9), respectively.

At the third and sixth menstruation cycle the worst pain intensity (group difference, –0.6, 95% CI, –1.2 to –0.02, and –1.4, 95% CI, –2.0 to –0.7), the number of days with pain (–0.4; 95% CI, –0.9 to –0.01, and –1.2; 95% CI, –1.6 to –0.7), and the proportion of women with pain medication (odds ratio, 0.5; 95% CI, 0.3–0.9, and 0.3; 95% CI, 0.2–0.5) was lower in the acupressure group. Hormonal contraceptive use was more common in the usual care group than in the acupressure group at the third cycle (odds ratio, 0.5; 95% CI, 0.3–0.97), but not statistically significant different at the sixth cycle (odds ratio, 0.6; 95% CI, 0.3–1.1). The number of sick leave days and body efficacy expectation (self-efficacy scale) did not differ between groups (Table 3).

On a scale from 0 to 6, the mean satisfaction with the intervention at the third cycle was 3.7 (SD, 1.3), recommendation of the intervention to others (4.3; SD, 1.5), appropriateness of acupressure for menstrual pain (3.9; SD, 1.4); and application of acupressure for other pain (4.3; SD, 1.5).

Findings were similar, and no relevant difference between results of primary, sensitivity, and subgroup analyses could be observed. The baseline characteristics of women in both groups who dropped out before the third menstruation cycle did not differ relevantly from those who did not drop out.

Safety data

In the self-acupressure group, 15 women reported having had at least 1 suspected adverse reaction (SAR). Over all cycles, the following SARs were mentioned: bruises (n = 5), deterioration (n = 3), pain in the hand (n = 1), pressure pain (n = 1), shift in menstruation cycle (n = 3), dizziness (n = 1), nausea (n = 1), pain in the legs (n = 1), and tingling in a finger (n = 2). Of those who mentioned a SAR, 10 women experienced a SAR at 1 cycle, 3 women at 2 cycles, and 2 women at 3 cycles. With the exception of 1 woman, all continued to apply self-acupressure. This woman stopped applying self-acupressure at the sixth cycle because of bruises, pressure pain, and tightness in the breast. She had already mentioned pressure pain at the first cycle, which had made it difficult to continue self-acupressure, although she did not report any SAR at the second and third cycles.

Two serious adverse events occurred in each treatment group (self-acupressure: hip surgery, hospitalization due to dizziness; usual care: surgery of the nose, appendix surgery). None was considered related to the trial or the trial intervention.

Adherence and practice time

Overall adherence was good, but declined slightly over time. At the first cycle, 108 (97.3%) of the women stated that they had practiced acupressure on at least 1 day during the menstruation cycle, and at the sixth cycle this number was 92 (82.9%). Fewer women practiced acupressure on all days with pain (first cycle 102 [91.9%]; second cycle 89 [80.1%]; third cycle 91 [82.0%]; and sixth cycle 75 [67.6%]). The mean duration of 1 practice session was similar over all cycles (first cycle: before menstruation, 5.3 minutes (mean; SD, 2.1); during menstruation, 5.4 (SD, 1.7); sixth cycle: before menstruation, 5.4 (SD, 1.5); during menstruation, 5.3 (SD, 1.5) (Table 3). Women spent about 82.5 minutes (95% CI, 73.2–91.7) for acupressure during the first cycle, and 78.8 minutes (95% CI, 68.8–88.8), 76.8 minutes (67.3–86.4), and 68.7 minutes

