INSTITUT PROF. KURSCHEID

Studies from practice for practice

Study Report

Reduction of menstrual pain by the medical device "Beurer EM 50"- an observational study (ReduSchmerz)

DRKS No. DRKS00024411

Version 1.4 (US)

Date 04.07.2022

Sponsor: Prof. Dr. med. Thomas Kurscheid

Evaluation: Bonn-Rhein-Sieg University of Applied Sciences

1 Summary

This is a multicenter observational study to evaluate the efficacy of the medical device "Beurer EM 50" (EM 50) in reducing period pain associated with primary dysmenorrhea (PD). The study was conducted in the period from 09.06.2021 - 21.01.2022 by the Institute Prof. Kurscheid in Bonner Straße 205, Cologne as sponsor.
The study screened 60 patients from which 59 were enrollend and included in the evaluation. Patients were asked to use the EM 50 for at least the first three days of the cycle and to document its use. Patients' intraindividual pain was assessed using Visual Analog Scale (VAS) and McGill score both before and after the use of the device. Furthermore, the result was compared with both scoring systems of the patients' previous cycle.
The patient cohort includes a broad age range from 18 to 47 years with a mean age of 29 years. Thus, the efficacy of the medical device could be investigated in all relevant age groups. Overall, a sustained improvement in perceived pain was observed regardless of age and pain score, indicating the effectiveness of the device in reducing individual pain perception.
Over the entire cycle, temporary side effects were reported in 3% of the applications. The majority of adverse events occurred on the first day of use and were caused by improper handling of the device. None of the adverse events were severe or persistent. Thus, the benefit of the device appears to be safe, especially after individual adjustment of the intensity level.

In summary, the majority of patients (>80%) reported pain relief from EM 50 during the first three days of the cycle. In parallel, a reduction in the use of analgesics was observed in 41% of patients. This result is confirmed by the high willingness to recommend the device by 96% (57 of 59 patients) and the fact that 98% (58 of 59 patients) stated that they would continue to use the device. Thus, it can be concluded that the medical device is useful for a broad user group.

2 Synopsis

Table 1 Tabular synopsis of the ReduSchmerz study.

Title	**Reduction of menstrual pain by the medical device "Beurer EM 50"- an observational study (ReduSchmerz)**
Short title	Observational study of "Beurer EM 50"
Studies Objective	Efficacy of "Beurer EM 50" in reducing menstrual pain associated with primary dysmenorrhea
Testing	Beurer EM 50
Indication	Primary dysmenorrhea
Study design	Application in one cycle: Observation of the pain profile with application of the Beurer EM 50
Duration of study	Approximately 35 days per patient / Total study duration 3 months
Inclusion criteria	• Willingness to participate in the study • Older than 18 years • Premenopausal • Primary dysmenorrhea in the lower abdomen (VAS ≥ 25) • Menstruation in the last 6 weeks with a cycle length of 3 to 6 weeks
Exclusion criteria	• Known pregnancy • Abdominal surgery in the 6 months prior to study inclusion • Injuries or exanthema of the abdominal wall • Known allergies to the plastic of the Beurer EM 50 • Wearing non-removable piercings • Wearing an intrauterine device (IUD)
Number of cases	59
Primary endpoint	• Average intraindividual improvement in pain score after use of the device on days 1, 2, and 3
Secondary endpoints	• Average intraindividual improvement of pain score after using the device (average values of all measurements) • Average intraindividual improvement in pain score during use of the device on days 1, 2, and 3 • Average intraindividual improvement in pain score during use of the device (averages of all measurements) • Duration of pain relief after using the device • Improvement in pain (VAS, McGill) compared to previous cycle (pre-cycle) • Limitation of daily life compared to pre-cycle • Use of painkillers compared to pre-cycle

	• Frequency of AEs • Frequency of use of the Beurer EM 50 • Handling device (one time day 5)

3 Summary

4 Abbreviations

Table 2. Overview of abbreviations.

AE	Adverse Event
CRF	Case Report Form
EM 50	Beurer EM 50
ITT	Intend-to-treat
IUD	Intrauterine device
NSAID	Non-steroidal anti-inflammatory drugs
PD	Primary dysmenorrhea
PMS	Premenstrual syndrome
PP	Per-protocol
QoL	Quality of Life
SAE	Serious Adverse Event
TENS	Transcutaneous electrical nerve stimulation
VAS	Visual analog scale

5 Ethics Submission

On March 18, 2021, the protocol version 1.0, the patient information and consent form version 1.0, as well as the questionnaires for the patients were submitted to the Ethics Committee of the Medical Association North Rhine in Cologne for review according to §15 of the professional code of conduct prior to the performance of biomedical research on humans and were rejected for the time being on May 12, 2021.
After the adjustment of the commission proposals, protocol version 1.1 entitled "Reduction of menstrual pain by the medical device "Beurer EM 50 Menstrual Relax "- an observational study (ReduSchmerz)" and the consent form version 1.0 received a positive vote on 09.06.2021.
The study physician ensured that this study was conducted according to key priniciples regulations and guidelines for good clinical practice (ICH- E6 (GCP), and according to the principles and the Declaration of Helsinki.
In order to increase the visibility of the study, an information flyer on the acquisition of participants was submitted to the Ethics Committee of the North Rhine Medical Association in

Düsseldorf for evaluation after the start of the study on September 1, 2021. The ethics committee gave this a positive vote on 17.09.2021.

6 Structure of the study implementation

The study was conducted in the period from 09.06.2021 - 21.01.2022 by the Institute Prof. Kurscheid in Bonner Straße 205, Cologne as sponsor. Responsible investigator and investigators were specialist in general medicine Prof. Dr. Thomas Kurscheid, specialist in gynecology and obstetrics Dr. Verena Ackemann and specialist in gynecology and obstetrics Edith Kern.

Table 3. Overview of responsibilities and contact details.

Sponsor	Prof. Dr. Thomas Kurscheid
Student financing	Beurer company (product manufacturer)
Study Centers	**Practice Dr. Thomas Kurscheid** Bonner Straße 205, 50968 Cologne Tel. 0221 800432-0 E-mail praxis@dr-kurscheid.de **Practice Dr. Verena Ackemann** Bonner Straße 205, 50968 Cologne Tel. 0221 37 97 380 E-mail mail@frauenmed.de **Practice Edith Kern** Schildergasse 84, 50667 Cologne Tel. 0221 27263794 E-mail info@gyn-kern.de
Study documentation	Prof. Dr. Sieber Bonn-Rhein-Sieg University of Applied Sciences
Data evaluation	Prof. Dr. Sieber Bonn-Rhein-Sieg University of Applied Sciences

7 Introduction

This study investigated the efficacy of "Beurer EM 50" (EM 50) in reducing primary dysmenorrhea (PD) associated menstrual pain.

PD describes cramping pain in the lower abdomen that occurs just before or during menstruation and is not a consequence of any other identifiable pelvic pathology[1] . Frequency data vary from 20% to 90% in women of childbearing age. This makes PD one of the most commonly complained of gynecological conditions in young women[2] . Pain typically lasts 8-72 hours, is most severe on the first or second day of menstruation, and may radiate to the back and thighs. Associated symptoms include fatigue, diarrhea, vomiting, and nausea. Affected individuals report a general impairment due to the pain in their professional and personal lives and an overall reduced quality of life (QoL)[3] .

Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently used for pain therapy. These are associated with side effects such as dizziness or digestive problems[4] . For this reason, many women look for alternative therapies to reduce their menstrual cramps. The application of heat to the abdominal area has also been shown to reduce pain[5] .

