Author's response to reviews

Title: Baclofen for stroke patients with persistent hiccups: a randomized, double-blind, placebo-controlled trial

Authors:

Cuie Zhang (1469058419@qq.com)
Ruifen Zhang (2072631381@qq.com)
Shuangyan Zhang (zhangshuangyan2014@163.com)
Meiling Xu (2627830420@qq.com)
Shuyan Zhang (2519220577@qq.com)

Version: 2
Date: 10 May 2014

Author's response to reviews: see over
Dear Editors and Reviewers,

Thank you for your letter and for the reviewers’ comments concerning our manuscript entitled “Baclofen for stroke patients with persistent hiccups: a randomized, double-blind, placebo-controlled trial” (ID: 2068767632119005). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewers’ comments are as follows:

Responds to the Editorial comments:

Comment 1: “1. Please include the trial registration number at the end of your abstract. If your research article reports the results of a controlled health care intervention, please list your trial registry, along with the unique identifying number and the date that your trial was registered.”
Answer: Thanks for the editor’s excellent advice. We have added the trial registration number at the end of your abstract. (Referred to the Abstract section in red color).

Comment 2: “2. Please include a list of abbreviations used in the manuscript and their meanings, after your Conclusions.”
Answer: Thanks for the editor’s excellent suggestion. We have added the Abbreviations part after your Conclusions. (Referred to the Abbreviations part after Conclusions section in red color).

Comment 3: “3. Please include a figure title and legend section after the reference list. The figures should not be included in the main body of the manuscript.”
Answer: Thanks for the editor’s great suggestion. We have added figure title and legend section after the reference list. (Referred to the end of References list in red color).

Responds to the reviewers’ comments:

Reviewer 1:
Comment 1: “Minor Essential Revisions:
Abstract (Methods)
Study medication was administered immediately after randomization and then three times daily for 5 days. >> administered should be revised as administrated.”
Answer: Thanks for the reviewer’s excellent suggestion. We have rewritten this sentence. (Referred to the second sentence, Abstract (Methods) section in red color).

Comment 2: “Methods
Inclusion and exclusion criteria
Exclusion criteria included: persistent hiccups mainly associated with cancer or other unclear mechanisms; Rejection of baclofen therapy; and failed to accept the completion of clinical treatment. >> Rejection should be revised as rejection.”
Answer. Thanks for the reviewer’s good advice. We have changed “Rejection” to “rejection”. (Referred to the Inclusion and exclusion criteria Part, Methods Section in red color).

Comment 3: “Intervention
Participants recruited to the baclofen group received 10 mg there times daily at the beginning and it was continued for 5 days. Participants assigned to the placebo group received 10 mg there times daily for 5 days. >> there should be revised as three.”
Answer: We have changed “there” to “three”. (Referred to the Intervention Part, Methods Section in red color).

Comment 4: “Results
Paragraph 1: One hundred and eleven patients initially entered the study. >> eleven should be revised as thirteen.”
Answer: Thanks for the reviewer’s great suggestion, and we have changed “eleven” to “thirteen” (Referred to Paragraph 1, Results Section in red color).

Comment 5: “Paragraph 2:
No patient in the baclofen group had no any amelioration relieved in the symptom of persistent hiccups compared with eight in placebo group (RR, 0.06, 95% CI 0.00-0.94, p=0.04). >> patient should be revised as patients.”
Answer: We have changed “patient” to “patients”. (Referred to Paragraph 2, Results Section in red color).

Comment 6: “Discussion
Our results suggest baclofen 10 mg three times daily was an acceptable dose and concur with findings by Mirijello [13]. >> this sentence should be revised as” “Our results suggest that baclofen 10 mg three times daily was an acceptable dose and concur with findings by Mirijello [13].”
Answer: Thanks for the reviewer’s excellent advice. We have revised the original sentence to ‘Our results suggest that 10 mg baclofen three times daily was an acceptable dose, and concur with the findings of Mirijello [13].’ (Referred to Paragraph 2, Discussion Section in red color).

