Moxibustion did not have an effect in a randomised clinical trial for version of breech position

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ABSTRACT

INTRODUCTION: In Chinese traditional medicine, the stimulation of acupuncture point no. 67 – the bladder meridian – is recommended to favour cephalic version in case of foetal breech presentation. The point can be stimulated by an acupuncture needle, ginger application, fingertip pressure, laser or moxibustion; moxibustion is heat generated by a burning stick containing the herb *Artemisia vulgaris.*
A Cochrane review concluded that more research on the effectiveness of moxibustion is needed. This study aimed to estimate the effectiveness of moxibustion for version of breech presentation.

METHODS: We included 200 women in gestational week 33 who had a singleton foetus in breech position. They were randomised to moxibustion treatment daily for two weeks or control without moxibustion. The randomisation was performed for nulliparous and parous women separately.

RESULTS: After the trial, which lasted on average 16 days, the breech position was confirmed in 68 of the 92 nulliparous and in 50 of the 108 parous women (74% versus 46%, $p < 0.01$); furthermore, cephalic position was verified in 76 women and other positions in six women. No significant difference regarding the incidence of breech position was found in the moxibustion group compared with the control group (risk ratio (RR) = 1.05, 95% confidence interval (CI): 0.8-1.38); nor in nulliparous (RR = 1.17, 95% CI: 0.77-1.76) or in parous women (RR = 1.0, 95% CI: 0.69-1.46); an RR > 1 favours moxibustion).

CONCLUSIONS: No significant effects of moxibustion were found in correcting the breech position in primiparous and parous women after their 33rd gestational week.

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TRIAL REGISTRATION: This trial was registered with ClinicalTrials.gov as NCT02251886.

Breech presentation is commonly suspected in mid-pregnancy and the incidence decreases to 3-4% as the pregnancy approaches term. External cephalic version (ECV) reduces the number of non-cephalic presentations at birth and the need for caesarean section. ECV is usually performed after 36 weeks [1]. Non-manipulative cephalic version has been evaluated in systematic reviews. Various alternative medical interventions, such as osteopathy, hypnosis and moxibustion, have been proposed to improve the likelihood of a cephalic presentation in terms of efficacy, acceptability and side-effects [2-6]. Postural techniques have been suggested, including the knee-chest position and the supine position with the pelvis elevated, with little evidence to support their efficacy [7, 8]. Few of these alternative interventions have been evaluated extensively in randomised trials except from moxibustion [4, 9-14]. A Cochrane review concluded that more research on the effectiveness of moxibustion is needed [15].

In Chinese traditional medicine, the stimulation of acupuncture point no. 67 of the bladder meridian (BL 67), located on the lateral side of the fifth toe, is recommended to favour cephalic version (**Figure 1**). The point can be stimulated by an acupuncture needle, ginger application, fingertip pressure, laser and by moxibustion.

Our aim was to estimate the effectiveness of moxibustion at week 33 to promote the version of breech presentation and to evaluate the acceptability of the method by the pregnant women. Our hypothesis was that moxibustion may reduce foetal breech presentation and its consequences. Thus, we registered the need for ECV and the alternatives offered to women refusing ECV, including caesarean section.

METHODS

At the Obstetrical Departments in Holstebro and Herning, Denmark, women were invited to participate in a randomised trial on moxibustion when a foetal breech position in a singleton pregnancy was verified at ultrasound in week 32. Women were enrolled in the study in the period from October 2003 to January 2010. The exclusion criteria were vaginal bleeding in the second and third trimester, placental insufficiency, cervical shortening, premature rupture of membranes, preeclampsia, high blood pressure, pelvic insufficiency, low placental position, placenta previa, uterine malformations, previous corrective uterine surgery and known foetal morbidity. The experimental design was a parallel trial with randomisation stratified for nulliparous and parous women. The randomisation was performed from a list of random numbers from the Geigy Scientific Tables, with even and odd numbers indicating moxibustion or not. The randomisation result was pre-packed in a sealed, non-transparent envelope and was drawn when the woman gave informed consent. There were two stacks: one with en-