TABLE 2
Baseline demographic and clinical characteristics of trial groups

Characteristic	Acupressure (n = 111), mean ± SD/n (%)	Usual care (n = 110), mean ± SD/n (%)
Age (y)	24.4 ± 3.3	23.7 ± 3.9
BMI (kg/m ²)	22.0 ± 3.8	21.8 ± 3.1
≥12 Years of school	98 (88.3)	100 (90.9)
Size of household		
Single-person	17 (15.3)	20 (18.2)
Multi-person	94 (84.7)	90 (81.8)
Partnership	87 (78.4)	71 (65.1)
Migrant background [40] ^a	20 (18.0)	17 (15.5)
Smartphone operating system		
iOS	45 (40.5)	38 (34.5)
Android	65 (58.6)	71 (64.5)
Duration of cycle (days)	28.7 ± 2.7	28.7 ± 2.5
Duration of menstruation (days)	5.4 ± 1.4	5.2 ± 1.0
Concomitant diseases	13 (11.7)	5 (4.5)
Complaints/pain ^b		
Abdominal cramps	98 (88.3)	88 (80.0)
Pain in lower abdomen	97 (87.4)	83 (75.5)
Back Pain	70 (63.1)	72 (65.5)
Headache	39 (35.1)	33 (30.0)
Nausea/vomiting	35 (31.5)	30 (27.3)
Other	31 (27.9)	40 (36.4)
Hormonal contraceptive	26 (23.4)	40 (36.4)
Sick leave days	0.6 ± 0.7	0.5 ± 0.7
Sport/Therapy against pain	41 (36.9)	48 (43.6)
Jogging	16 (14.4)	16 (14.5)
Fitness/gymnastics	13 (11.7)	20 (18.2)
Yoga	12 (10.8)	12 (10.9)
Meditation/relaxation	9 (8.1)	7 (6.4)
Dancing	2 (1.8)	8 (7.3)
Other	16 (14.4)	26 (23.6)
Mean pain (NRS 0–10) ^c	6.3 ± 1.6	6.1 ± 1.6
Worst pain (NRS 0–10) ^c	7.6 ± 1.1	7.5 ± 1.1
Number of days with pain	2.6 ± 1.2	2.7 ± 1.1
Pain medication intake	89 (80.2)	90 (81.8)
Body efficacy expectation	2.8 ± 0.5	2.8 ± 0.5

BMI, body mass index; NRS, numeric rating scale.

^a Determination by assessment of primary language, place of birth, and place of mother's and father's birth; ^b Multiple answers possible; ^c Higher values indicate worst possible pain.

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TABLE 3

Primary and secondary outcomes at first, second, third, and sixth menstruation cycle (adjusted for baseline value)

	Acupressure, mean (95% CI)/ proportion (95% CI)	Usual care, mean (95% CI)/ proportion (95% CI)	Differences acupressure vs usual care, mean (95% CI)/OR (95% CI)	P
Mean pain intensity during third menstruation cycle (NRS) [primary outcome]	4.4 (4.0–4.7)	5.0 (4.6–5.3)	–0.6 (–1.2 to –0.1)	.026
Mean pain intensity (NRS)				
First cycle	4.9 (4.5–5.2)	5.2 (4.9–5.5)	–0.3 (–0.8 to 0.1)	.171
Second cycle	4.6 (4.2–5.0)	4.9 (4.5–5.3)	–0.4 (–0.9 to 0.2)	.197
Sixth cycle	3.5 (3.1–4.0)	5.0 (4.5–5.4)	–1.4 (–2.0 to –0.8)	<.001
Worst pain intensity				
First cycle	6.2 (5.9–6.6)	6.4 (6.1–6.8)	–0.2 (–0.7 to 0.3)	.383
Second cycle	5.8 (5.4–6.2)	6.1 (5.7–6.5)	–0.3 (–0.8 to 0.3)	.374
Third cycle	5.6 (5.2–6.0)	6.2 (5.8–6.6)	–0.6 (–1.2 to –0.02)	.043
Sixth cycle	4.9 (4.4–5.4)	6.3 (5.8–6.8)	–1.4 (–2.0 to –0.7)	<.001
Number of days with pain				
First cycle	2.7 (2.4–3.0)	2.8 (2.4–3.1)	–0.05 (–0.5 to 0.4)	.828
Second cycle	2.3 (2.0–2.6)	3.1 (2.8–3.4)	–0.8 (–1.2 to –0.3)	.001
Third cycle	2.3 (2.0–2.6)	2.7 (2.4–3.0)	–0.4 (–0.9 to –0.01)	.047
Sixth cycle	1.9 (1.6–2.2)	3.1 (2.7–3.4)	–1.2 (–1.6 to –0.7)	<.001
Women with pain medication intake ^{a,b}				
First cycle	0.5 (0.4–0.6)	0.7 (0.6–0.8)	0.4 (0.2–0.8)	.004
Second cycle	0.6 (0.5–0.7)	0.7 (0.6–0.8)	0.6 (0.3–0.1)	.051
Third cycle	0.6 (0.5–0.7)	0.7 (0.6–0.8)	0.5 (0.3–0.9)	.029
Sixth cycle	0.5 (0.4–0.6)	0.8 (0.7–0.8)	0.3 (0.2–0.5)	<.001
Number of days with pain medication				
First cycle	1.2 (1.0–1.4)	1.4 (1.2–1.6)	–0.2 (–0.6 to 0.1)	.110
Second cycle	1.1 (0.9–1.3)	1.5 (1.3–1.8)	–0.4 (–0.7 to –0.1)	.015
Third cycle	1.1 (0.9–1.3)	1.5 (1.2–1.7)	–0.4 (–0.7 to –0.1)	.021
Sixth cycle	0.9 (0.7–1.0)	1.6 (1.4–1.9)	–0.7 (–1.1 to –0.4)	<.001
Women with hormonal contraceptives ^{a,b}				
First cycle	0.3 (0.2–0.3)	0.3 (0.3–0.4)	0.6 (0.3–1.1)	.116
Second cycle	0.2 (0.2–0.3)	0.3 (0.3–0.4)	0.6 (0.3–1.1)	.088
Third cycle	0.2 (0.2–0.3)	0.4 (0.3–0.5)	0.5 (0.3–0.97)	.040
Sixth cycle	0.2 (0.2–0.3)	0.4 (0.3–0.5)	0.6 (0.3–1.1)	.084
General change in menstrual pain ^c				
Third cycle	2.1 (1.9–2.2)	2.8 (2.6–2.9)	–	<.001
Sixth cycle	1.8 (1.7–2.0)	2.8 (2.7–3.0)	–	<.001
Responder rate ^{a,b,d}				
First cycle	0.2 (0.1–0.3)	0.1 (0.05–0.2)	2.3 (1.0–5.2)	.040