Another proven, pharmaceutical therapy option is transcutaneous electrical nerve stimulation (TENS)[6] . Here, the pain-relieving effect is achieved primarily by two factors. Firstly, by suppressing the transmission of pain into the nerve fibers, and secondly, by increasing the release of endorphins produced naturally in the body, which reduce the sensation of pain through their action in the central nervous system[7] .

The EM 50 product combines TENS technology with a heat function and is CE marked for self-application for menstrual cramps. It has 15 TENS intensity levels and a heat program of 43°C, which is separately adjustable.

The special feature of this product is that it has a battery function (6 x à20 min) and can therefore be worn anywhere and at any time. Furthermore, the device is particularly cuddly to the body shape due to its soft and flexible structure and thus very discreet. Thus, the Beurer EM 50 can also be used on the go.

The aim of this study is to record the effectiveness of "Beurer EM 50" by means of an observational study.

The patients included were asked to use the Beurer EM 50 during their next menstruation and to document their pain sensation as well as the application itself by means of questionnaires. The main focus was on pain reduction during the first three days of the menstrual cycle.

8 Study Goal

The study objective is to investigate the efficacy of the medical device "Beurer EM 50" in reducing primary dysmenorrhea - associated menstrual pain. The endpoints investigated are described in 9.2 und 9.2 listed.

9 Study plan

Interested potential patients were fully informed about the study by an attending study physician. Written informed consent was obtained prior to performing any study-specific procedures.

The screening questionnaire was used to verify that the patient met all inclusion criteria and had no exclusion criteria. Eligible patients were allowed to participate in the study and were assigned a study number. They received the "Beurer EM 50" device and the questionnaires (CRF) for self-completion.

QoL during the last menstrual period (reference cycle) was recorded in **questionnaire I.**

The EM 50 was applied by the patient herself according to the instructions for use.

For PD-related complaints, pain before and after EM 50 use was recorded in **questionnaire II** (menstruation day 1, 2, 3, 4). Medications taken for pain relief were also documented.

The handling of the device was recorded once on day 5 at the end of menstruation in **questionnaire III.** In addition, QoL was assessed during menstruation with use of the EM 50 (Figure 1).

Schedule of activities: Exemplified by a cycle with a 5-day menstrual period. Subjects are included in the study during cycle 0 (reference cycle). Applications of the EM 50 take place during menstruation of the following cycle 1.

Cycle 0 (Reference Cycle)						Cycle 1				
1	2	3	4	5	X	1	2	3	4	5
Menstruation Cycle 0						**Menstruation Cycle 1**				
					Screening Visit	**Use of EM 50 by patient**				
					Informed Concent	**Questionnaire** II (QoL, Pain) (day 1,2,3,4)				
						Questionnaire III (QoL, Pain, Usability) (day 5)				
					Inclusion/Exclusion Criteria					
					Screening questionnaire	**Questionnaire II**				
					Questionnaire I	**Questionnaire III**				

Figure 1. *Schedule of activities: Exemplified by a cycle with a 5-day menstrual period. Subjects are included in the study during cycle 0. Application of EM 50 takes place during menstruatial cycle 1.*

9.1 Design

This is a non-interventional, unblinded, multicenter, single-arm study.

The study duration was approximately 35 days per patient. The study was considered terminated when the data of the last patient were recorded.

9.2 Study population

The study population is composed of 59 women with menstrual symptoms.

Patients who were eligible for the study were given detailed information about the study by the study physician.

9.3 Primary endpoint

The primary endpoint of the study was the mean intraindividual improvement in pain score (VAS, McGill) after use of the device on cycle days 1, 2, and 3.

9.4 Secondary endpoints

Secondary endpoints were:

- Average intraindividual improvement in pain score after using the device (averages of all measurements)
- Duration of pain relief after using the device
- Improvement in pain (VAS, McGill) compared to pre-cycle
- Limitation of daily life compared to pre-cycle
- Use of painkillers compared to pre-cycle
- Frequency of AEs
- Frequency of use of the EM 50
- Handling device (one time day 5)

9.5 Inclusion criteria

Study participants were only allowed to participate in the study if the following criteria were met:

- Willingness to participate in the study
- older than 18 years
- Premenopausal
- Primary dysmenorrhea in the lower abdomen (VAS $\geq$ 25)
- Menstruation in the last 6 weeks with a cycle length of 3 to 6 weeks

9.6 Exclusion criteria

Study participants were excluded from study participation as soon as one or more of the following applied to them:

- Known pregnancy
- Abdominal surgery in the 6 months prior to study inclusion
- Injuries or exanthema of the abdominal wall
- Known allergies to the plastic of the EM 50
- Wearing non-removable piercings
- Wearing an intrauterine device (IUD)

9.7 Statistical analysis plan

9.7.1 Case Estimation

The number of study participants was derived from the following estimates:

An average reduction in pain of approximately 15 points on the VAS pain score with a standard deviation of 20 points on the VAS has been reported in the literature with comparable medical devices. We do not consider a decrease of 5 or less on the VAS pain score to be relevant in such a study. The significance level is set at 0.05, and the power is set at 90%. For the case number calculation using one-sided paired t-test, the number of patients is 44.
With a screening failure rate of 20% and a drop out rate of 15%, the number of patients to be included in the study is 58.

9.7.2 Details of the statistical analysis

The study was analyzed using Microsoft Excel according to the statistical analysis plan.

9.7.3 Data basis of the analysis

Statistical analysis was performed after study end. The end of the study is defined as the receipt of the last questionnaire (questionnaire III) from the last patient. Data from the questionnaires and case reports were included in the analysis.

9.7.4 Data sets for analysis

For the analysis, 3 different data sets were defined: *Intend-to-treat* (ITT), *per-protocol* (PP), and application dataset.
The *Intend-to-treat dataset* contains all patients who were included in the study (signed informed consent).
The *per-protocol* set includes all patients who were included in the study (signed informed consent), used the TENS device according to protocol, and completed all questionnaires or submitted them to the appropriate study center.
Data from patients will be excluded from the per-protocol analysis set if at least one of the following criteria is met:

- Inclusion or exclusion criteria violated
- Desire of the patient to leave the study
- Not all questionnaires were submitted by the patient

The used data set includes data from patients who wore the device for at least 10 minutes and had a VAS of at least 35 before device use.

9.7.5 Endpoints

The endpoints as described in 9.3 und 9.4 are taken into account in the statistical evaluation.

9.7.6 Software

Data is collected and analyzed using Microsoft Excel (Microsoft Redmond, WA, USA).

9.7.7 Data Handling

Missing values were not replaced, the corresponding value was set to "missing". Outliers were not expected due to the questionnaire structure.

9.7.8 Primary Endpoint Analysis

In accordance with the primary study objective, the following hypotheses were formulated:

H_0 : VAS score before using the device is equal to the VAS score after using the device is tested against the alternative hypothesis H_1

H_1 : VAS score before using the device is greater than VAS score after using the device.

For the analysis of the primary endpoint, the change in intraindividual pain before use of the device was compared with pain after use of the device on cycle days 1, 2, and 3 using a t-test (the analysis assumed that the distribution of the pain score was normally distributed).
The significance level was set at $\alpha = 0.05$, and the power was set at 90%. For descriptive statistics, mean and standard deviation, 95% confidence interval, minimum and maximum were calculated.
Measurements after 10 min of application with VAS score before application >45 are used for the analysis. If an insufficient number of observations is obtained, the application data set is used.

9.7.9 Secondary Endpoint Analysis

The *intend-to-treat* (ITT), *per-protocol* (PP), and application data sets were used for analysis of secondary endpoints.
Pain score analyses were performed for both the VAS and McGill.