Reviewer 2:
Comment 7: “1. Is the question posed by the authors new and well defined?
Moretto EN, Wee B, Wiffen PJ, Murchison AG. Interventions for treating persistent and intractable hiccups in adults.Cochrane Database of Systematic Reviews 2013, Issue 1. Art. No.: CD008768. DOI: 10.1002/14651858.CD008768.pub2. concluded that "There is insufficient evidence to guide the treatment of persistent or intractable hiccups with either pharmacological or non-pharmacological interventions. The paucity of high quality studies indicate a need for randomized placebo-controlled trials of both pharmacological and nonpharmacological treatments. As the symptom is relatively rare, trials would need to be multi-centred and possibly multi-national.” Hence the question posed by the authors whilst not new deserves attention. More effort is needed to define the question in the light of previous work eg referring to cochrane reviews’”
**Answer:** Thanks for the reviewer’s excellent comment. We have responded this excellent comment in the **Background section** (*Paragraph 3, Background Section in red color*).

**Comment 8:** “2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?
There should be more specific inclusion and exclusion criteria for example, what is the definition of “persistent hiccups after stroke” is it >=48 hours prior to randomisation or >=48 hours after stroke onset?
**Answer:** Thanks for the reviewer’s very excellent comment. We have revised and added the specification and details into the inclusion and exclusion section. (**Referred to Inclusion and exclusion criteria, Methods Section in red color**).

There is also inadequate description of the trial medications - how was the placebo manufactured and what was it composed of?

**Answer:** Thanks for the reviewer’s great suggestion. We have added the description of placebo manufactured and composed of it in the **Intervention** section. (**Referred to Intervention, Methods Section in red color**).

the choice of outcome measures should be better described and justified – are the outcomes used conventional, have they been validated? what is the reliability?”

**Answer:** Thanks for the reviewer’s excellent advice. The outcome measures we have chosen, according to the standard criteria of Chinese Medicine Medical Association which has been validated. (**Referred to Assessments, Methods Section in red color**).

**Comment 9:** “3. Are the data sound and well controlled?
As this is a small study, confounders are likely and the omission of any details of the stroke and co-morbidities is of concern - what was the stroke subtype(s), duration, severity etc; did the groups differ in vascular risk factors, concomitant medications etc
The survey results were not reported in any detail. This should be rectified.
The lack of any adverse events is disturbing - whilst serious adverse events may be absent given the short trial duration, the lack of any adverse events suggests that either the patients were remarkably well or that there is some misunderstanding as to how AEs are defined”

**Answer:** Thanks for the reviewer’s excellent comment. We have added the details of the stroke and hiccups. In addition, we have also added adverse events, although they were mild. (**Referred to the second and fourth paragraphs, Section Results in red color**).

**Comment 10:** “4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
the authors should state that they have complied with the CONSORT guidelines (http://www.consort-statement.org/). As so many patients did not meet inclusion criteria, it would be important to list the reasons. also as the study was conducted over 15 months and only 113 patients were assessed for eligibility, it would be important to ascertain how many were screened - clearly hiccups after stroke is not common and such data would allow better planning for larger trials”
**Answer**: We have stated that this study complied with the CONSORT guidelines in study design section. In addition, we have also listed the reasons of exclusion in Figure 1 and paragraph 1 of the Results section. *(Referred to Part Study design, Methods Section; and Figure 1 and Paragraph 1, Section Results in red color)*.

**Comment 11**: “5. Are the discussion and conclusions well balanced and adequately supported by the data? lack of further details on the patient casemix (see above) hampers the discussion”

**Answer**: We have added some details in the Discussion section *(Referred to Paragraph 3, Discussion Section in red color)*.

**Comment 12**: “6. Do the title and abstract accurately convey what has been found?”

**Answer**: Thanks for the reviewer’s excellent comment.

**Comment 13**: “7. Is the writing acceptable? the authors should seek advice on english usage - there are a number of grammatical errors and certain terms would be better re-phrased eg "null and void" as an outcome might be "no effect"; "yellow" for ethnicity might be "Han Chinese"”

**Answer**: Thanks for the reviewer’s excellent advice. We have asked a local native speaker to revise the grammatical errors and certain terms *(Marked in red color in the text)*

**Comment 14**: “All the above would be Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)”

**Answer**: Thanks for the reviewer’s valuable and very helpful comment. We have responded all the above comments in the revised manuscript *(Marked in red color in the text)*.

**Specific comments (numbers in reviewer section indicate lines in the original manuscript):**

**Original Manuscript**: 16&17—page 2: Results of preclinical studies suggest that baclofen may be useful in treatment of stroke patients with persistent hiccups.

**Answer**: ‘The results’ instead ‘Results’ before of preclinical studies suggest’;

Insert ‘the’ between ‘may be useful in’ and ‘treatment of stroke patients with persistent hiccups’.