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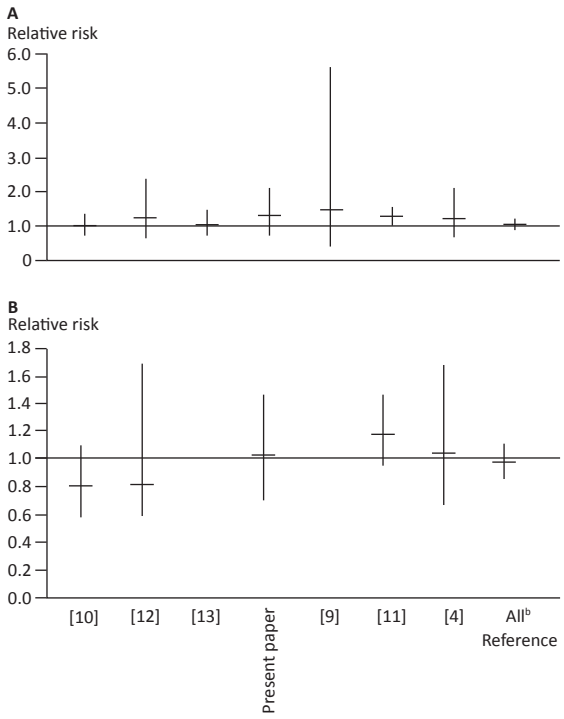
FIGURE 1



Plots of effect of moxibustion for version of breech position analysed with relative risk[a] by parity with 95% confidence interval in seven European studies. **A.** Nulliparous women. **B.** Parous women.

a) Relative risk > 1 indicates favourable effect of moxibustion on breech version to non-breech position.
b) All studies combined adjusted according to number of women included.

velopes for nulliparous and one with envelopes for parous women. Eligible non-participants were not registered. The women were instructed to apply moxibustion daily for 15-20 minutes, preferably in the evening (Figure 1). Moxibustion is the stimulation with heat generated by a burning stick containing the herb *Artemisia vulgaris* (mugwort). The treatment took place from inclusion in week 33, and was intended to continue for a minimum of two weeks. The control group had no other treatment instead of moxipustion. The partner was also instructed in how to give the moxibustion treatment. No moxibustion treatment was given in the ambulatory clinic after the initial instruction. The study was non-blinded. Ultrasound examination would end the experiment three weeks later, and ECV was offered according to current guidelines. The position, non-breech or breech, was noted. The foetuses with an oblique position at this gestational week were counted as cephalic as all were subsequently delivered vaginally in the cephalic position. Follow-up ended at the last delivery in 2010.

The study was approved by the local Scientific Ethical Committee and by the Danish Data Protection Agency (R. no.: 1-16-02-587-14), registered with ClinicalTrials.gov (NCT02251886), and conducted in accordance with the Helsinki Declaration and the Guidelines for Good Clinical Practice.

Statistical analysis

Sample size calculation indicated that 45 women were needed in each group, based on $\alpha = 0.05$ and a power of 80 ($\beta = 0.2$). We assumed a 30% effect of moxibustion on top of 20% of spontaneous version in nulliparous control women and a 30% effect of moxibustion on top of 60% of spontaneous version in parous control women. Consequently, we intended to include 90 nulliparous and 90 parous women. All randomised women were assessed under the intention-to-treat principle. Women who had performed three days of moxibustion were analysed according to the per-protocol principle.

All analyses were performed in IBM SPSS Statistics 20. The difference between two means was tested with Student's t-test if Gaussian distribution could be assured. Otherwise, Mann-Whitney's or Wilcoxon's test was used for unpaired and paired analysis, respectively. Differences between two proportions were tested with Fisher's exact test or the chi-squared test, as appropriate. Results are given as mean ± standard deviation if not otherwise stated. Relative risks (RR) are given with 95% confidence intervals (CI). A two-sided p-value of 0.05 was the level of significance.

Trial registration: The trial was registered with ClinicalTrials.gov (NCT02251886).

