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A randomised controlled trial of moxibustion for breech presentation

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Objectives To evaluate the efficacy of moxibustion for the correction of fetal breech presentation in a non-Chinese population.

Design Single-blind randomised controlled trial (RCT).

Setting Six obstetric departments in Italy.

Sample Healthy non-Chinese nulliparous pregnant women at 32–33 weeks + 3 days of gestational age with the fetus in breech presentation.

Methods Random assignment to treatment or observation. Treatment consisted of moxibustion (stimulation with heat from a stick of *Artemisia vulgaris*) at the BL 67 acupuncture point (Zhiyin) for one or two weeks. Two weeks after recruitment, each participant was subjected to an ultrasonic examination of the fetal presentation.

Main outcome measure Number of participants with cephalic presentation in the 35th week.

Results The study was interrupted when 123 participants had been recruited (46% of the planned sample). Intermediate data monitoring revealed a high number of treatment interruptions. At this point no difference was found in cephalic presentation in the 35th week (treatment group: 22/65, 34%; control group: 21/58, 36%; RR 0.95; 99% CI 0.59–1.5).

Conclusions The results underline the methodological problems evaluating of a traditional treatment transferred from a different cultural context. They do not support either the effectiveness or the ineffectiveness of moxibustion in correcting fetal breech presentation.

INTRODUCTION

Moxibustion is a traditional Chinese therapy consisting of stimulation of acupuncture points with heat from the slow combustion of mixtures of medicinal grasses, most often *Artemisia vulgaris* (the Japanese name for which is 'moxa'). Little is known about the possible mechanism of this treatment.[1–4] Moxibustion of the BL 67 point (Zhiyin), situated beside the outer corner of the fifth toenail, is traditionally proposed in China for the correction of anomalous presentation of the fetus.[5–8] The treatment is simple and can also be performed at home by the pregnant women. After publication of the (positive) results of the only randomised controlled trial (RCT) of its efficacy,[9] this treatment has become popular in several Western countries, including Italy, where it is recommended by doctors and midwives in public and private hospitals for women with fetal malposition during the third trimester. The original trial, performed in China between 1995 and 1996 on the basis of a protocol designed in Italy, showed that in the treatment group there were more fetal cephalic versions and a substantial increase of fetal movements in respect of the control group. The study hypothesised a positive relation between the two outcomes: the increased fetal activity could facilitate the cephalic version. The Italian multicentre RCT reported here was planned as a confirmatory trial of the therapy's efficacy, and as an assessment of the ability to transfer a traditional Chinese treatment outside of the original ethnic, social and cultural context. The rationale of the two studies was the same and is described in the original report. The protocol used in the present study was virtually identical to that of the first in order to obtain the most comparable results. Both studies were performed with primigravid women, a population with a low probability of the late spontaneous cephalic version.

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METHODS

A randomised single-blind trial (the evaluator was blinded to the participant's group allocation) was performed in six obstetric departments of public hospitals in northern and central Italy. It was funded by the University of Turin, site of the main research centre. The protocol was approved by the Ethics Committee of the Piedmont Region.

The participants were 123 non-Chinese nulliparous pregnant women, in good health, with normal fetal biometry, at 32–33 weeks + 3 days of gestational age (confirmed by early ultrasound), and ultrasound diagnosis of breech presentation within the preceding 24 hours. They were recruited and randomised by the investigators (doctors or midwives) during routine pregnancy assessment in ultrasound clinics of the participating hospitals. Each participant was thoroughly informed about the aims and procedures of the study and signed a written consent form.

The women were randomly assigned to two groups by computer generated random numbers (PACT, Version 2.0, Glaxo Welcome, London, England) and the randomisation was concealed with numbered sealed opaque envelopes: treated (moxa group) and non-treated (control group). The reasons for exclusion from the study were refusal of randomisation or treatment, defective pelvis, previous uterine surgery, recognised fetal or uterine malformation or fibroid >4 cm diameter, twin pregnancy, current or previous tocolytic therapy and any other pregnancy complications.

The procedures were carried out by doctors or midwives who had been trained in the technique of administration of moxibustion for the correction of anomalous fetal presentation by an expert acupuncturist (the first author of this article).

Neither the treatment administrators nor the participants were blinded to group assignment; only the evaluator was blinded to the participant's group. The participants were told to avoid any treatment that might influence the results of the trial: only treatment with moxibustion was allowed and only for the participants of the moxa group.