**Original Manuscript**: 17&18—page 2: This study was aimed at assessing the possible efficacy of baclofen for treatment of persistent hiccups after stroke.

**Answer**: ‘to assess’ instead ‘at assessing’ between ‘This study was aimed’ and ‘the possible efficacy’;

Insert ‘the’ between ‘the possible efficacy of baclofen for’ and ‘treatment of persistent hiccups after stroke.’.

**Original Manuscript**: 19&20—page 2: A total of 30 persistent hiccups after stroke were randomly assigned to receive baclofen (n=15) or placebo (n=15) in a double-blind, parallel group trial.
Answer: ‘stroke patients with persistent hiccups’ instead ‘persistent hiccups after stroke’ between ‘A total of 30’ and ‘were randomly assigned to receive baclofen (n=15) or placebo (n=15)’;

Insert a space on either side of “=” in the “baclofen (n=15) or placebo (n=15)”;

Insert ‘a’ between ‘baclofen (n=15) or’ and ‘placebo (n=15)’.

Original Manuscript: 20&21—page 2: Study medication was administered immediately after randomization and then three times daily for 5 days.

Answer: ‘Participants in the baclofen group received 10 mg baclofen three times daily for 5 days. Participants assigned to the placebo group received 10 mg placebo three times daily for 5 days.’ instead ‘Study medication was administered immediately after randomization and then three times daily for 5 days.’

Original Manuscript: 22&23—page 2: The primary outcome measure was persistent hiccups cessation. Secondary outcome measures included the total efficacy, improvement, and null and void of persistent hiccups.

Answer: ‘cessation of hiccups’ instead ‘persistent hiccups cessation’;

‘efficacy in the two groups and adverse events.’ instead ‘the total efficacy, improvement, and null and void of persistent hiccups.’ after ‘Secondary outcome measures included’.

Original Manuscript: 24—page 2: Results: Thirty patients completed the study.

Answer: ‘All 30’ instead ‘Thirty’ before ‘patients completed the study’.

Original Manuscript: 24-28—page 2: When baclofen was compared with placebo, significant difference in favor of cessation of hiccups (Relative Risk (RR) 7.00, 95% confidence interval (CI) 1.91-25.62, p=0.003). The same findings applied to the total efficacy of baclofen when compared with placebo (RR, 2.07, 95% CI 1.22-3.51, p= 0.007). With respect to safety, no adverse events were documented.

Answer: ‘The number of patients in whom the hiccups completely stopped was higher in the baclofen group than in the placebo group (relative risk, 7.00; 95% confidence interval: 1.91–25.62, P = 0.003). Furthermore, efficacy was higher in the baclofen group than in the placebo group (P< 0.01). No serious adverse events were documented in either group. One case each of mild transient drowsiness and dizziness was present in the baclofen group.’ instead ‘When baclofen was compared with placebo, significant difference in favor of cessation of hiccups (Relative Risk (RR) 7.00, 95% confidence interval (CI) 1.91-25.62, p=0.003). The same findings applied to the total efficacy of baclofen when compared with placebo (RR, 2.07, 95% CI 1.22-3.51, p= 0.007). With respect to safety, no adverse events were documented.’.

Original Manuscript: 29&30—page 2: Conclusions: In summary we demonstrated that baclofen was more effective than placebo for stroke patients with persistent hiccups.

Answer: ‘Baclofen was more effective than a placebo for the treatment of persistent hiccups in stroke patients.’ instead ‘In summary we demonstrated that baclofen was more effective than placebo for stroke patients with persistent hiccups.’;

Insert ‘Trial registration: Chinese Clinical Trials Register: ChiCTR-TRC-13004554’ after ‘Conclusions: In summary we demonstrated that baclofen was more effective than placebo
for stroke patients with persistent hiccups.’.

Original Manuscript: 31—page 2: Keywords: Baclofen; Stroke; hiccups: Randomized controlled trial
Answer: ‘Hiccups;’ instead ‘hiccups;’ between ‘Stroke;’ and ‘Randomized controlled trial’.

Original Manuscript: 33&34—page 3: Hiccups are caused by involuntary multiple spastic contractions of the diaphragm and intercostal muscles.
Answer: ‘Hiccups’ instead ‘Hiccups’ before ‘are caused by involuntary multiple spastic contractions of the diaphragm and intercostal muscles.’.