RESULTS

In total, 200 women were included in the study (**Table 1**). The groups had similar clinical characteristics when nulliparous and parous were analysed separately. The trial lasted an average of 16 days and version to cephalic position was found to be independent of moxibustion, but highly dependent on parity. Breech position was confirmed in 68 of the 92 nulliparous and in 50 of the 108 parous women (74% versus 46%, $p < 0.01$); cephalic position was verified in 76 women and other positions were detected in six women. Similar incidences of breech position were found in the moxibustion groups and the control women combined (RR = 1.05, 95% CI: 0.8-1.38); in nulliparous (RR = 1.17, 95% CI: 0.77-1.76) as well as in parous women (RR = 1.0, 95% CI: 0.69-1.46); an RR > 1 favours moxibustion (Table 1).

In the moxibustion groups, ten women admitted giving treatment for less than four days. The per-protocol analysis excluded these women; thus, 90% of the moxibustion group were included for this analysis (Table 1). In total, 32 women had less than ten days of moxibustion including the above ten women. In seven cases,

TABLE 1

Clinical data of 200 women randomised to moxibustion or control treatment.

	Nulliparous women		Parous women	
	moxibustion	control	moxibustion	control
n	48	44	54	54
Age, mean ± SD, yrs	28 ± 4	29 ± 4	31 ± 3	31 ± 3
Body weight, mean ± SD, kg	76 ± 14	75 ± 12	78 ± 14	74 ± 15
Gestational age at randomisation, mean ± SD, days	229 ± 6	230 ± 7	229 ± 6	231 ± 7
Exposure, mean ± SD, days of trial	15 ± 4	15 ± 3	16 ± 5	17 ± 6
Primary outcome, n (%)				
Breech at end of study, intention-to-treat	34 (71)	34 (77)	25 (46)	25 (46)
Breech at end of study, per-protocol/reduced denominator[a]	32/45 (71)	34 (77)	18/47 (38)	25 (46)
Breech, ≥ 10 days of moxibustion[b]/reduced denominator[c]	28/35 (80)	34 (77)	20/35 (57)	25 (46)
ECV performed after end of trial, n	10	13	11	13
Successful ECV, n	0	2	3	3
Breech after attempted ECV, n	34	32	22	22
Breech at birth, n	33	31	17	17
Elective caesarean section, n	28	29	17	18
Acute caesarean section, n	6	7	1	2
Vaginal birth, n	14	8	36	42
Birth weight, mean ± SD, g	3,358 ± 471	3,332 ± 522	3,652 ± 379	3,699 ± 494
Apgar at 1 min. ≤ 7, n	1	1	1	2
Apgar at 5 min. ≤ 7, n	1	0	0	0
Apgar at 10 min. ≤ 7, n	1	0	0	0

ECV = external cephalic version; SD = standard deviation.
a) Reduced number of women in moxibustion group (10 women excluded): per protocol; 45 (3 women excluded) and 47 (7 women excluded), nulliparaous and parous women, respectively.
b) Clinical data of women randomised to moxibustion treatment in per-protocol analysis and if moxibustion treatment was continued for a minimum of 10 days.
c) Reduced number of women (32 women excluded): all moxibustion women who had ≥ 10 days of treatment; 35 (13 women excluded) and 35 (19 women excluded), nulliparaous and parous women, respectively.

a cephalic position was suspected and verified; in the remaining 25 of the 32 women, the compliance was deemed to be insufficient. Thus, only 70 women (69%) remained with sufficient treatment to anticipate a likely effect of moxibustion (Table 1).

The per-protocol analysis gave similar results on breech position irrespective of moxibustion treatment (Table 1). The incidence of breech position was not significantly lower in women who had been treated with moxibustion for ten days or longer than among the control women (Table 1), or among all other women combined as controls (nulliparous 28/35 versus 40/57, p = 0.43; parous: 20/35 versus 30/73, p = 0.17). The breech position was confirmed at the end of trial in 31% (11 of 32) of cases, in women who had received less than ten days of moxibustion (Table 1).

