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Moxibustion for the treatment of pressure ulcers: Study protocol for a pilot, multicenter, randomized controlled trial

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Abstract

Introduction: Pressure ulcers are common in the elderly and immobile. Currently, there are few proven effective treatments for pressure ulcers. This trial aims to evaluate the feasibility efficacy, and safety of moxibustion for pressure ulcers.

Methods/analysis: This is a multicenter, two-armed, parallel-design, randomized controlled trial (RCT). Thirty eligible patients with pressure ulcers will be randomized in a ratio of 1:1 to the treatment group and control group. The participants in the treatment group will undergo indirect moxibustion for 30 minutes before application of a dressing, one session daily, five sessions weekly for four weeks. The patients in the control group will only receive a dressing, applied in the same way as in the treatment group. Both groups will be followed up for three months. The primary outcome measures will be wound surface area (WSA) and proportion of ulcers healed within trial period (PUHTP). The secondary outcomes will be the Pressure Ulcer Scale for Healing (PUSH Tool), Visual Analogue Scale (VAS), and adverse events. All outcomes will be evaluated at the beginning of the study, at the end of the second week, at four weeks after randomization, and at one and three months after treatment cessation.

Ethics/dissemination: This trial has undergone ethical scrutiny and been approved by the ethics review boards of First Affiliated Hospital of Heilongjiang University of Chinese Medicine and Second Affiliated Hospital of Heilongjiang University of Chinese Medicine (Permission numbers: LLP2014025 and LLP2013115). The results of this study will provide clinical evidence for the feasibility, efficacy, and safety of moxibustion for pressure ulcers.

Trial registration number: ChiCTR-TRC-13003959

Keywords: moxibustion; pressure ulcers; bedsores; randomized controlled trial

Background

A pressure ulcer (i.e., bedsore, pressure sore, decubitus ulcer) is defined as a localized injury to the skin and underlying tissue layers affecting the muscle, tendon, and bone as a result of constant pressure due to impaired mobility [1, 2]. Pressure ulcers are often caused by pressure, shear, friction, or a combination of these [3]. Common sites for pressure ulcers include the back of the head, shoulder blade, elbow, lower back, hip, pelvic bone, ankle, and heel [4]. Pressure ulcers are generally classified into four stages (stage I, II, III, and IV) according to the European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel guidelines (EPUAP/NPUAP) [3].

The prevalence of pressure ulcers across studies varies from 8.8% to 53.2% [5-8], and incidence rates range from 7% to 71.6% [7-10]. It has been estimated that the annual treatment cost of pressure ulcers ranges from GBP £1.4 to 2.1 billion, which is broadly equal to the total UK National Health Service expenditure on mental illness, or the total cost of community health services [11]. Effective and adequate prevention is an important issue for patients, clinicians, and policy makers.

Moxibustion is a popular and safe intervention used to manage various conditions, such as breech presentation [12], facial paralysis [13], chronic fatigue [14], knee osteoarthritis [15], and type 2 diabetes mellitus [16]. In addition, moxibustion has been found to be effective in treating pressure ulcers [17, 18], which suggests that moxibustion may be an effective treatment for pressure ulcers. However, most prior studies were case reports, case series, or clinical trials without a control group, resulting in poor quality of these studies. Considering these methodological flaws, we will conduct a multicenter RCT to investigate the effectiveness and safety of moxibustion. The results of this study will provide evidence for the feasibility of a large clinical trial, and yield data to determine the appropriate sample size for future large scale RCTs of moxibustion in patients with pressure ulcers.

Methods/Design

Objective

The primary objective of this study is to assess the feasibility of moxibustion treatment for pressure ulcers and obtain preliminary safety and efficacy data to inform a future, larger, randomized controlled trial in the same patient population.

Design

This is an assessor- and analyst-blinded, randomized, controlled clinical trial with two parallel arms. The trial will be conducted at two clinical centers in China: First Affiliated Hospital of Heilongjiang University of Chinese Medicine and Second Affiliated Hospital of Heilongjiang University of Chinese Medicine, between December 31, 2013, and December 31, 2016. This protocol has been approved by the ethics review boards of First Affiliated Hospital of Heilongjiang University of Chinese Medicine and Second Affiliated Hospital of Heilongjiang University of Chinese Medicine with permission numbers LLP2014025 and LLP2013115, respectively. Written informed consent will be obtained from all study participants prior to enrollment.

Eligible patients will be randomized in a ratio of 1:1 to the treatment group (moxibustion plus dressing) and control group (dressing), and receive treatment for four weeks. Patients will be followed up for three months (Figure 1, Table 1). Outcome measures will be assessed at baseline, as well as at the end of the second and fourth week after randomization, and at one and three months after treatment cessation. Results will be analyzed by professionals blinded to the group allocation. This protocol has been registered with the Chinese Clinical Trials Register, a registry in the World Health Organization (WHO) Registry Network.

Eligibility

Inclusion Criteria

Participants will be included if they fulfill the following criteria: (1) aged 18 to 75 years; (2) pressure ulcers belonging to stage II or III according to the EPUAP/NPUAP

guidelines [3]; and (3) at least one pressure ulcer.