Original Manuscript: 34-36—page 3: This action is rapidly accompanied by uncontrollable inhalation and a sudden closure of the respiratory tract by the epiglottis, resulting in the classic “hic” sound [1, 2].
Answer: ‘with’ instead ‘by’ between ‘This action is rapidly accompanied’ and ‘uncontrollable inhalation’.

Original Manuscript: 38-40—page 3: They often classified under three categories dependent on the episode duration, such as acute, and persistent and intractable hiccups.
Answer: ‘Hiccups are’ instead ‘They often’ before ‘classified under three categories’;
‘depending on their duration: acute, persistent, and intractable hiccups.’ instead ‘dependent on the episode duration, such as acute, and persistent and intractable hiccups.’ after ‘They often classified under three categories’.

Original Manuscript: 40-42—page 3: Acute hiccups defined as the episode lasts for minutes to hours; persistent hiccups involves the episode lasts for more than 48 hours; and intractable hiccups last for more than one month.
Answer: Insert ‘are’ between ‘Acute hiccups’ and ‘defined as’;
‘a hiccupping episode that’ instead ‘the episode’ between ‘Acute hiccups defined as’ and ‘lasts for minutes to hours’;
Delete ‘involves the episode’ between ‘persistent hiccups’ and ‘lasts for more than 48 hours’.

Original Manuscript: 42&43—page 3: They not only confined to the adults but also observed among the infants [3, 4] and children [5].
Answer: ‘Hiccups are’ instead ‘They’ before ‘not only confined to the adults’;
Insert ‘are’ between ‘but’ and ‘observed among the infants [3, 4]’;
Delete ‘the’ between ‘also observed among’ and ‘infants [3, 4] and children [5].’.

Original Manuscript: 45-47—page 3: Some of the most complications encountered in the practice include pressure ulcers [6-8], depression [9], motor disability [10], insomnia [11], and hiccups [12].
Answer: ‘commonly encountered’ complications in clinical’ instead ‘complications encountered in the’ between ‘Some of the most’ and ‘practice include pressure ulcers [6-8]’.
‘—’ Instead ‘-‘ between ‘6’ and ‘8’ of ‘pressure ulcers [6-8]’.

**Original Manuscript:** 48-50—page 3: A wide range of pharmacological interventions has been used to treat persistent and intractable hiccups, such as baclofen [13-15], gabapentin [16], chlorpromazine [17], haloperidol [18], metoclopramide [19] and so on.

**Answer:** ‘—’ instead ‘-‘ between ‘13’ and ‘15’ of ‘baclofen [13–15]’;

‘and metoclopramide [19]’ instead ‘metoclopramide [19] and so on’ after ‘such as baclofen [13-15], gabapentin [16], chlorpromazine [17], haloperidol [18],’.

**Original Manuscript:** 50&51—page 3: Several clinical studies support the idea that baclofen may help for maintaining hiccups after stroke [13-15].

**Answer:** ‘have reported’ Instead ‘support the idea’ between ‘Several clinical studies’ and ‘that baclofen may help’;

‘treat persistent hiccups occurring after a stroke [13–15].’ instead ‘for maintaining hiccups after stroke [13-15].’ After ‘Several clinical studies support the idea that baclofen may help’;

Insert ‘Although a Cochrane systematic review found that no sufficient evidence for the treatment of persistent or intractable hiccups with either pharmacological or non-pharmacological interventions, all four included studies in the review had focused on acupuncture, and not baclofen, or even other pharmacological interventions [20].’ After ‘Several clinical studies support the idea that baclofen may help for maintaining hiccups after stroke [13-15].’

**Original Manuscript:** 51-53—page 3: To the best of our knowledge, there are few randomized controlled trials and only with minor sample that has evaluated the efficacy of baclofen for persistent hiccups after stroke.

**Answer:** ‘only a’ instead ‘there are’ between ‘To the best of our knowledge,’ and ‘few randomized controlled trials’;

‘small sample sizes have’ instead ‘minor sample that has’ between ‘few randomized controlled trials with’ and ‘evaluated the efficacy of baclofen for persistent hiccups after stroke.’

**Original Manuscript:** 54&55—page 3: We conducted a randomized, double blind, placebo-controlled, 5-day clinical trial to evaluate the possible benefit of baclofen in maintaining persistent hiccups after stroke.

**Answer:** Insert ‘-‘ between ‘double’ and ‘blind’;

‘treatment’ instead ‘maintaining’ between ‘the possible benefit of baclofen in’ and ‘persistent hiccups after stroke.’