Increased foetal activity and uterine contractions were reported in nearly half of the women who received moxibustion, but this did not increase the likelihood of a non-breech position (27/47 versus 32/55, p = 0.94), **Table 2**. Similarly, the women had no less breech position with low versus good compliance in the trial when they felt increased foetal activity and uterine contractions (6/16 versus 21/31, women with low compliance versus ≥ 10 days moxibustion treatment, p = 0.09), Table 2.

TABLE 2

Symptoms reported in moxibustion group. Data are given as number of women (breech at end of trial).

	General symptoms, all women	Stopped prematurely < 10 days	Moxibustion treatment ≥ 10 days
Increased foetal activity, uterine contractions	47 (27)	16 (6)	31 (21)
Verified non-breech position within 10 days of trial	-	7	-
Bad smell	31 (21)	10 (5)	21 (16)
Headache	8 (5)	6 (5)	6 (0)
Nausea	6 (4)	3 (2)	3 (2)
No symptoms indicated	28 (15)	6 (1)	22 (14)
Total	102 (59)[a]	32 (10)[a]	70 (49)[a]

a) > 1 symptom per woman.

After the moxibustion trial, 47 out of 118 women (40%) had ECV of whom 17% (8/47) succeeded in a cephalic position at delivery; the remaining women had a caesarean section. Eleven percent of the foetuses turned spontaneously to cephalic position after week 36, as observed in 12 of the 110 women who initially

(week 369 had their foetal breech position confirmed or who received an unsuccessful ECV. The most common reason for not attempting ECV was the woman's preference for caesarean section over ECV. Similar perinatal data and exposure time were seen from inclusion to end of trial within the two parity groups (Table 1). The birth weights were higher in women who delivered vaginally or were intended to deliver vaginally than in the women who had elective caesarean section (3,712 ± 516 versus 3,304 ± 358 g, $p < 0.01$). This difference was due to the lower gestational age at surgery in the latter women rather than to the position of the foetus.

DISCUSSION

This randomised trial included pregnant women at 32 gestational week with foetal breech position in a singleton pregnancy. Daily treatment for 20 minutes with moxibustion during a three-week period did not affect the primary outcome, which was cephalic presentation at the end of the treatment period. This was the case for both nulliparous and parous participants. The secondary outcomes were also not affected by the treatment, i.e. ECV and caesarean section rate. After the trial, we found 11% spontaneous version of breech position even after week 36, a moderate ECV success, and a low acceptance of ECV when delivery mode was discussed with the women. A limitation of this study is the non-blinding of the participants. One way to adjust for the potential effect of non-blinding could be moxibustion at sham points in the control as done by Vas et al [11]. During the trial, non-participants were not registered, and therefore we do not know whether our study group represents the women with breech properly. We were able to include the intended number of women from our sample size calculation and keep the stratification for parity for further analysis. The follow-up was complete and the per-protocol rate was acceptable with 90% in the moxibustion group, but 21% had received less than ten days of treatment.

The breech position incidence tended to increase in the per-protocol analysis or when excluding women due to low compliance (Table 1). This suggested either a rapid effect of moxibustion or a high rate of spontaneous version to non-breech position. We suspect the latter is more likely due to the observation that women felt increased foetal movements, uterine contractions and early spontaneous versions. Increased foetal movements are common symptoms observed mainly in the moxibustion group as their comfort is scrutinised more [3, 4, 9, 13, 16] (Table 2). In Cardini's trial, 22% of women interrupted the trial due to non-compliance and premature exit [13]. Cardini experienced more initial resistance to enter the trial out of concern for the foetus, whereas Danish women gladly accepted the trial when asked. The side-effects of fumes by moxibustion are well-known and were the prime reason for withdrawal in other studies [9, 13]. Trial compliance improved if the partner was involved.

Three Chinese trials have reported an effect of moxibustion for breech position compared with postural techniques [15, 17-19]. This may be associated with the earlier and longer intervention time of these studies, in which the intervention usually took place in gestational weeks 28 to 37, with an unclarified parity issue or with a better effect of moxibustion (90% version in the moxibustion group). The version percentage was unexpect-

TABLE 3

European studies since 2004 on the effect of moxibustion on breech position. Spontaneous version of breech in control group and diference between control and moxibustion group (moxa effect).