- Average intraindividual difference in pain before and after use of the device compared across all time points using a t-test
- Average intraindividual difference in pain before using the device compared with pain after using the device on cycle day 1 using t-test
- Average intraindividual difference in pain before using the device compared with pain after using the device on cycle day 2 by t test
- Average intraindividual difference in pain before using the device compared with pain after using the device on cycle day 3 by t test
- Average intraindividual difference in pain before using the device compared with pain after using the device on cycle day 4 by t test
- Average intraindividual difference in pain before using the device compared with pain after using the device on cycle day 5 by t test

- Average intraindividual difference of pain before using the device with pain after using the device on cycle days 1, 2, and 3 by t-test
- Difference in improvement in pain compared to previous cycle (pre-cycle) using paired, one-tailed t-test
- Difference in limitation of daily life compared to pre-cycle
- Difference in the use of painkillers compared to pre-cycle
- Descriptive analysis of duration of use, using mean and standard deviation, 95% confidence interval, minimum and maximum
- Descriptive analysis of duration of pain relief after application using mean and standard deviation, 95% confidence interval, minimum and maximum
- Descriptive analysis of onset and degree of pain relief over the day, using mean and standard deviation, 95% confidence interval, minimum and maximum
- Descriptive frequency of AEs by number, mean and standard deviation, 95% confidence interval, minimum and maximum
- Descriptive analysis of frequency of EM 50 use using mean and standard deviation, 95% confidence interval, minimum and maximum
- Descriptive analysis of each instrument handling scale item using mean and standard deviation, 95% confidence interval, minimum and maximum

9.7.10 Analysis of exploratory endpoints

Subgroup analysis of primary and secondary endpoints by pain score, analgesic use, satisfaction, AEs, the "pain score pre-cycle (cycle 0)", duration of use, frequency of use, function of use, etc. For the analysis of exploratory endpoints, the Intend-to-treat (ITT), Per-Protocol (PP) and application dataset were used. Analysis of pain was performed for both the VAS and McGill.

10 Study participants

10.1 Epidemiology of the patients

The study was planned with 58 participants. A total of 60 patients were screened, of which 59 were included. 52 of the included patients were classified as PP and 59 as ITT. One patient was not included due to lack of data. Patients were included at 3 study centers, 48 at the Dr. Kurscheid study center, 1 patient at the study center of Kern, and 10 at the study center of Dr. Ackemann.

Table 4. Summary of patient characteristics by study center. Previous cycle pain score, age, age group, and recruitment period.

Multicenter	Study center Dr. Ackemann: 11 Patients Study center Dr. Kern: 1 Patient Study center Prof. Kurscheid: 48 Patients
Recruitment period	24.06.21 - 21.01.22
Average pain (VAS 0-100)	70
Average pain (McGill)	3.2
Average age (years)	29
Median age (years)	28
Youngest patient (years)	18
Oldest patient (years)	47

The pain pattern of the reference cycle was rated by the patients on average as 70 on the VAS score and 3.2 on the McGill score. The mean age was 29 years with an age range of 18 to 47 years.

10.1.1 Protocol deviations

A participant is classified as PP if the EM 50 was used over the first three days of the cycle.
In 7 cases (12%), the EM 50 was not used beyond the first three days of the cycle. These participants are considered ITT. Furthermore, one participant was excluded from the study due to insufficient data.

11 Evaluation

11.1 Primary endpoint: change in intraindividual pain before and after use of the device on cycle days 1, 2, and 3 on the Visual Analog Scale (VAS).

During the first 3 days of the study, 155 fully documented pain scores were recorded by the 59 female patients before and after application. On average, pain was rated as 62 on the VAS score before application, and the use of the EM 50 reduced this to an average of 44 (Figure 2). This corresponds to a decrease of 18 points on the VAS score. Since the decrease in pain is highly significant with a $p<0.001$, the null hypothesis "VAS score before using the device is equal to the VAS score after using the device" could be rejected.

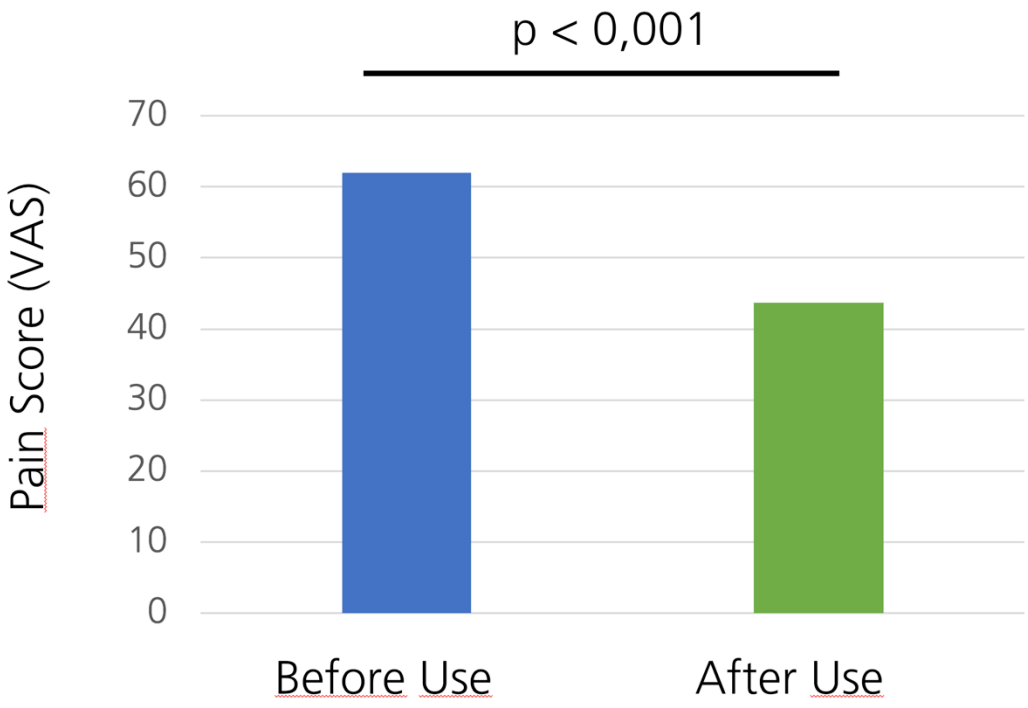

Figure 2. *Average intraindividual improvement in pain score VAS before and after use of the device at sum of days 1, 2, and 3. Sum of 155 fully documented pain scores evaluated.*

Of 155 fully documented applications, 143 showed improvement and 9 showed no improvement in VAS pain score (3 patients reported a VAS of 1 (no Pain) before the use). 126 applications (81%) showed improvement of ≥ 10 VAS points; 94 applications (61%) showed improvement of ≥ 15 VAS points; and 72 applications (47%) showed improvement of ≥ 20 VAS points.

11.2 Secondary endpoints

11.2.1 Average intraindividual difference in pain before and after use of the device compared across all time points.

During the 5 study days, 241 fully documented pain scores were recorded by the 59 female patients before and after application (Figure 3). Before application, the pain score averaged 52 points on the VAS score and 35 after application. This represents a decrease of 16 points on the VAS score. The decrease in pain was highly significant according to a p<0.001.