Exclusion criteria

Patients with any of the following conditions will be excluded because of safety concerns and possible sensation loss interfering with evaluation of pain intensity: (1) undergoing other therapies that might interfere with the ability to heal, such as corticosteroid therapy, radiation therapy, or chemotherapy for cancer; (2) infected pressure ulcers; (3) complications of diabetes mellitus; and (4) severe diseases, such as liver, cardiac, and kidney diseases, and relevant serious complications.

Randomization and allocation concealment

In this trial, randomization will be performed at the Good Clinical Practice (GCP) Center of Second Affiliated Hospital of Heilongjiang University of Chinese Medicine. Thirty participants who meet the eligibility criteria will be assigned in a ratio of 1:1 to the treatment group and control group. Patients will be randomized using a computerized number generator through the stratified block randomization method of the Statistical Analysis System (SAS) package (Version 9.1.3; SAS Institute Inc., Cary, North Carolina, USA) by a statistician with no clinical involvement in this trial. The allocation will be concealed in sequentially numbered, opaque, sealed envelopes containing the randomization assignments. Allocation concealment will be broken only after the participant has met all selection criteria and completed the baseline assessments. The participants will know the allocated group, but the outcome assessors and data analysts will be masked to the intervention allocation [19].

Blinding

In moxibustion research, it is not feasible to conceal allocation from the practitioners. In addition, it is not possible to prevent participants from knowing if they have received moxibustion treatment or dressing intervention, or both. The treatment and assessment will be performed independently. The outcome assessors and the data statistical analysts will be blinded to treatment allocation throughout the study.

Intervention

Treatment group (moxibustion plus dressing)

The participants receiving moxibustion treatment will be treated indirectly at a distance of 2 to 3 cm from the wound surface for 30 minutes per session, one session daily, five sessions weekly for four weeks. In addition, a dressing will be applied in one session daily, five sessions weekly for four weeks.

Control group (dressing)

The format of the dressing intervention will be the same as in the treatment group.

Outcome measures

The wound surface area (WSA), proportion of ulcers healed within trial period (PUHTP), Pressure Ulcer Scale for Healing (PUSH Tool), and Visual Analogue Scale (VAS) will be the outcomes used to assess efficacy. Adverse events will be recorded to assess safety.

Primary outcomes

1) Wound surface area

The WSA [20] of the pressure ulcers will be measured by the use of acetate tracing and subsequent planimetric determination. Ulcer tracings will be accomplished by outlining the pressure ulcer circumference onto a transparent film applied directly over the wound. Each ulcer will be traced three times by two assessors, respectively, in order to improve the accuracy of these tracings. A third assessor will determine the ulcer surface area from the wound tracing using a planimeter (KP-21C). All three assessors will be blinded to the identities of the patients and to the treatment group assignments.

2) Proportion of ulcers healed within trial period

Completely healed ulcers will be defined as 100% epithelization or skin closure

without drainage [20].

Secondary outcomes

1) Pressure Ulcer Scale for Healing

The PUSH Tool [21] was developed by the NPUAP as a quick, reliable tool to monitor the change in pressure ulcer status. This tool categorizes ulcers with respect to surface area, exudate, and type of wound tissue. Subscores for each of these ulcer characteristics will be recorded, and then added to obtain the total score. A comparison of total scores measured over time provides an indication of the improvement or deterioration in pressure ulcer healing.

2) Visual Analogue Scale

The pain intensity of pressure ulcers will be assessed using the 100-mm VAS (0, absence of pain; 100, the worst pain of imaginable) [22, 23]. In order to evaluate the clinical severity and impact on activities of daily life in patients with bedsores, the VAS is selected as a secondary outcome measurement.

Statistical methods

Sample Size

Although several studies have investigated the effects of moxibustion on pressure ulcers, no RCTs have assessed the effects of moxibustion on pressure ulcers. There is no previous study on which to base the sample size calculation. Therefore, this pilot study will evaluate the efficacy and safety of moxibustion and feasibility of clinical trials. Taking into account the minimum number of subjects necessary to evaluate the efficacy of moxibustion, this pilot study will include 36 participants (18 in each group) with an expected dropout rate of 20% [24].

Statistical analysis

Data will be analyzed by a statistician blinded to the group allocations using the Statistical Package for the Social Sciences (SPSS) 17.0 statistical software package.

Significant levels will be reported at $P < 0.05$. Data analysis of baseline characteristics and of primary and secondary outcomes will be based on the intention-to-treat (ITT) principle. If an adjustment for possible baseline incomparability is needed, analysis of covariance will be conducted. If the measurement data of WSA, PUSH, and VAS have non-normal distributions, the Wilcoxon rank sum test will be used. If the measurement data have normal distributions, the *t*-test will be used. In the case of proportions, the chi-square or Fisher exact test will be applied (e.g., PUHTP).

Patient safety

Any adverse events (known as unfavorable or unintended signs, symptoms, or diseases occurring after treatment) related to moxibustion treatment will be observed and reported by patients and practitioners during each patient visit. In addition, all vital signs and adverse events will be measured and recorded at each visit.

Quality control

All staff will be required to undergo special training before participating in the trial. For example, staff will be trained to select participants and to conduct the moxibustion intervention. The monitors will check study protocol compliance and informed consent documents, and assess the progress of the study, including participant recruitment, moxibustion intervention, and data quality, at each center once a month. Dropouts and withdrawals from the study will be recorded through the intervention and follow-up periods.