					Spontaneous version from breech to non-breech position, %			Moxa effect: spontaneous breech to non-breech, %		
Reference	Country	Weeks of trial	Women, n	Nulli-parous, n	all women	nulliparous	parous	all women	nulliparous	parous
Neri et al [9]	Italy[a, e]	34-36	226	?	38	–	–	16	–	–
Cardini et al [13]	Italy[b, c]	32-35	123	123	36	36	–	– 2	– 2	–
Neri et al [14]	Italy[d]	33-36	39	39	20	20	–	11	11	–
Millereau et al [12]	France[c]	33-37	68	38	49	32	69	– 3	5	– 12
Guittier et al [4]	Switzerland[e]	34-36	212	139	16	13	21	2	3	2
Vas et al [11]	Spain[e, f]	34-35	406	228	44	30	63	14	15	10
Coulon et al [10]	France[a]	33-35	328	187	37	21	57	– 9	– 4	–13
Present paper	Denmark	33-35	200	92	40	23	54	2	6	0

a) Moxibustion + acupuncture vs. no treatment/placebo.
b) Replication study of a study performed in China.
c) Trial was stopped prematurely.
d) Moxibustion + acupuncture vs. moxibustion.
e) Data on parity from personal communication.
f) Moxibustion vs. sham moxibustion and postural treatment.
?: Author could not retrieve data on parity any more.

Two moxa sticks approaching the lateral side of the fifth toes at acupuncture point BL 67.

edly high; most women are expected to be nulliparous due to China's one-child policy. As all studies are in Chinese, they were not scrutinised first-hand and omitted from further comparison. Cardini et al. performed a trial on nulliparous in China in 1995-1996 with an effect of moxibustion of 28% and a spontaneous version of 48% from gestational week 33 to 35; both version rates were higher than in later European studies [20].

According to two European studies, moxibustion has a significant effect [9, 11]. Neri et al applied moxibustion and acupuncture combined, but did not state the number of nulliparae. Moreover, nulliparity is somewhat skewed with 48 versus 60% in the control versus the moxibustion group, respectively, which is probably due to non-stratified randomisation. The version rate of 54% in the treatment group was more astonishing as the treatment group held more nulliparous women than the control group did [9]. Vas et al found a 14% difference in favour of moxibustion and included two control groups that received either postural treatment or sham moxibustion [11]. Only Vas' trial had the power ($1 - \beta = 76\%$) to support the significant results (Figure 1) and had a high version rate of 45% in nulliparous and 73% in parous women. An effect of moxibustion was observed in both parity groups (15% and 10% for nulliparous and parous, respectively), **Table 3**.

On the other hand, four European studies found no effect [4, 10, 12, 13], Figure 1. Guittier et al performed their study at a later gestational age (weeks 34 to 38) and Cardini et al replicated a Chinese study on primigravidae in Italy. Coulon and Millereau found even less cephalic positions in the moxibustion group than in their control group. Coulon used an inactive laser probe as placebo, while Millereau and Cardini stopped prematurely due to a lack of effect and drop-outs (Table 3). The observation suggests that Southern European women may have higher spontaneous version rates and may be susceptible to moxibustion; still, the trial of Cardini et al did not find any effect in nulliparous women. No significant effect of moxibustion was found when all European studies were combined and stratified for parity (Figure 1).

From the Cardini replication study, one lesson learned was the difficulties of a multicentre study to assure homogeneity at inclusion, information and treatment. Even though our trial is a single-centre study, the interest and enthusiasm for moxibustion cooled when several of the European studies and a Cochrane meta-analysis were published [4, 9-13, 15] (Table 3).

The difference in spontaneous version rates in parous versus nulliparous is a potential source of error if stratification is not performed, preferably at randomisation and publication. For comparison of effect, we obtained data on parity which were not reported in the original publications (Table 3, Figure 1).

CONCLUSIONS

We found no effects of moxibustion for correction of breech position in primiparous and parous women after the 33rd gestational week.

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CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

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