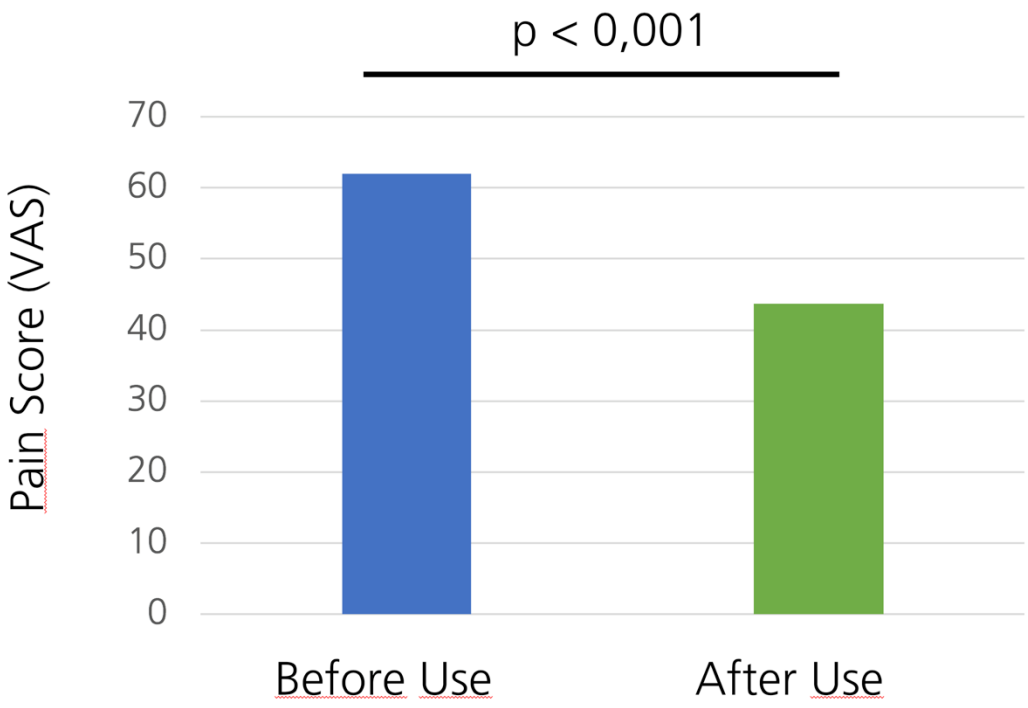

Figure 3. *Average intraindividual improvement in pain score VAS before and after use of the device as the sum of days 1 to 5. Sum of evaluated fully documented pain scores is 241.*

During the 5 study days, 263 fully documented pain scores were recorded by the 59 female patients before and after application using McGill score (Figure 4). Before application, the average pain score was 11 on the McGill score and 6 after application. This corresponds to a decrease of 5 points on the McGill score. The decrease in pain was highly significant according to a p<0.001.

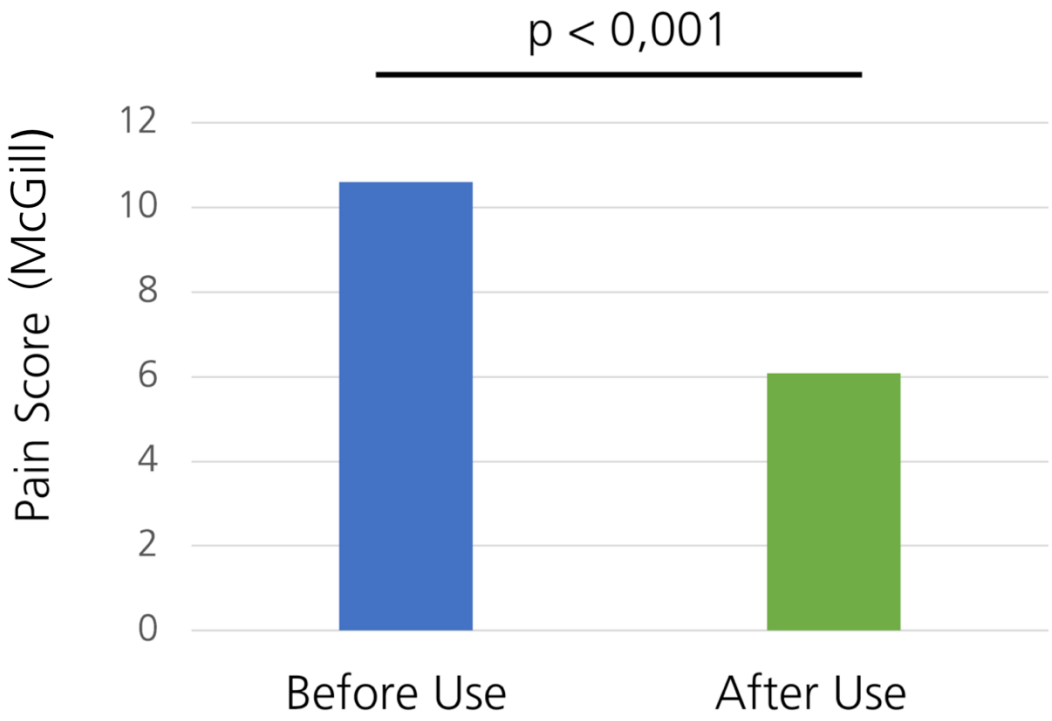

Figure 4. *Average intraindividual improvement in pain score McGill before and after use of the device at sum of day 1 to 5. Total of evaluated complete documented pain scores is 263.*

11.2.2 Average intraindividual difference of pain before and after using the device for each cycle day.

The study included the change in pain over 5 days after using the device. On all days, a significant decrease was observed on the VAS score (*Table 5*). On day 1, a pain score of 71 (95% CI 67 - 76) was recorded before use and of 51 (95% CI 45 - 56) after use. This represents a significant decrease in pain of 21 points on the VAS score ($p < 0.05$). The observed pain before and after application and the difference decreased over the observation days. At day 5, a pain score of 27 (95% CI 21–34) was reported before application and of 15 (95% CI 11 - 19) after application. This corresponds to a significant decrease in pain of 12 points on the VAS score ($p < 0.05$) (*Table 5 & Figure 5*).

Table 5. Average intraindividual pain difference for each cycle day .

	Pain before application (VAS)		Pain after application (VAS)		Reduction pain (VAS)	Significance
	Medium	95% CI	Medium	95% CI		
Day 1	71	67-76	50	45-56	21	$p < 0.05$
Day 2	64	60-68	45	40-50	19	$p < 0.05$
Day 3	50	44-56	35	30-40	14	$p < 0.05$
Day 4	39	33-44	25	25-20	13	$p < 0.05$
Day 5	27	21-34	15	11-19	12	$p < 0.05$

As a second pain score, pain was determined by McGill score. A significant decrease on the McGill score was observed on all days. On day 1, a pain score of 18 (95% CI 15 - 21) was recorded before application and of 12 (95% CI 9 - 14) after application. This represents a significant decrease in pain of 6 points on the McGill score ($p< 0.05$). The observed pain before and after application and the difference decreased over the observation days. At day 5, a pain score of 3.3 (95% CI 2.1 - 4.4) was reported before application and of 1.6 (95% CI 0.9 – 2.3) after application. This corresponds to a significant decrease in pain of 1.7 points on the McGill Score ($p< 0.05$) (*Table 6 & Figure 5*).