Ethics

Written informed consent will be obtained from each participant. This study is approved by the ethics review boards of First Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine and Second Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine.

Discussion

The objective of this study is to evaluate the effectiveness and safety of moxibustion for treating pressure ulcers. We designed this study to determine the efficacy and safety of moxibustion in the treatment group (moxibustion plus dressing) versus the control group (dressing). The results of this study will determine if moxibustion is an effective therapy for pressure ulcers.

The outcomes of WSA, PUHTP, PUSH Tool, and VAS are well-evaluated pressure ulcers. This pilot study will provide data on the efficacy of moxibustion for pressure ulcers through a follow-up period of three months after the completion of the treatment. An assessment of these outcomes will also be needed in a future, long-term, clinical trial.

In addition to appropriate outcome measures, the use of an appropriate control group is a critical issue in designing a high quality clinical trial. The purpose of this study is to clarify whether moxibustion is effective in patients with pressure ulcers, and we have planned a pragmatic design using a dressing intervention in the control group. This pragmatic trial comparing moxibustion plus dressing with dressing alone can provide evidence focused on the effectiveness of moxibustion.

In conclusion, this pilot, assessor- and analyst-blinded, multicenter RCT will investigate the efficacy and safety of moxibustion for pressure ulcers, assess the feasibility and relevance of a moxibustion therapy study design, and provide a clinical foundation for future, large-scale, multicenter clinical trials.

Trial status

The trial is currently recruiting subjects.

List of abbreviations

ChiCtr: Chinese Clinical Trials Register; EPUAP/NPUAP: European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel; RCT: randomized controlled trial; GCP: Good Clinical Practice; WSA: Wound surface area; PUHTP: Proportion of ulcers healed within trial period; PUSH Tool: Pressure Ulcer Scale for Healing; VAS: Visual Analogue Scale; ITT: intention-to-treat.

Acknowledgements

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Author's contributions

JHY and QHZ contributed equally to this work. QHZ and ZRS conceived the study, designed the study protocol. JHY and CRL drafted the manuscript. QHZ and ZRS sought funding and ethical approval. All authors contributed to the further writing of the manuscript as well as read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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Table 1 Time of visits and data collection

	-1 week	0 week	2 weeks	4 weeks	1 month	3 months
	Baseline	Treatment phase			Follow-up phase (End-of-treatment)	
Patients						
Informed consent	×					
Sign the informed consent		×				
Medical history	×					
Physical examination	×					
Randomization		×				
Intervention						
Treatment group (n = 18)		20 sessions of moxibustion plus dressing				
Comparison						
Control group (n = 18)		20 sessions of dressing				
Outcomes[a]						
WSA		×	×	×	×	×
PUHTP		×	×	×	×	×
PUSH Tool		×	×	×	×	×
VAS		×	×	×	×	×
Participant safety						
Adverse events		×	×	×	×	×

a. WSA: Wound surface area; PUHTP: Proportion of ulcers healed within trial period; PUSH Tool: Pressure Ulcer Scale for Healing; VAS: Visual Analogue Scale.

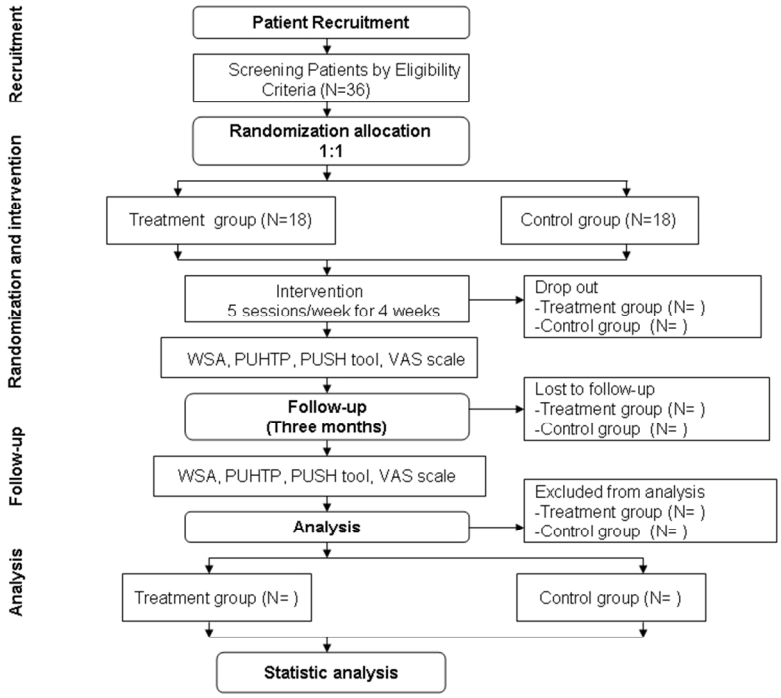

Figure 1 Flow chart of study process

254x190mm (96 x 96 DPI)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3
	2b	Specific objectives or hypotheses	3-4
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	4
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	Not completed
Participants	4a	Eligibility criteria for participants	4-5
	4b	Settings and locations where the data were collected	4
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	5-6
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	6-7
	6b	Any changes to trial outcomes after the trial commenced, with reasons	Not completed
Sample size	7a	How sample size was determined	7
	7b	When applicable, explanation of any interim analyses and stopping guidelines	7
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	5
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	5
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	5
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to	5

		interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	5
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	7
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	7
Results (This trial does not complete, so no results were provided)			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	
	13b	For each group, losses and exclusions after randomisation, together with reasons	
Recruitment	14a	Dates defining the periods of recruitment and follow-up	
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	
Discussion (This trial does not complete, so no results found-related discussed)			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	No
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	No
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	No
Other information			
Registration	23	Registration number and name of trial registry	
Protocol	24	Where the full trial protocol can be accessed, if available	Not completed
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	9