All the participants were asked to compile two weekly forms to count active fetal movements (AFM). Each form had to be completed twice a day for 7 days with the number of AFM counted in one hour. All the participants were asked to undergo an ultrasound evaluation of fetal presentation two weeks after the randomisation. In the participating centres where external cephalic version (ECV) was routinely performed, participants with persistent breech presentation could request this treatment after the 37th week. Finally, each participant was contacted (in person or by telephone) during the puerperium to gather information about the final stage of pregnancy and the delivery.

On the day of randomisation, the moxa group participants were trained in moxibustion treatment (alone or accompanied by the partner or helper). The training consisted of presentation of the necessary material (sticks of *A. vulgaris*), location of the BL 67 acupuncture point (Zhiyin) and performance of the first stimulation. The participant was asked to perform the treatment in a comfortable sitting or semi-sitting position for 30 minutes (15 minutes per side), twice a day for seven days. She was free to choose the time of day for the treatment to ensure tranquillity and absence of interruptions. The intensity of stimulation was the maximum tolerated by the participant (i.e. able to provoke brief local hyperaemia without burning). At the end of the training, the participant received enough *Artemisia* sticks for one week of treatment and a form to count the AFM. The AFM had to be counted for one hour starting from the second quarter of an hour of each of the two daily treatments. The participant was asked to immediately inform the researcher of any difficulty or undesired effect and to undergo an ultrasound control of fetal presentation after the first week of treatment. In the case of persistence of breech presentation at this intermediate control, the participant was asked to continue the same treatment for another seven days. She received the necessary materials and a second form to count the AFM, and an appointment was made for the ultrasound control after the second week of treatment. The reasons for interruption of treatment, real or presumed side effects and adverse events associated with treatment were recorded on the clinical charts.

The main outcome was the proportion of cephalic presentations in both groups evaluated by ultrasound in the 35th week (i.e. two weeks after randomisation). The secondary outcomes were as follows: the number of cephalic presentations at delivery, the fetal motor activity (AFM count), the compliance with treatment (assessed subjectively by the researchers and by the participants, and objectively based on the number of participants who interrupted treatment) and the adverse events in both groups.

The sample size was set at 260 participants (130 per group). In fact, a hypothetical difference between the two groups of 27% for the main outcome (the value found in the previous trial executed in China)[9] could have been identified with a power of 90% and level of significance $\alpha = 0.05$ if 74 participants per group completed the study. However, an unpredictable number of women could have requested ECV after the 37th week, which could have been a confounding factor with regard to evaluation of fetal presentation at delivery. Therefore, the number of recruited participants was empirically raised to 130 per group. Suspension of treatment did not lead to exclusion from the analysis because the main outcome of all participants were evaluated on the basis of 'intention to treat'. An interim analysis of the main outcomes measures was planned when at least 40% of the sample would have been recruited and treated or observed, to enable the study to be stopped early if, as indeed occurred, a clear result emerged.

The analysis was performed with the Stata 7.0 programme (StataCorp, College Station, Texas). Comparisons of continuous variables were carried out with Student's t test and those of qualitative variables with the χ^2 test. Evaluation of the main outcome was described in terms of relative

risk (RR) with a confidence interval (CI) of 99%. Other results were reported as rough data and %, as the study is underpowered, thus their value is just to indicate trends, useful for further studies on the same topic.

RESULTS

Recruitment began in March 2001 and ended in February 2003. One hundred and fifty-seven women were assessed for eligibility. The study was interrupted by majority decision of the participating centres when 123 participants had been enrolled (46% of the planned sample size); the intermediate data monitoring revealed a bad compliance to the treatment and a high number of treatment's interruptions, so that major doubts raised among the investigators about the adequacy of the study protocol for evaluating the treatment's efficacy.

The trial flowchart is shown in Fig. 1. Among the 157 women assessed for eligibility, 3 did not meet inclusion criteria, 24 refused to participate because they were wary of the treatment, 7 refused to be randomised because they wanted to be treated by moxibustion (6 cases) or by caesarean section at term (1 case). Two recruited participants (both belonging to the control group) were included in the analysis of the main outcome (but not of the secondary outcomes), despite the first left the study after deciding to undergo treatment and was lost to follow up, and the second was found (at delivery) to have a breech baby in a bicornuate uterus. Following the 'intention to treat', the missing data of the first were considered as a positive result (cephalic version occurred).

Twenty-one participants with persistent breech presentation requested ECV treatment after the 37th week, 12 of whom had successful version.

The randomised groups were comparable at baseline. There were no significant differences at recruitment (for maternal age and height, educational level, family history of breech presentation, extended legs of the fetus, placental location and grading, amniotic fluid index) or at delivery (for neonate sex, weight, length, cranial circumference, umbilical cord loops).