**Original Manuscript:** 58&59—page 4: **Methods**

**Design**

**Answer:** ‘Study design’ Instead ‘Design’ after ‘Methods’.

**Original Manuscript:** 60—page 4: This study was a two parallel arm blinded randomized controlled trial.

**Answer:** Insert ‘-‘ between ‘two’ and ‘parallel’;
Insert ‘;’ between ‘arm’ and ‘blinded’;

Insert ‘;’ between ‘blinded’ and ‘randomized controlled trial’.

**Original Manuscript**: 60-64—page 4: The trial conducted at the clinical research center in China in accordance with the Declaration of Helsinki and the Guidelines for Good Clinical Practice: the Evidence-Based Medicine Center of the Fourth affiliated hospital of Harbin Medical University. Inclusion took place between August 2012 and November 2013.

**Answer**: ‘was conducted’ instead ‘conducted at the clinical research center in China’ between ‘The trial’ and ‘in accordance with the Declaration of Helsinki and the Guidelines for Good Clinical Practice’;

‘at’ instead ‘:’ between ‘Good Clinical Practice’ and ‘the Evidence-Based Medicine Center’;

‘Affiliated Hospital’ instead ‘affiliated hospital’ between ‘the Fourth’ and ‘of Harbin Medical University’;

Insert ‘, a clinical research center in China’ between ‘the Fourth affiliated hospital of Harbin Medical University’ and ‘.’;

‘Patients were recruited’ instead ‘Inclusion took place’ before ‘between August 2012 and November 2013’.

**Original Manuscript**: 64&65—page 4: The study was approved by the Medical Ethical Committee of the Fourth affiliated hospital of Harbin Medical University.

**Answer**: ‘Ethics’ instead ‘Ethical’ between ‘the Medical’ and ‘Committee of the Fourth affiliated hospital of Harbin Medical University.’;

‘Affiliated Hospital’ instead ‘affiliated hospital’ between ‘the Fourth’ and ‘of Harbin Medical University’.

**Original Manuscript**: 65-67—page 4: Eligibility participants were randomly allocated into the baclofen group or the placebo group at a 1:1 allocation ratio and received treatment for 5 days, with 15 days of follow-up.

**Answer**: ‘Eligible’ instead ‘Eligibility’ before ‘participants were randomly allocated into’;

‘to’ instead ‘into’ between ‘Eligibility participants were randomly allocated’ and ‘the baclofen group or the placebo group’;

Insert ‘This study complied with CONSORT guidelines.’ after ‘Eligibility participants were randomly allocated into the baclofen group or the placebo group at a 1:1 allocation ratio and received treatment for 5 days, with 15 days of follow-up.’.

**Original Manuscript**: 68—page 4: *Inclusion and exclusion criteria*

**Answer**: ‘*Inclusion and exclusion criteria’ instead ‘Inclusion and exclusion criteria’.

**Original Manuscript**: 69—page 4: We included participants aged 18-65 years with persistent hiccups after stroke.

**Answer**: ‘–’ instead ‘:’ between ‘18’ and ‘65’ of ‘18-65 years’;

Insert ‘(more than 48 hours but less than 1 month)’ between ‘We included participants aged 18-65 years with persistent hiccups’ and ‘after stroke’.
**Original Manuscript**: 69-71—page 4: In addition, no baclofen was taken within the last 15 days prior to study entry; and informed consent document has been signed.

**Answer**: ‘participants were required to not have taken baclofen within’ instead ‘no baclofen was taken within the last’ between ‘In addition,’ and ‘15 days’;

‘and were required to sign an informed consent form’ instead ‘; and informed consent document has been signed’ between ‘15 days prior to study entry’ and ‘.’.

**Original Manuscript**: 71-73—page 4: Exclusion criteria included: persistent hiccups mainly associated with cancer or other unclear mechanisms; Rejection of baclofen therapy; and failed to accept the completion of clinical treatment.

**Answer**: ‘The exclusion’ instead ‘Exclusion’ before ‘criteria included’;

Delete ‘; between ‘Exclusion criteria included’ and ‘persistent hiccups’;

cancer [21], multiple sclerosis [22], meningitis [23], brain abscess [24], traumatic brain injury [25], encephalitis [26], spinal cord lesions [27], kidney failure [28], pneumonia [29], laryngitis [30], and cardiopulmonary arrest [31]; instead ‘cancer or other unclear mechanisms’ between ‘persistent hiccups mainly associated with’ and ‘Rejection of baclofen therapy’;

‘rejection’ instead ‘Rejection’ before ‘of baclofen therapy’;

‘failure to complete’ instead ‘failed to accept the completion of’ between ‘and’ and ‘clinical treatment.’.