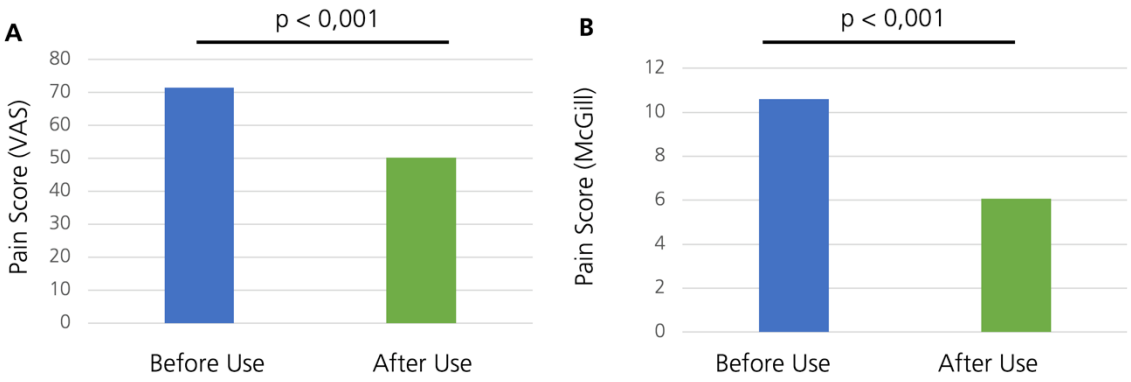

Figure 5. Difference in improvement of pain compared before and after using at day 1 EM 50 by VAS score (A) and McGill (B) using paired t-test. A significant decrease in the both pain scores was observed after the use of EM 50 ($p<0.001$).

Table 6. Average intraindividual pain difference for each cycle day by McGill scores:

	Pain before Application (McGill Scores)		Pain after application (McGill Scores)		Reduction Pain (McGill Scores)	Significance
	Medium	95% CI	Medium	95% CI		
Day 1	17,5	14,5-20,5	11,5	9,0-14,0	6.0	$p < 0.05$
Day 2	15,8	13,1-18,5	9,4	7,5-11,3	6.4	$p < 0.05$
Day 3	9,2	7,3-11,2	5,7	4,1-7,4	3.5	$p < 0.05$
Day 4	5,4	3,9-7,0	0,8	0,6-1,0	4.7	$p < 0.05$
Day 5	3,3	2,1-4,4	1,6	0,9-2,3	1.7	$p < 0.05$

11.2.3 Difference in improvement of pain compared to pre-cycle

In the study, both VAS score and McGill score were used to compare the difference in average pain perception between the current cycle and the pre-cycle. The pre-cycle was assessed with an average score of 70 (VAS) and 3.2 (McGill). The examined cycle was evaluated with a score of 55 (VAS) and 2 (McGill), respectively. This results in a decrease in pain of 15 (VAS) and 1.2 (McGill) points, respectively (*Figure 6*).

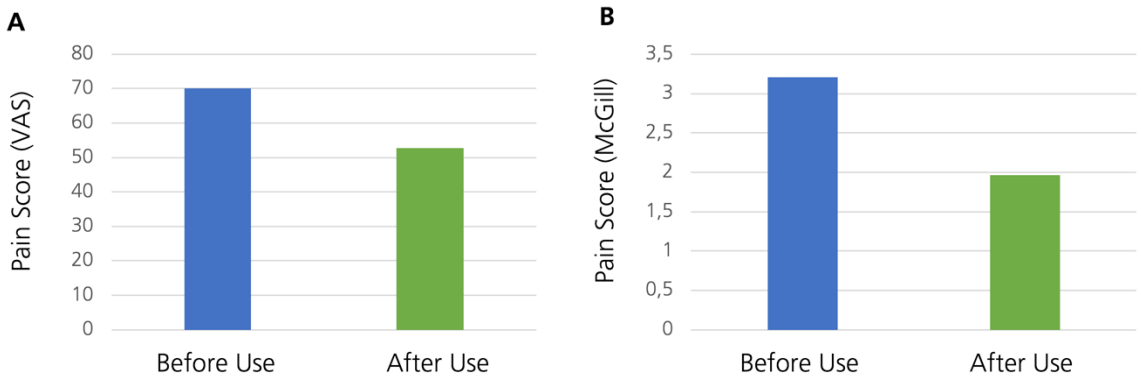

Figure 6: Difference in improvement of pain compared to pre-cycle between VAS score (A) and McGill (B) using paired t-test. Thus, it can be concluded that the use of the EM 50 resulted in an improvement in pain compared to the pre-cycle.

11.2.4 Difference in the restriction of daily life compared to pre-cycle.

Furthermore, the restriction of daily life due to menstrual pain was measured compared to the pre-cycle. 54% of patients (29 of 54) reported a reduction in restriction compared with the pre-

cycle. 2% of patients (3 of 59) reported increased restriction compared with the pre-cycle (Figure 7).

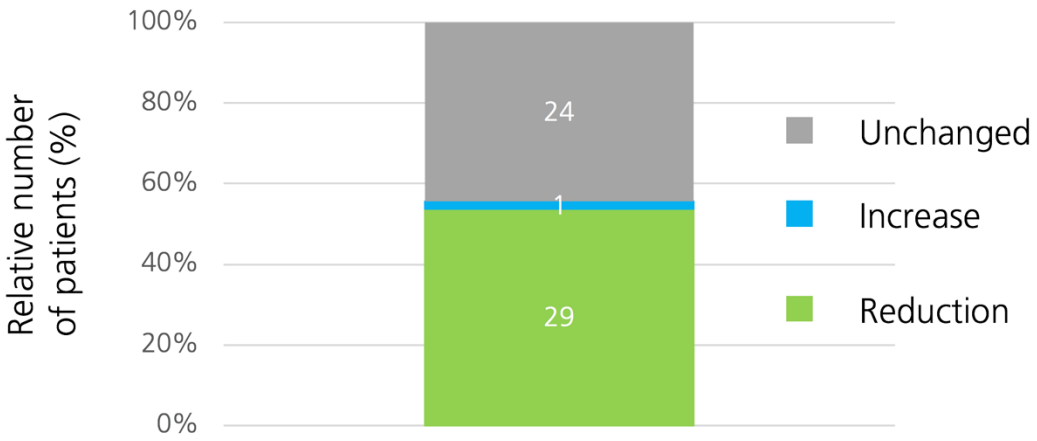

Figure 7. *Difference in limitation of daily life compared to the pre-cycle. The proportion of patients who reported perceiving a reduction in limitations as a result of using the EM 50 is shown in green (29 patients). 1 of the patients experienced a greater restriction during the period in which the device was used. 24 patients stated that they did not perceive any change in restriction (gray). In total, 54 patients provided information on this.*

11.2.5 Descriptive analysis of the duration of use

In the study, the duration of use was investigated. On average, the device was used for 48 min or longer across all cycle days. Specifically, the device was applied on day 1 40 min, day 2 54 min, day 3 58 min, day 4 49 min, and day 5 38 min. On day 1, the device was used by 19 patients for more than 1 hour at a time. On day 2, the device was used by 20 patients for more than 1 hour at a time. On day 3, 17 patients used the device for more than 1 hour at a time *(Figure 9).*