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(continued)

TABLE 3

Primary and secondary outcomes at first, second, third, and sixth menstruation cycle (adjusted for baseline value)

(continued)

	Acupressure, mean (95% CI)/proportion (95% CI)	Usual care, mean (95% CI)/proportion (95% CI)	Differences acupressure vs usual care, mean (95% CI)/OR (95% CI)	P
Second cycle	0.3 (0.2–0.4)	0.2 (0.2–0.3)	1.6 (0.9–3.0)	.109
Third cycle	0.4 (0.3–0.5)	0.2 (0.2–0.3)	2.0 (1.1–3.6)	.023
Sixth cycle	0.6 (0.5–0.7)	0.2 (0.2–0.3)	4.4 (2.5–7.9)	<.001
Sick leave days				
First cycle	0.3 (0.2–0.4)	0.3 (0.2–0.4)	0.04 (–0.1 to 0.2)	.497
Second cycle	0.2 (0.1–0.3)	0.2 (0.1–0.3)	0.01 (–0.1 to 0.1)	.854
Third cycle	0.3 (0.2–0.4)	0.3 (0.2–0.4)	–0.01 (–0.1 to 0.1)	.870
Sixth cycle	0.2 (0.1–0.3)	0.2 (0.2–0.3)	–0.1 (–0.2 to 0.04)	.250
Body efficacy expectation				
First cycle	2.8 (2.8–2.9)	2.9 (2.8–2.9)	–0.02 (–0.1 to 0.1)	.629
Second cycle	2.8 (2.7–2.9)	2.8 (2.7–2.9)	0.02 (–0.1 to 0.1)	.698
Third cycle	2.9 (2.8–3.0)	2.8 (2.7–2.9)	0.1 (–0.04 to 0.2)	.195
Sixth cycle	2.9 (2.8–3.0)	2.8 (2.7–2.9)	0.05 (–0.1 to 0.2)	.424

CI, confidence interval; NRS, numeric rating scale; OR, odds ratio.

^a Proportion (95% CI); ^b Odds ratio; ^c Scale of 1–5 (menstrual pain had: 1 = improved significantly, 2 = improved slightly, 3 = no change, 4 = worsened slightly, 5 = worsened significantly); ^d Responder rate = mean pain reduced by at least 50%.

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(57.7–79.7) for the second, third, and sixth cycle, respectively.

Comment

Participating women with menstrual pain who applied self-acupressure supported by a smartphone app experienced statistically significant different pain relief after 3 menstruation cycles in comparison to women who received usual care. After 6 menstruation cycles, in the intervention group pain further decreased, resulting in a clinically relevant difference between groups.

The strengths of this trial include the randomized study design, the large number of participants for an interventional randomized trial on acupressure, and the high adherence and follow-up rates. By using a smartphone app for the delivery of the intervention and for data collection, the trial used a novel study approach. Moreover, we consider the results to be transferrable to standard care settings, because this pragmatic trial resulted from an extensive stakeholder engagement process.²⁹