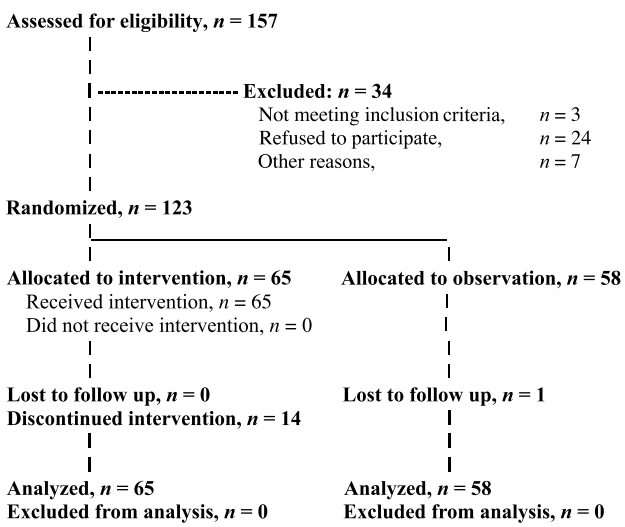

Fig. 1. Trial flow diagram.

At the interim statistical analysis (executed independently of the clinical investigators) no difference was found between the two groups with regard to the main outcome (proportion of cephalic presentations in both groups in the 35th week) (treatment group: 22/65, 34%; control group: 21/58, 36%; RR 0.95; 99% CI 0.59–1.5). Cephalic presentations at delivery were 34/65 (52%) in the moxa group and 29/57 (51%) in the control group. The variation of the presentation after the 35th week was due partly to the use of ECV (12 cases, see above) and partly to spontaneous version to cephalic or to breech (7 cases, see below).

There was an appreciable but non-significant difference between the two groups in AFM count during the first week of treatment/observation (mean: moxa group 254, control group 220; median: 209 and 121, respectively) ($t = 0.6$, $P = 0.4$).

The compliance of the Italian participants with the moxibustion treatment was judged by the investigators as 'good' in 45 cases (69%), 'acceptable' in 13 cases (20%) and 'poor' in 7 cases (11%). Of the 65 moxa group participants, 27 complained the treatment being unpleasant and associated physical disturbances, usually unpleasant odour with or without nausea and throat problems (14 cases, see Fig. 1), abdominal pain because of contractions (11 cases) and other less frequent problems; 14 participants (22%) temporarily or definitively interrupted the treatment because of these symptoms.

During treatment in the moxa group, there were two cases of preterm delivery at 34 weeks. The first was caused by premature rupture of the membranes (PROM) after 5 days of treatment. In the second case, uterine contractions began on the 10th day of treatment, just after sexual intercourse, and were preceded by blood loss and suspected PROM. There was also a case of bleeding at 37 weeks of gestational age in the moxa group following an ECV, presumably due to an excess of pressure on the anterior placenta.

No PROM was recorded in the control group. However, there was a delivery at 37 weeks after bleeding from placenta abruption at the marginal sinus.

The delivery for all four cases described in this section was by caesarean section and there were no pathological consequences for the neonates.

Fetuses with 'extended legs' at the first ultrasound (performed at recruitment) showed a much lower percentage of cephalic versions than those with 'flexed legs': 18/68 (27%) *versus* 22/48 (46%). This was true for the total recruited population and for the two groups separately, thus confirming the results of the original study (10).

The median age of the recruited population was 31 years. Women younger than 31 had better results than those older than 31, independently of the group: 25/56 (45%) cephalic

versions at 35 weeks in the younger women *versus* 17/64 (27%) in the older women.

There were generally more cephalic versions at 35 weeks in women with a low educational level (max. grade 8) than in those with a high school or university education: 14/30 (47%) *versus* 26/89 (29%). The difference in the moxa group was 56% *versus* 26%, whereas in the control group both subgroups had the same percentage of cephalic versions at 35 weeks (33%).

DISCUSSION

Compared with those of the original study[9] the only two protocol differences were the exclusion of Chinese women and the upper limit of gestational age at recruitment, which was the 33rd week in the original study. We think it unlikely that this can explain the different results.

The percentages of spontaneous cephalic version (control group) between the 33rd and the 35th week are clearly different in the Italian (21/56; 36%) and Chinese (62/130; 48%) samples. However this difference disappears when the confounding factor of age is eliminated. In fact the percentages of spontaneous cephalic version in the untreated Italian women less than the median age (mean age 26.2 years) and in the untreated Chinese women of the original trial (mean age 25.2 years) are very similar (respectively 44.6% and 47.7%). As far as we know no data are available in the literature about the influence of maternal age on the probability of cephalic version.