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

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Keywords: moxibustion; pressure ulcers; bedsores; randomized controlled trial

Abstract

Introduction: Pressure ulcers are common in the elderly and immobile. Currently, there are few proven effective treatments for pressure ulcers. This trial aims to evaluate the feasibility efficacy, and safety of moxibustion for pressure ulcers.

Methods/analysis: This is a multicenter, two-armed, parallel-design, randomized controlled trial (RCT). Thirty eligible patients with pressure ulcers will be randomized in a ratio of 1:1 to the treatment group and control group. The participants in the treatment group will undergo indirect moxibustion for 30 minutes before application of a dressing, one session daily, five sessions weekly for four weeks. The patients in the control group will only receive a dressing, applied in the same way as in the treatment group. Both groups will be followed up for three months. The primary outcome measures will be wound surface area (WSA) and proportion of ulcers healed within trial period (PUHTP). The secondary outcomes will be the Pressure Ulcer Scale for Healing (PUSH Tool), Visual Analogue Scale (VAS), and adverse events. All outcomes will be evaluated at the beginning of the study, at the end of the second week, at four weeks after randomization, and at one and three months after treatment cessation.

Ethics/dissemination: This trial has undergone ethical scrutiny and been approved by the ethics review boards of First Affiliated Hospital of Heilongjiang University of Chinese Medicine and Second Affiliated Hospital of Heilongjiang University of Chinese Medicine (Permission number: HZYEYLP2014). The results of this study will provide clinical evidence for the feasibility, efficacy, and safety of moxibustion for pressure ulcers.

Trial registration number: ChiCTR-TRC-13003959

Background

A pressure ulcer (i.e., bedsore, pressure sore, decubitus ulcer) is defined as a localized injury to the skin and underlying tissue layers affecting the muscle, tendon, and bone as a result of constant pressure due to impaired mobility [1, 2]. Pressure ulcers are often caused by pressure, shear, friction, or a combination of these [3]. Common sites for pressure ulcers include the back of the head, shoulder blade, elbow, lower back, hip, pelvic bone, ankle, and heel [4]. Pressure ulcers are generally classified into four stages (stage I, II, III, and IV) according to the European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel guidelines (EPUAP/NPUAP) [3].

The prevalence of pressure ulcers across studies varies from 8.8% to 53.2% [5-8], and incidence rates range from 7% to 71.6% [7-10]. It has been estimated that the annual treatment cost of pressure ulcers ranges from GBP £1.4 to 2.1 billion, which is broadly equal to the total UK National Health Service expenditure on mental illness, or the total cost of community health services [11]. Effective and adequate prevention is an important issue for patients, clinicians, and policy makers.

Moxibustion is a popular and safe intervention used to manage various conditions, such as breech presentation [12], facial paralysis [13], chronic fatigue [14], knee osteoarthritis [15], and type 2 diabetes mellitus [16]. In addition, moxibustion has been found to be effective in treating pressure ulcers [17, 18], which suggests that moxibustion may be an effective treatment for pressure ulcers. However, most prior studies were case reports, case series, or clinical trials without a control group, resulting in poor quality of these studies. Considering these methodological flaws, we will conduct a multicenter RCT to investigate the effectiveness and safety of moxibustion. The results of this study will provide evidence for the feasibility of a large clinical trial, and yield data to determine the appropriate sample size for future large scale RCTs of moxibustion in patients with pressure ulcers.

Methods/Design

Objective

The primary objective of this study is to assess the feasibility of moxibustion treatment for pressure ulcers and obtain preliminary safety and efficacy data to inform a future, larger, randomized controlled trial in the same patient population.

Design

This is an assessor- and analyst-blinded, randomized, controlled clinical trial with two parallel arms. The trial will be conducted at two clinical centers in China: First Affiliated Hospital of Heilongjiang University of Chinese Medicine and Second Affiliated Hospital of Heilongjiang University of Chinese Medicine, between May 29, 2014, and December 31, 2016. This protocol has been approved by the ethics review boards of First Affiliated Hospital of Heilongjiang University of Chinese Medicine and Second Affiliated Hospital of Heilongjiang University of Chinese Medicine with permission number HZYEYLP2014. Written informed consent will be obtained from all study participants prior to enrollment. Author JHY will approach potential participants and invite them to participate in the study, and author CRL will ask them to complete the consent process.

Eligible patients will be randomized in a ratio of 1:1 to the treatment group (moxibustion plus dressing) and control group (dressing), and receive treatment for four weeks. Patients will be followed up for three months (Figure 1, Table 1). Outcome measures will be assessed at baseline, as well as at the end of the second and fourth week after randomization, and at one and three months after treatment cessation. Results will be analyzed by professionals blinded to the group allocation. This protocol has been registered with the Chinese Clinical Trials Register, a registry in the World Health Organization (WHO) Registry Network.