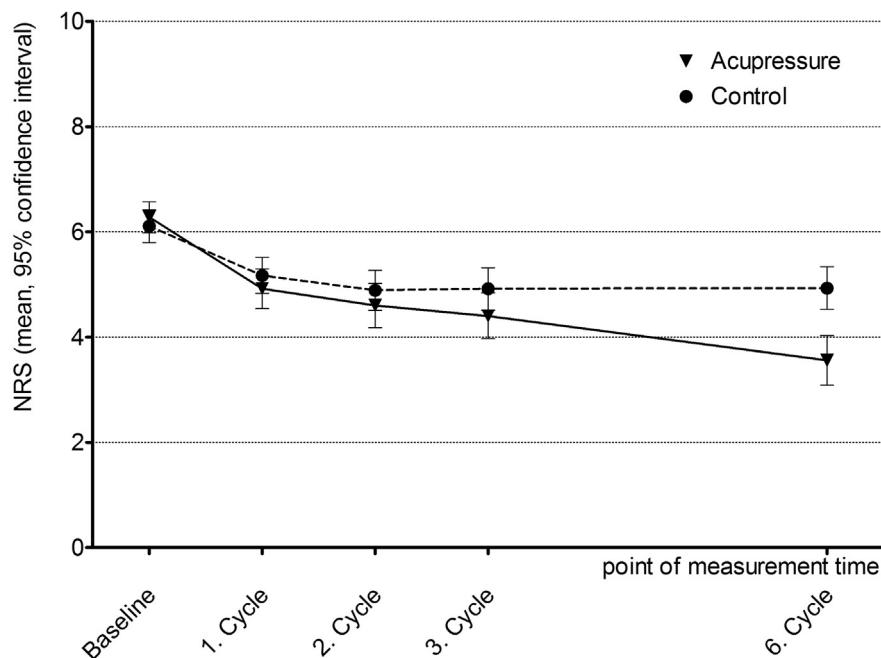
However, the results of our trial might have been influenced by the selection of our sample. Although we aimed at a diverse sample by advertising on public transportation, almost 90% percent of participants had at least 12 years of school education, which is more than the average population. Furthermore, one-third of the screened women failed eligibility criteria. These aspects do affect the generalizability of the results. Our outcome assessment was reduced to a minimum²⁹ because stakeholders suggested that the outcome assessment should be short and patient-relevant, and that data should be collected by an app.

The whole trial duration, including the preparation for the app, took 4.5 years, which is a long time for a trial on consumer technology.³⁵ In contrast, a longer follow-up time might have provided more insight about long-term use. Based on the development of the primary outcome over time, a longer follow-up might have shown an even higher effect. However, due to the relatively short follow-up time, it is also possible that we have

overestimated the impact of treatment. Recruitment for this trial was difficult, and a longer study duration might have had a further inhibiting impact on recruitment. For future studies, ways to accelerate recruitment are needed. To keep the intervention standardized, our app received no major updates. However, an advanced development of the app for future studies is already in progress.

Considering the large number of available mobile Health (mHealth) apps for smartphones, only a few have been evaluated in an randomized controlled trial setting.^{27,28,36,37} To our knowledge, no randomized controlled trial evaluating a smartphone app using acupressure or targeting menstrual pain had previously been conducted. According to the updated Cochrane Review “Acupuncture for dysmenorrhoea,” which included acupressure trials, evidence is insufficient to demonstrate whether or not acupuncture or acupressure is effective in treating primary dysmenorrhea because of the methodological limitations of the

FIGURE 2
Mean pain intensity (unadjusted mean, 95% confidence interval).



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included studies.¹³ Although our rigorously designed trial might support the evidence base in favor of acupressure, it might also be associated with a high risk of bias because of the lack of blinding.³⁸ However, we think that our trial can contribute valuable data to its effectiveness in usual care.

Our results might have practical implications, because they could add a self-care option to the recommended treatment options of oral contraceptives and nonsteroidal anti-inflammatory drugs, which are effective but have limitations because of associated side effects^{7,10} and failure rates.⁵ Moreover, self-care treatments such as rest, medication, heating pads, tea, exercise, and herbs are already used by women with menstrual pain.¹⁰ Therefore an additional nondrug and self-care treatment option might fit well into women's perceptions of how to treat menstrual pain³⁹ and might further support self-empowerment of affected women.

In our trial, for self-care acupressure, the effect increased over time, showing clinical relevance on the pain scale after

6 cycles³⁴ and a responder rate of about 60%. A similar increase was also shown by a trial from Chen et al.¹⁹ However, most trials on acupressure and dysmenorrhea have had shorter follow-ups.¹⁴ The findings that the adherence was still high after 3 months and that the effect increased over time are encouraging. Regarding the high prevalence of menstrual pain, a treatment option with a modest-to-moderate effect and a good safety profile might have a considerable public health impact and should be further evaluated. It would be interesting to compare app-based self-acupressure with other active treatment in future research.

To conclude, self-acupressure supported and evaluated by a smartphone app was able to achieve a sustainable reduction in pain and medication in comparison to usual care. This self-care intervention showed a high retention rate and was safe. We suggest that future trials should provide long-term data and compare acupressure with other active treatments options among a more diverse target group. ■

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