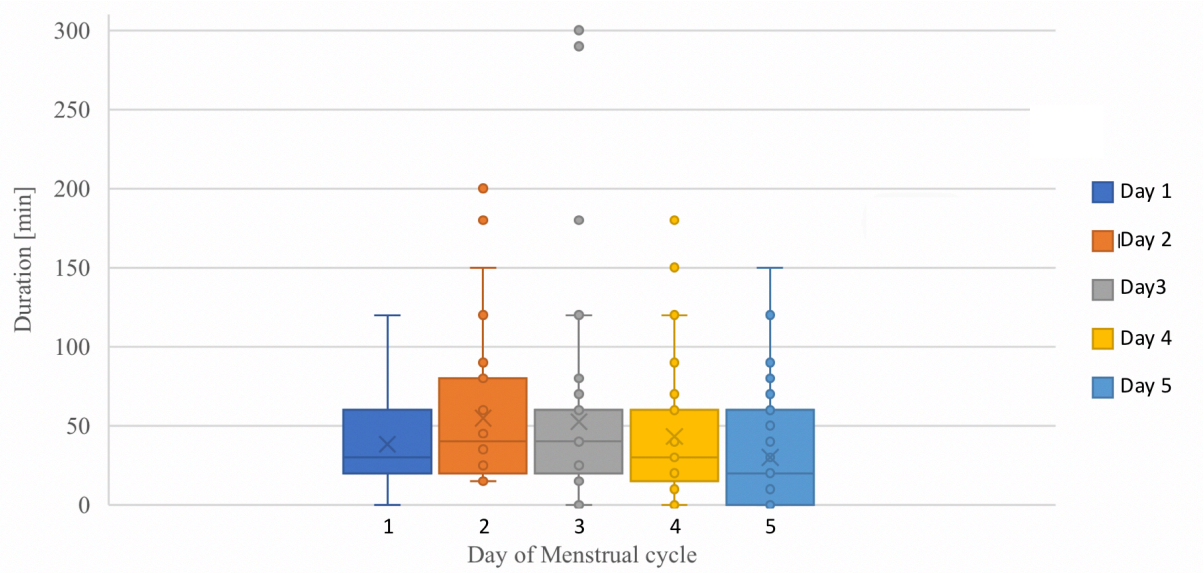

Figure 9. *Descriptive analysis of duration of use of the total population using mean (cross) and standard deviation (box), 95% confidence interval (antennas), minimum and maximum (points). On average, the duration of use decreased from the third day of the cycle. None of the patients used the device for longer than 300 min. In particular, on the last two days of the cycle, 7 patients did not use the device at all. Included were 56patients.*

11.2.6 Descriptive analysis of duration of pain relief after application.

In the study the duration of pain relief after application was investigated. On all days, pain relief from 2 to 6 hours was reported as a mean value. In detail, there was recorded a pain relief of 130 min on day 1, 143 min on day 2, 175 min on day 3, 405 min on day 4 and a pain relief of 422 min on day 5 *(Figure 10)*.

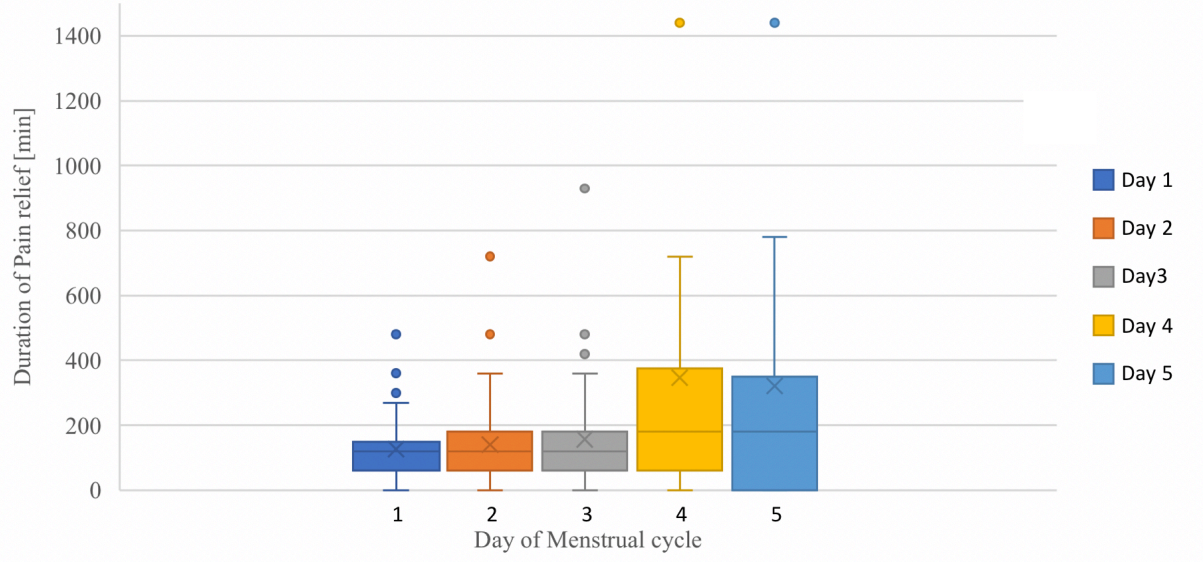

Figure 10. *Descriptive analysis of duration of pain relief after application of the total population using mean (cross) and standard deviation (box), 95% confidence interval (antennas), minimum, and maximum (points). On average, the duration of relief increased over the cycle. Some of the patients did not use the device after the third day of the cycle; accordingly, these patients reported no relief. On day 4, one patient reported that her pain relief lasted 2100 min; this value was considered an outlier and was not included in the chart. Fifty-nine patients were included.*

11.2.7 Descriptive analysis of the onset and degree of pain relief over the day.

Furthermore, the subjective assessment of the observed pain relief was recorded. Patients were asked about pain relief and its quality. The majority of patients 82% (on day 1), 93% (on day 2) and 80% (on day 3) reported pain relief on day 1-3. The fact that some patients (up to 25%) stopped using the device on cycle days 4 and 5 also reduced the percentage of patients who experienced pain relief to as low as 71% *(Figure 11)*.

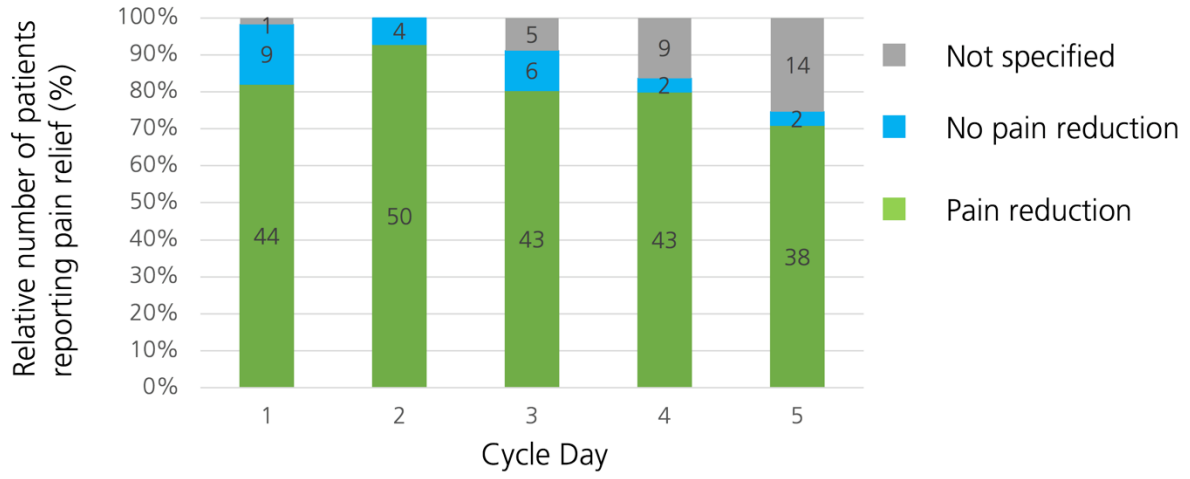

Figure 11*. Descriptive analysis of the onset of pain relief per study day. Pain relief was noted in a large majority of patients, especially on the first three days of the cycle. Due to the fact that 11 patients did not use the device on the 4th and 15 on the 5th day of the cycle, no data were reported here by 16% and 25%, respectively. Nevertheless, even on these days at least 71% reported pain relief with the EM 50.*

More than 35% of all patients reported good and very good pain relief. Especially on day 3, a very high satisfaction of pain relief was observed *(Figure 12)*.