Eligibility

Inclusion Criteria

Participants will be included if they fulfill the following criteria: (1) aged 18 to 75

years; (2) pressure ulcers belonging to stage II or III according to the EPUAP/NPUAP guidelines [3]; and (3) at least one pressure ulcer.

Exclusion criteria

Patients with any of the following conditions will be excluded because of safety concerns and possible sensation loss interfering with evaluation of pain intensity: (1) undergoing other therapies that might interfere with the ability to heal, such as corticosteroid therapy, radiation therapy, or chemotherapy for cancer; (2) infected pressure ulcers; (3) complications of diabetes mellitus; and (4) severe diseases, such as liver, cardiac, and kidney diseases, and relevant serious complications.

Randomization and allocation concealment

In this trial, randomization will be performed at the Good Clinical Practice (GCP) Center of Second Affiliated Hospital of Heilongjiang University of Chinese Medicine. Thirty participants who meet the eligibility criteria will be assigned in a ratio of 1:1 to the treatment group and control group. Patients will be randomized using a computerized number generator through the stratified block randomization method of the Statistical Analysis System (SAS) package (Version 9.1.3; SAS Institute Inc., Cary, North Carolina, USA) by a statistician with no clinical involvement in this trial. The allocation will be concealed in sequentially numbered, opaque, sealed envelopes containing the randomization assignments. Allocation concealment will be broken only after the participant has met all selection criteria and completed the baseline assessments. The participants will know the allocated group, but the outcome assessors and data analysts will be masked to the intervention allocation [19].

Blinding

In moxibustion research, it is not feasible to conceal allocation from the practitioners. In addition, it is not possible to prevent participants from knowing if they have received moxibustion treatment or dressing intervention, or both. The treatment and assessment will be performed independently. The outcome assessors and the data

statistical analysts will be blinded to treatment allocation throughout the study.

Intervention

Treatment group (moxibustion plus dressing)

The participants receiving moxibustion treatment will be treated indirectly at a distance of 2 to 3 cm from the wound surface for 30 minutes per session, one session daily, five sessions weekly for four weeks. In addition, a dressing will be applied in one session daily, five sessions weekly for four weeks.

Control group (dressing)

The format of the dressing intervention will be the same as in the treatment group.

Outcome measures

The wound surface area (WSA), proportion of ulcers healed within trial period (PUHTP), Pressure Ulcer Scale for Healing (PUSH Tool), and Visual Analogue Scale (VAS) will be the outcomes used to assess efficacy. Adverse events will be recorded to assess safety.

Primary outcomes

1) Wound surface area

The WSA [20] of the pressure ulcers will be measured by the use of acetate tracing and subsequent planimetric determination. Ulcer tracings will be accomplished by outlining the pressure ulcer circumference onto a transparent film applied directly over the wound. Each ulcer will be traced three times by two assessors, respectively, in order to improve the accuracy of these tracings. A third assessor will determine the ulcer surface area from the wound tracing using a planimeter (KP-21C). All three assessors will be blinded to the identities of the patients and to the treatment group assignments.

2) Proportion of ulcers healed within trial period

Completely healed ulcers will be defined as 100% epithelization or skin closure without drainage [20].

Secondary outcomes

1) Pressure Ulcer Scale for Healing

The PUSH Tool [21] was developed by the NPUAP as a quick, reliable tool to monitor the change in pressure ulcer status. This tool categorizes ulcers with respect to surface area, exudate, and type of wound tissue. Subscores for each of these ulcer characteristics will be recorded, and then added to obtain the total score. A comparison of total scores measured over time provides an indication of the improvement or deterioration in pressure ulcer healing.

2) Visual Analogue Scale

The pain intensity of pressure ulcers will be assessed using the 100-mm VAS (0, absence of pain; 100, the worst pain of imaginable) [22, 23]. In order to evaluate the clinical severity and impact on activities of daily life in patients with bedsores, the VAS is selected as a secondary outcome measurement.

Statistical methods

Sample Size

Although several studies have investigated the effects of moxibustion on pressure ulcers, no RCTs have assessed the effects of moxibustion on pressure ulcers. There is no previous study on which to base the sample size calculation. Therefore, this pilot study will evaluate the efficacy and safety of moxibustion and feasibility of clinical trials. Taking into account the minimum number of subjects necessary to evaluate the efficacy of moxibustion, this pilot study will include 36 participants (18 in each group) with an expected dropout rate of 20% [24].

Statistical analysis

Data will be analyzed by a statistician blinded to the group allocations using the

Statistical Package for the Social Sciences (SPSS) 17.0 statistical software package. Significant levels will be reported at $P < 0.05$. Data analysis of baseline characteristics and of primary and secondary outcomes will be based on the intention-to-treat (ITT) principle. If an adjustment for possible baseline incomparability is needed, analysis of covariance will be conducted. If the measurement data of WSA, PUSH, and VAS have non-normal distributions, the Wilcoxon rank sum test will be used. If the measurement data have normal distributions, the *t*-test will be used. In the case of proportions, the chi-square or Fisher exact test will be applied (e.g., PUHTP).