Compliance was lower; 14/65 (22%) Italian women interrupted the treatment compared with 9/30 (6.9%) in the original study. Many Italian moxa group participants complained about the treatment being unpleasant and/or physical disturbances associated to it. Further studies are necessary to establish how much of this was due to the effects of the stimulation and how much to cultural or contextual factors, which could have negatively influenced the researchers and/or the participants. The last hypothesis is suggested also by the high number of eligible women (24/157) who refused to participate in the study because of mistrust in the treatment and fear to harm the fetus. Considering with hindsight all these unexpected problems of compliance, the choice of proposing the treatment at home, without a strict follow up whether women were practicing the technique effectively, appears as a major defect of the study protocol.

We recorded increased fetal motor activity after moxibustion, but there was no positive association between AFM and cephalic versions. If future studies confirm the efficacy of moxibustion, the hypothesis that it facilitates the cephalic version through an increase of AFM should be examined. In this regard, a recent Italian study[10] of cardiotocographic variability after stimulation of the BL 67 point with a different technique (moxibustion on a needle) recorded less AFM than with placebo.

It should also be mentioned that in the original study, no fetus changed its presentation after the 35th week, whereas in this study the late spontaneous version occurred in 7/122 cases (5.7%) (i.e. six versions from breech to cephalic presentation and one from cephalic to breech). Therefore, in a Caucasian population, the 'number of cephalic presentations at the 35th week' is unstable also in first pregnancies (although not as frequently as in subsequent ones) and it should not be used as a main outcome in future studies.

Finally, in the moxa group we recorded two cases of preterm delivery at 34 weeks associated with PROM (certain in one case, suspected in the other). In the original study, there were three cases of PROM at 37 weeks (i.e. two weeks after the end of treatment). With the available data, it is not possible to decide if there is a significant association between the use of moxibustion in pregnancy and preterm birth with or without PROM. Nevertheless, given the widespread use of this therapy in Italy, further studies are necessary to assess the frequency of this adverse event.

So far we have reported the main results of our study in comparison with those of the original trial. The following exploratory analysis concerns subgroups not included in the study's protocol and thus is not intended to evaluate the efficacy of the treatment. Its purpose is to suggest hypotheses for future studies of moxibustion, as well as suitable methods for clinical research on traditional medicine.

Moxibustion treatment produced favourable results in the subgroup of women with a low educational level. The lower level of schooling could have led to better compliance with a therapy deriving from a different culture (more trust and acceptance, better adherence to the procedure).

In contrast, cultural factors (like the higher education, the professional status and the consequent difficulty in prescribing a treatment rather different from the daily routine) could have limited the ability of the researchers to be clear and convincing in their communication and relationship with the pregnant women, for instance in the critical phase of teaching the treatment procedure.

These remarks, related to so-called aspecific factors of the efficacy of any treatment, could partly explain the null result of this study. The apparent simplicity of moxibustion, described in the original study[9] as 'easy to teach, learn and perform', has led to the expectation that its transfer to a new context would occur without difficulty. Instead the results of this pragmatic study indicate the complexity of the factors involved in even a simple treatment. Therefore, when a traditional treatment (be it simple or complex) is under study in a new context, it should be prescribed and performed (or taught) by a person with a solid background in that tradition and in obstetrics as well (or collaborating with experts in obstetrics) and within a suitable and more controllable setting.

In addition the protocol should involve not only the participant's consent to participation in the study but also

the recording (before randomisation) of her opinion and expectations with regard to the treatment[11] and her attitudes in respect of the type of delivery (vaginal or caesarean).

CONCLUSIONS

The results of this study do not confirm those of the original study with regard to the efficacy of moxibustion in correcting breech presentation of the fetus in primigravid women at the 33rd week of pregnancy. On the other hand, because the study was interrupted and is underpowered and given the methodological weaknesses of the protocol, no conclusion can be made regarding the efficacy and safety of moxibustion. Indeed, the significance of this study is to underline several problems concerning the ability to transfer the investigated treatment from the original ethnic, social and cultural context to the typical context of an Italian public hospital and draw some deductions on methodology of clinical research in traditional medicine. Further experimental research, adequately designed for the adoptive context, is needed for confirming the efficacy, safety and transferability of the investigated treatment.

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Competing interests

All authors declare that they have no competing interests; therefore, they have nothing to declare.

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