**Original Manuscript**: 74—page 4: Randomization

**Answer**: ‘Randomization’ instead ‘Randomization’.

**Original Manuscript**: 75—page 4: Randomisation was computer generated, and concealed in opaque sealed envelopes.

**Answer**: ‘Randomization was performed using a computer, and group allocation instructions were’ instead ‘Randomisation was computer generated, and’ before ‘concealed in opaque sealed envelopes’.

**Original Manuscript**: 76&77—page 4: Participants were allocated to a study group baclofen or placebo by the practitioner taking the next sequentially numbered envelope.

**Answer**: ‘For assignment to the baclofen or placebo group, participants were required to select one of the sequentially numbered envelopes’ instead ‘Participants were allocated to a study group baclofen or placebo by the practitioner taking the next sequentially numbered envelope’.

**Original Manuscript**: 78—page 4: Participants and recruitment

**Answer**: ‘Participants and recruitment’ instead ‘Participants and recruitment’.

**Original Manuscript**: 79&80—page 4: The plan was to conduct the research in the Fourth affiliated hospital of Harbin Medical University.

**Answer**: ‘We planned’ instead ‘The plan was’ before ‘to conduct the research’;

‘our’ instead ‘the’ between ‘conduct’ and ‘research in the Fourth affiliated hospital of Harbin Medical University’.
‘Affiliated Hospital’ instead ‘affiliated hospital’ between ‘the Fourth’ and ‘of Harbin Medical University.’.

Original Manuscript: 80&81—page 4: In preparing for this research, we identified that this center offered baclofen or placebo treatment to 30 people between August 2012 and November 2013.
Answer: Insert ‘had’ between ‘this center’ and ‘offered baclofen or placebo treatment’.

Original Manuscript: 81-83—page 4: This enabled a fair test of the feasibility criteria and, if recruitment was good, potentially permitted a reliable calculation of the effect size of the intervention for computing the later sample size.
Answer: ‘, and’ instead ‘and,’ between ‘This enabled a fair test of the feasibility criteria’ and ‘if recruitment was good,’;
‘subsequent’ instead ‘later’ between ‘the effect size of the intervention for computing the’ and ‘sample size.’.

Original Manuscript: 84&85—page 4&5: Those individuals who were accepted for baclofen treatment were informed about the research and given an information sheet.
Answer: ‘elected to undergo’ instead ‘were accepted for’ between ‘Those individuals who’ and ‘baclofen treatment were informed’.

Original Manuscript: 85&86—page 5: For those agreeing to participate, consent was taken at the next appointment.
Answer: ‘From’ instead ‘For’ before ‘those agreeing to participate,’;
‘agreed’ instead ‘agreeing’ between ‘For those’ and ‘to participate,’.

Original Manuscript: 86-88—page 5: After the clinical assessment, participants were randomized to receive the baclofen or placebo, which delivered by the service’s therapists, all of whom were trained in its delivery.
Answer: ‘baclofen or a placebo, both of which were given by therapists, who were trained in their administration.’ instead ‘the baclofen or placebo, which delivered by the service’s therapists, all of whom were trained in its delivery.’ after ‘After the clinical assessment, participants were randomized to receive’.

Original Manuscript: 89—page 5: Intervention

Original Manuscript: 90&91—page 5: The comparison groups were baclofen and placebo. Participants recruited to the baclofen group received 10 mg there times daily at the beginning and it was continued for 5 days.
Answer: Delete ‘The comparison groups were baclofen and placebo.’ before ‘Participants recruited to the baclofen group received 10 mg there times daily at the beginning and it was continued for 5 days.’;
‘three’ instead ‘there’ between ‘10 mg’ and ‘times daily’;
Delete ‘at the beginning and it was continued’ between ‘10 mg three times daily’ and ‘for 5 days.’.

Original Manuscript: 92—page 5: Participants assigned to the placebo group received 10 mg there times daily for 5 days.
Answer: ‘of a placebo three’ instead ‘there’ between ‘10 mg’ and ‘times daily for 5 days’.