Patient safety

Any adverse events (known as unfavorable or unintended signs, symptoms, or diseases occurring after treatment) related to moxibustion treatment will be observed and reported by patients and practitioners during each patient visit. In addition, all vital signs and adverse events will be measured and recorded at each visit.

Quality control

All staff will be required to undergo special training before participating in the trial. For example, staff will be trained to select participants and to conduct the moxibustion intervention. The monitors will check study protocol compliance and informed consent documents, and assess the progress of the study, including participant recruitment, moxibustion intervention, and data quality, at each center once a month. Dropouts and withdrawals from the study will be recorded through the intervention and follow-up periods.

Ethics

Written informed consent will be obtained from each participant. This study is approved by the ethics review boards of First Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine and Second Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine.

Discussion

The objective of this study is to evaluate the effectiveness and safety of moxibustion for treating pressure ulcers. We designed this study to determine the efficacy and safety of moxibustion in the treatment group (moxibustion plus dressing) versus the control group (dressing). The results of this study will determine if moxibustion is an effective therapy for pressure ulcers.

The outcomes of WSA, PUHTP, PUSH Tool, and VAS are well-evaluated pressure ulcers. This pilot study will provide data on the efficacy of moxibustion for pressure ulcers through a follow-up period of three months after the completion of the treatment. An assessment of these outcomes will also be needed in a future, long-term, clinical trial.

In addition to appropriate outcome measures, the use of an appropriate control group is a critical issue in designing a high quality clinical trial. The purpose of this study is to clarify whether moxibustion is effective in patients with pressure ulcers, and we have planned a pragmatic design using a dressing intervention in the control group. This pragmatic trial comparing moxibustion plus dressing with dressing alone can provide evidence focused on the effectiveness of moxibustion.

In conclusion, this pilot, assessor- and analyst-blinded, multicenter RCT will investigate the efficacy and safety of moxibustion for pressure ulcers, assess the feasibility and relevance of a moxibustion therapy study design, and provide a clinical foundation for future, large-scale, multicenter clinical trials.

Trial status

The trial is currently recruiting subjects.

List of abbreviations

ChiCtr: Chinese Clinical Trials Register; EPUAP/NPUAP: European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel; RCT: randomized controlled trial; GCP: Good Clinical Practice; WSA: Wound surface area; PUHTP: Proportion of ulcers healed within trial period; PUSH Tool: Pressure Ulcer Scale for Healing; VAS: Visual Analogue Scale; ITT: intention-to-treat.

Acknowledgements

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Author's contributions

JHY and QHZ contributed equally to this work. QHZ and ZRS conceived the study, designed the study protocol. JHY and CRL drafted the manuscript. QHZ and ZRS sought funding and ethical approval. All authors contributed to the further writing of the manuscript as well as read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Figure 1: Flow Chart of Study Process

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Table 1 Time of visits and data collection

	-1 week	0 week	2 weeks	4 weeks	1 month	3 months
	Baseline	Treatment phase			Follow-up phase (End-of-treatment)	
Patients						
Informed consent	×					
Sign the informed consent		×				
Medical history	×					
Physical examination	×					
Randomization		×				
Intervention						
Treatment group (n = 18)		20 sessions of moxibustion plus dressing				
Comparison						
Control group (n = 18)		20 sessions of dressing				
Outcomes[a]						
WSA		×	×	×	×	×
PUHTP		×	×	×	×	×
PUSH Tool		×	×	×	×	×
VAS		×	×	×	×	×
Participant safety						
Adverse events		×	×	×	×	×

a. WSA: Wound surface area; PUHTP: Proportion of ulcers healed within trial period; PUSH Tool: Pressure Ulcer Scale for Healing; VAS: Visual Analogue Scale.

Moxibustion for the treatment of pressure ulcers: Study protocol for a pilot, multicenter, randomized controlled trial

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Abstract

Introduction: Pressure ulcers are common in the elderly and immobile. Currently, there are few proven effective treatments for pressure ulcers. This trial aims to evaluate the feasibility efficacy, and safety of moxibustion for pressure ulcers.

Methods/analysis: This is a multicenter, two-armed, parallel-design, randomized controlled trial (RCT). Thirty eligible patients with pressure ulcers will be randomized in a ratio of 1:1 to the treatment group and control group. The participants in the treatment group will undergo indirect moxibustion for 30 minutes before application of a dressing, one session daily, five sessions weekly for four weeks. The patients in the control group will only receive a dressing, applied in the same way as in the treatment group. Both groups will be followed up for three months. The primary outcome measures will be wound surface area (WSA) and proportion of ulcers healed within trial period (PUHTP). The secondary outcomes will be the Pressure Ulcer Scale for Healing (PUSH Tool), Visual Analogue Scale (VAS), and adverse events. All outcomes will be evaluated at the beginning of the study, at the end of the second week, at four weeks after randomization, and at one and three months after treatment cessation.

Ethics/dissemination: This trial has undergone ethical scrutiny and been approved by the ethics review boards of First Affiliated Hospital of Heilongjiang University of Chinese Medicine and Second Affiliated Hospital of Heilongjiang University of Chinese Medicine (Permission number: HZYEYLP2014). The results of this study will provide clinical evidence for the feasibility, efficacy, and safety of moxibustion for pressure ulcers.