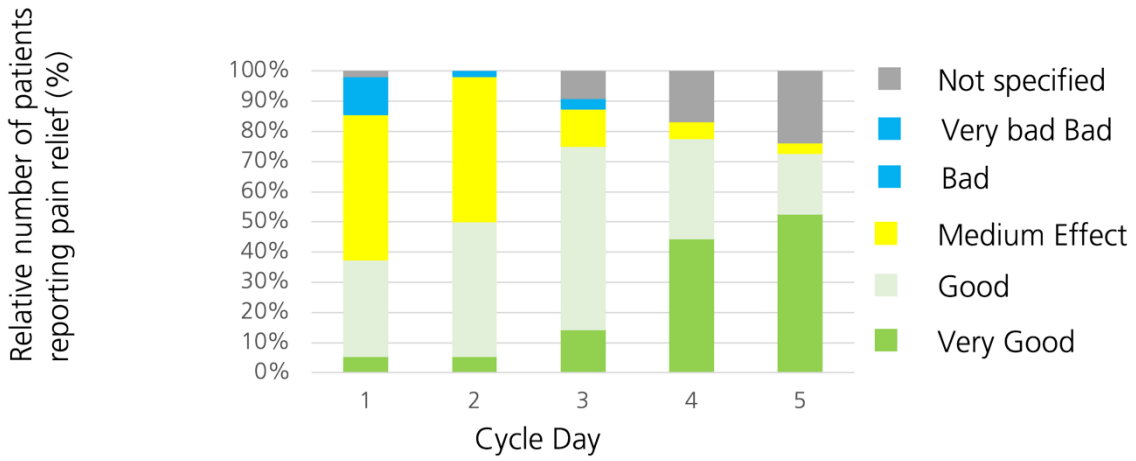

Figure 12. *Descriptive analysis of the degree of pain relief over the day. Moderate or better than moderate pain relief was seen in more than 85% of patients, especially on the first two days of the cycle. The highest degree of pain relief was achieved on the third day of the cycle. Due to the fact that 4 patients ended the use of the device prematurely, no information was provided here by 8%. Nevertheless, even on these days more than 85% reported a moderate or better pain relief by the EM 50.*

11.2.8 Descriptive frequency of AEs

Side effects were reported in isolated cases. Most side effects occurred on the first two days of use. Whereby 7 patients (8% of the uses) reported side effects on day 1 and 2 patients (5% of the uses) on day 2. The majority of patients did not report side effects. The most common side effect reported by patients was reddening of the skin, justified by excessive heat setting. The second most frequent side effect (3 patients) was slight pain due to the TENS function being set too high. Other observed side effects were slight pruritus (2), slight tingling (1) and slight sensitivity of the skin (2) (Table 7).

Table 7. Occurred side effects and their frequency.

Side effect	Frequency
Redness	5
Mild pruritus	2
Slight pain or uncomfortable at higher TENS intensity	4
Body weakness (dizziness, circulatory problems) with repeated use	1
Skin Sensitive due to heat function	2
Tingling/Tickle	1

11.2.9 Descriptive analysis of the frequency of use of the EM 50.

The study participants used the device on average twice per day on all 5 observation days. The use decreased slightly with decreasing pain intensity. Thus, on the first day of the cycle, the

device was used approximately 2.4 times and on the fifth day of the cycle only 2 times (*Figure 13*). 95% of the users used the device between 1 and 4 times on days 1 and 2. In isolated cases, up to 10 uses per day were recorded.

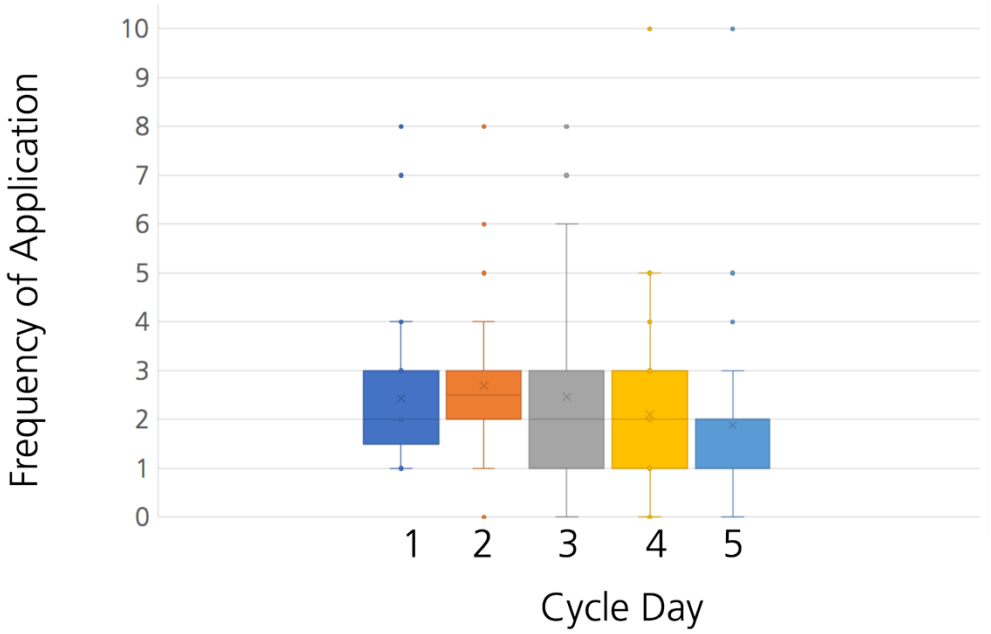

Figure 13. *Descriptive analysis of frequency of EM 50 use, using mean (cross) and standard deviation (box), 95% confidence interval (antennas), minimum and maximum (dots). Frequency of use decreased over menstruation. This decrease likely paralleled the reduction in menstrual symptoms. On average, the device was used 2.4 times per day. Evaluated questionnaires: 54.*

11.2.10 Descriptive analysis of the individual scale points on the handling of the device.

The majority of patients rated both handling and design as good or very good. 35 female patients (63%) rated the design and 26 (46%) the handling as very good (*Figure 14*). 54 female patients (98%) stated that they would continue to use the device and 54 of the female patients (96%) would recommend the device to others (*Figure 15)*.