Trial registration number: ChiCTR-TRC-13003959

Keywords: moxibustion; pressure ulcers; bedsores; randomized controlled trial

Background

A pressure ulcer (i.e., bedsore, pressure sore, decubitus ulcer) is defined as a localized injury to the skin and underlying tissue layers affecting the muscle, tendon, and bone as a result of constant pressure due to impaired mobility [1, 2]. Pressure ulcers are often caused by pressure, shear, friction, or a combination of these [3]. Common sites for pressure ulcers include the back of the head, shoulder blade, elbow, lower back, hip, pelvic bone, ankle, and heel [4]. Pressure ulcers are generally classified into four stages (stage I, II, III, and IV) according to the European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel guidelines (EPUAP/NPUAP) [3].

The prevalence of pressure ulcers across studies varied from 8.8% to 53.2% [5-8], and incidence rates ranged from 7% to 71.6% [7-10]. It had been estimated that the annual treatment cost of pressure ulcers ranged from GBP £1.4 to 2.1 billion, which was broadly equal to the total UK National Health Service expenditure on mental illness, or the total cost of community health services [11]. Effective and adequate prevention is an important issue for patients, clinicians, and policy makers.

Moxibustion is a popular and safe intervention used to manage various conditions, such as breech presentation [12], facial paralysis [13], chronic fatigue [14], knee osteoarthritis [15], and type 2 diabetes mellitus [16]. In addition, several previous studies reported that moxibustion has been found to be effective in treating pressure ulcers [17, 18]. However, most prior studies were case reports, case series, or clinical trials without a control group, resulting in poor quality of these studies. Considering these methodological flaws, we will conduct a multicenter RCT to investigate the effectiveness and safety of moxibustion. The results of this study will provide evidence for the feasibility of a large clinical trial, and yield data to determine the appropriate sample size for future large scale RCTs of moxibustion in patients with pressure ulcers.

Methods/Design

Objective

The primary objective of this study is to assess the feasibility of moxibustion treatment for pressure ulcers and obtain preliminary safety and efficacy data to inform a future, larger, randomized controlled trial in the same patient population.

Design

This is an assessor- and analyst-blinded, randomized, controlled clinical trial with two parallel arms. The trial will be conducted at two clinical centers in China: First Affiliated Hospital of Heilongjiang University of Chinese Medicine and Second Affiliated Hospital of Heilongjiang University of Chinese Medicine, between May 29, 2014, and December 31, 2016. This protocol has been approved by the ethics review boards of First Affiliated Hospital of Heilongjiang University of Chinese Medicine and Second Affiliated Hospital of Heilongjiang University of Chinese Medicine with permission number HZYEYLP2014. Written informed consent will be obtained from all study participants prior to enrollment.

Eligible patients will be randomized in a ratio of 1:1 to the treatment group (moxibustion plus dressing) and control group (dressing), and receive treatment for four weeks. Patients will be followed up for three months (Figure 1, Table 1). Outcome measures will be assessed at baseline, as well as at the end of the second and fourth week after randomization, and at one and three months after treatment cessation. Results will be analyzed by professionals blinded to the group allocation. This protocol has been registered with the Chinese Clinical Trials Register, a registry in the World Health Organization (WHO) Registry Network.

Eligibility

Inclusion Criteria

Participants will be included if they fulfill the following criteria: (1) aged 18 to 75 years; (2) pressure ulcers belonging to stage II or III according to the EPUAP/NPUAP guidelines [3]; and (3) at least one pressure ulcer and last two weeks.

Exclusion criteria

Patients with any of the following conditions will be excluded because of safety concerns and possible sensation loss interfering with evaluation of pain intensity: (1) undergoing other therapies that might interfere with the ability to heal, such as corticosteroid therapy, radiation therapy, or chemotherapy for cancer; (2) infected pressure ulcers; (3) complications of diabetes mellitus; and (4) severe diseases, such as liver, cardiac, and kidney diseases, and relevant serious complications.

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Blinding

In moxibustion research, it is not feasible to conceal allocation from the practitioners. In addition, it is not possible to prevent participants from knowing if they have received moxibustion treatment or dressing intervention, or both. The treatment and assessment will be performed independently. The outcome assessors and the data statistical analysts will be blinded to treatment allocation throughout the study.

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Treatment group (moxibustion plus dressing)

The participants receiving moxibustion treatment will be treated indirectly at a distance of 2 to 3 cm from the wound surface for 30 minutes per session, one session daily, five sessions weekly for four weeks. In addition, a dressing will be applied in one session daily, five sessions weekly for four weeks.

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The format of the dressing intervention will be the same as in the treatment group.

Outcome measures

The wound surface area (WSA), proportion of ulcers healed within trial period (PUHTP), Pressure Ulcer Scale for Healing (PUSH Tool), and Visual Analogue Scale (VAS) will be the outcomes used to assess efficacy. Adverse events will be recorded to assess safety.

Primary outcomes

1) Wound surface area

The WSA [20] of the pressure ulcers will be measured by the use of acetate tracing and subsequent planimetric determination. Ulcer tracings will be accomplished by outlining the pressure ulcer circumference onto a transparent film applied directly over the wound. Each ulcer will be traced three times by two assessors, respectively, in order to improve the accuracy of these tracings. A third assessor will determine the ulcer surface area from the wound tracing using a planimeter (KP-21C). All three assessors will be blinded to the identities of the patients and to the treatment group assignments.

2) Proportion of ulcers healed within trial period

Completely healed ulcers will be defined as 100% epithelization or skin closure without drainage [20].

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Statistical methods

Sample Size

Although several studies have investigated the effects of moxibustion on pressure ulcers, no RCTs have assessed the effects of moxibustion on pressure ulcers. There is no previous study on which to base the sample size calculation. Therefore, this pilot study will evaluate the efficacy and safety of moxibustion and feasibility of clinical trials. Taking into account the minimum number of subjects necessary to evaluate the efficacy of moxibustion, this pilot study will include 36 participants (18 in each group) with an expected dropout rate of 20% [24].

Statistical analysis

Data will be analyzed by a statistician blinded to the group allocations using the Statistical Package for the Social Sciences (SPSS) 17.0 statistical software package. Significant levels will be reported at $P < 0.05$. Data analysis of baseline

characteristics and of primary and secondary outcomes will be based on the intention-to-treat (ITT) principle. If an adjustment for possible baseline incomparability is needed, analysis of covariance will be conducted. If the measurement data of WSA, PUSH, and VAS have non-normal distributions, the Wilcoxon rank sum test will be used. If the measurement data have normal distributions, the *t*-test will be used. In the case of proportions, the chi-square or Fisher exact test will be applied (e.g., PUHTP).

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Written informed consent will be obtained from each participant. This study is approved by the ethics review boards of First Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine and Second Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine. The consent and ethics have approached by peer-review and ethics review board meeting at May 29, 2014.

Discussion

The objective of this study is to evaluate the effectiveness and safety of moxibustion for treating pressure ulcers. We designed this study to determine the efficacy and safety of moxibustion in the treatment group (moxibustion plus dressing) versus the control group (dressing). The results of this study will determine if moxibustion is an effective therapy for pressure ulcers.

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In addition to appropriate outcome measures, the use of an appropriate control group is a critical issue in designing a high quality clinical trial. The purpose of this study is to clarify whether moxibustion is effective in patients with pressure ulcers, and we have planned a pragmatic design using a dressing intervention in the control group. This pragmatic trial comparing moxibustion plus dressing with dressing alone can provide evidence focused on the effectiveness of moxibustion.

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Trial status

The trial is currently recruiting subjects.

List of abbreviations

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Author's contributions

JHY and QHZ contributed equally to this work. QHZ and ZRS conceived the study, designed the study protocol. JHY and CRL drafted the manuscript. QHZ and ZRS sought funding and ethical approval. All authors contributed to the further writing of the manuscript as well as read and approved the final manuscript.

Competing interests

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Table 1 Time of visits and data collection

	-1 week	0 week	2 weeks	4 weeks	1 month	3 months
	Baseline	Treatment phase			Follow-up phase (End-of-treatment)	
Patients						
Informed consent	×					
Sign the informed consent		×				
Medical history	×					
Physical examination	×					
Randomization		×				
Intervention						
Treatment group (n = 18)		20 sessions of moxibustion plus dressing				
Comparison						
Control group (n = 18)		20 sessions of dressing				
Outcomes[a]						
WSA		×	×	×	×	×
PUHTP		×	×	×	×	×
PUSH Tool		×	×	×	×	×
VAS		×	×	×	×	×
Participant safety						
Adverse events		×	×	×	×	×

a. WSA: Wound surface area; PUHTP: Proportion of ulcers healed within trial period; PUSH Tool: Pressure Ulcer Scale for Healing; VAS: Visual Analogue Scale.

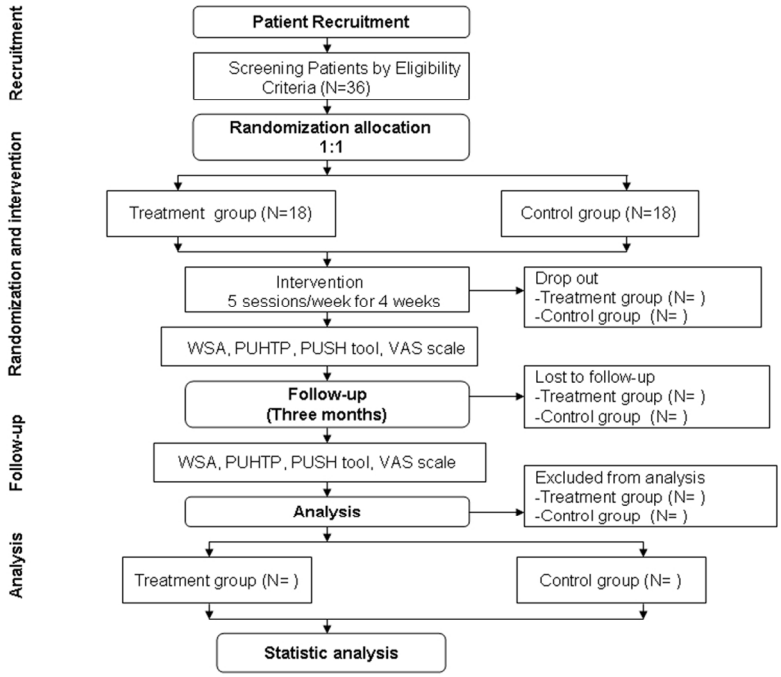

Figure 1 Flow chart of study process

Flow chart of study process
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