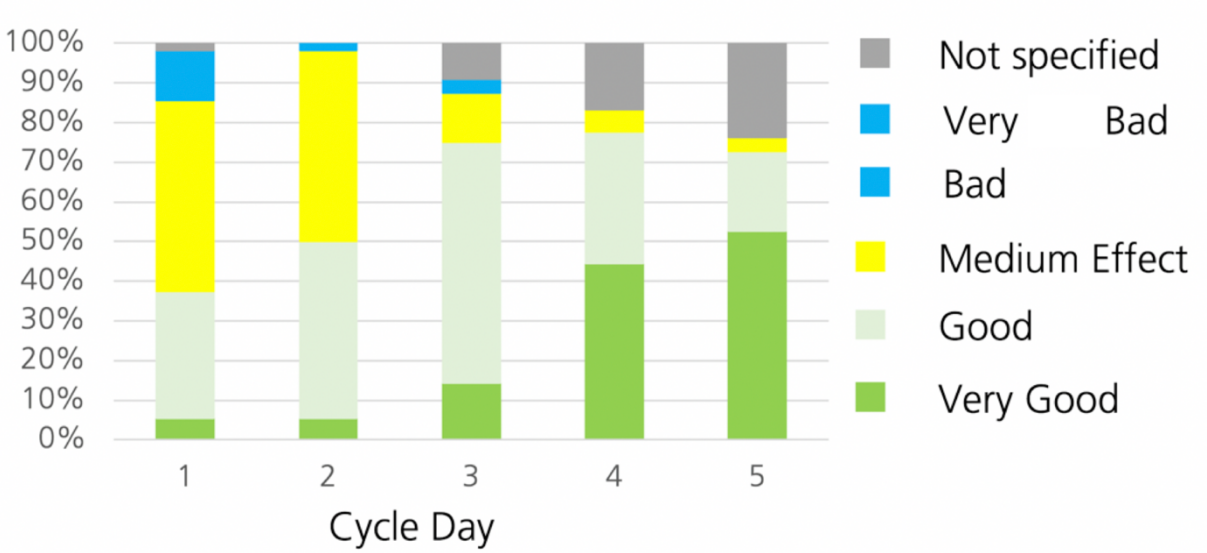

Figure 14. *Analysis of patients' opinion about the device. The majority of patients said they evaluate the design (93%) and the handling (93%) good or better. None of the patients rated the design or manageability as poor or very poor.*

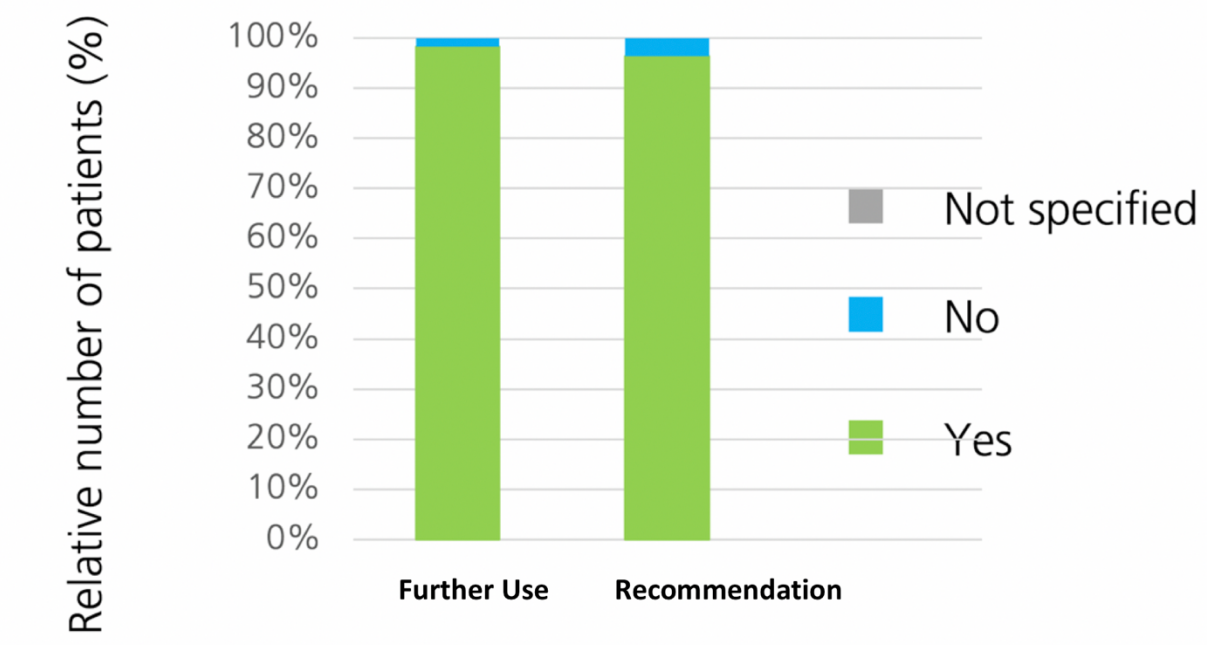

Figure 15. *Opinion of patients regarding continued use and recommendation of the EM 50. More than 98% of patients said they would continue to use the device and more than 96% would recommend the EM 50 to others.*

12 Discussion

The aim of the multicenter observational study was to investigate the effectiveness of the medical device "Beurer EM 50" in reducing menstrual pain associated with primary

dysmenorrhea (ReduSchmerz). For this purpose, 54 patients from 3 study centers were included in the application observation during the period 6.24.21 – 01.21.22. The patient cohort covers a broad age range from 18 to 47 years with a mean age of 29 years. Thus, the efficacy of the medical device could be investigated in all relevant age groups and a **benefit of the medical device** in **a broad user group** could be **concluded.** Regarding menstrual pain, participants reported a high menstrual pain score of 70 on the 100 VAS scale. This high pain score was not expected, but is confirmed by the large number of pain relievers listed. **Thus, a benefit for patients with high menstrual pain can also be expected**.

In terms of reduction in pain, the (i) improvement in pain score after use of the device, (ii) improvement in pain compared with previous cycle, (iii) duration of pain relief, and (iv) change in amount of analgesics taken were observed. Pain was determined using the independent and validated VAS and McGill scoring systems.

The change in pain score VAS and McGill were consistent in the observations. This therefore strengthens the statement about the change in pain. **A statistically significant improvement in pain score was observed both after use of the device and compared to the previous cycle**. An improvement in pain over all days of 18 points on the VAS score is considered a **medically relevant decrease**. An improvement of 18 or more points was observed in 43% of the applications. This improvement was observed across all days of observation (days 1 to 5). Day 1 of menstruation also recorded the greatest average reduction in VAS score (47% ≥ 18). This was to be expected, as the greatest baseline pain was also recorded on this day. As pain decreased over the cycle, the average use of the device also decreased. Thus, it can be concluded that with **greatest menstrual pain comes greatest benefit in use**. The similar reduction in pain from a TENS unit has also been observed in other publications.[9, 10,11]

The participants reported a reduction in pain that lasted for about two hours. Thus, the reduction is not only limited to the immediate heat or TENS effect, but a **lasting effect** can be assumed. This persistent effect and the reduction of pain can also be seen as the reason for the reported reduction in the intake of analgesics.

Overall, it can be said that all data on the reduction of pain are consistent. Thus, the use of the device really seems to go hand in hand with a reduction in pain. The success of the application is also reflected in the high number of uses and the willingness to use the device, as well as the high degree of recommendation.

In the study, there were isolated reports of mild and temporary side effects after or during the use of the medical device. Essentially, short-term reddening of the skin or pain of the skin were described. Furthermore, patients reported that they had used the device at too high level and

that this had caused the reactions. This need to adapt the settings also fits with the observation that the majority of adverse events were observed on the first day of use and did not recur with more accurate setting of the device. None of the adverse events were severe or persistent. Thus, the benefit of the device appears to be safe especially after individual adjustment of the level.

In the observational study, a sustained improvement in perceived pain was observed regardless of age and pain score, indicating the effectiveness of the device in reducing individual pain perception. However, the study only made intraindividual comparisons before and after use of the EM 50, with no control group. Secondly, the patients were not blinded to the use. Both of these factors offer the risk, especially in pain studies, that the reduction in pain is caused in whole or in part by the placebo effect. This risk of the placebo effect could only be more delineated by a controlled, blinded study. However, by its nature, it is almost impossible to blind the use of heat and TENS stimulation in a placebo controlled study. Studies with TENS alone were controlled and showed a similar positive effect[9, 10,11] . Also, the changes are medically relevant and thus it is not relevant to the participant's perception of pain whether the pain is brought about by a physiological change or by a placebo effect. This is because, as a rule, an underestimation of pain by the patient due to a placebo effect is not accompanied by a medical risk.

13 Literature

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