Original Manuscript: 93&94—page 5: Participants were then asked to identify obstacles to the goal attainment and consider the possibility that therapy could help them overcome these obstacles.
Answer: ‘The participants’ instead ‘Participants’ before ‘were then asked to identify obstacles’;
Insert ‘any’ between ‘asked to identify’ and ‘to the goal attainment’;
Insert ‘the’ between ‘consider the possibility that’ and ‘therapy could help them overcome these obstacles.’.

Original Manuscript: 94&95—page 5: This was intended to enhance participants’ motivation to engage in therapy.
Answer: ‘motivate the participants to engage in the’ instead ‘enhance participants’ motivation to engage in’ between ‘This was intended to’ and ‘therapy.’
Insert a new paragraph of ‘The placebo tablets used in this study were composed of hydroxypropyl cellulose, pregelatinized starch, dextrin, starch, silicon dioxide, magnesium stearate, sodium carboxymethyl starch, sucrose, talcum powder, gelatin, silicone oil, and Chinese wax. The tablets were produced by Changzhou Siyao Pharmaceuticals Co. Ltd. and had the same dose, taste, and color as baclofen.’ after ‘his was intended to enhance participants’ motivation to engage in therapy.’

Original Manuscript: 96—page 5: Assessments

Original Manuscript: 97—page 5: The achieved outcomes were assessed with the following criteria [12].
Answer: ‘Patients outcomes were evaluated using the Chinese Medicine Medical Association standard criteria [12] and classified as follows’ instead ‘The achieved outcomes were assessed with the following criteria [12]’.

Original Manuscript: 97-101—page 5: Cured: Cessation of persistent hiccups within intervention period, with no relapse in one week; Improved: Reduction in the frequency, severity, and other morbid conditions (such as abdominal discomfort); Null and void: No any amelioration relieved in the symptom of hiccups. Total efficacy included the persistent hiccups cured and improved.
Answer: ‘cure: cessation’ instead ‘Cured: Cessation’ before ‘of persistent hiccups within intervention period’;
Insert ‘the’ between ‘within’ and ‘intervention period’;
‘improvement: reduction’ instead ‘Improved: Reduction’ before ‘in the frequency,’;
‘and severity of hiccups’ instead ‘, severity,’ between ‘frequency’ and ‘and other morbid conditions’;
‘symptoms’ instead ‘morbidity conditions’ between ‘and other’ and ‘(such as abdominal discomfort);’
‘and no effect: no amelioration of hiccups.’ instead ‘Null and void: No any amelioration relieved in the symptom of hiccups.’ before ‘Total efficacy included the persistent hiccups cured and improved.’;
Delete ‘Total efficacy included the persistent hiccups cured and improved.’.

**Original Manuscript:** 102—page 5: **Data collection and analysis**
**Answer:** ‘**Data collection and analysis**’ instead ‘Data collection and analysis’.

**Original Manuscript:** 103&104—page 5: Clinical outcomes included cessation of persistent hiccups within intervention period, hiccups improvement and null and void.
**Answer:** ‘In addition to the clinical outcomes, the efficacy and side effects in the two groups were recorded and analyzed.’ instead ‘Clinical outcomes included cessation of persistent hiccups within intervention period, hiccups improvement and null and void.’.

**Original Manuscript:** 104-106—page 5: We collected data on the number of eligible participants with persistent hiccups, willingness of participants to be randomized, compliance with intervention and aimed to estimate the effect size for a fully powered trial.
**Answer:** Insert ‘the’ between ‘willingness of’ and ‘participants to be randomized,’;
Insert ‘and’ between ‘willingness of participants to be randomized,’ and ‘compliance with intervention’;
Insert ‘the’ between ‘compliance with’ and ‘intervention’;
Insert ‘,’ between ‘compliance with intervention’ and ‘and aimed to estimate the effect size for a fully powered trial.’.

**Original Manuscript:** 107—page 5: **Sample size and analysis**
**Answer:** ‘**Sample size and analysis**’ instead ‘Sample size and analysis’.

**Original Manuscript:** 108&109—page 5: This was a feasibility study, and it was estimated that a sample of 30 participants would be sufficient to provide data to answer our study questions [20].
**Answer:** ‘feasibility study’ instead ‘was a feasibility study, and it was’ between ‘This’ and ‘estimated that a sample of 30 participants’;
‘[32]’ instead ‘[20]’ between ‘30 participants would be sufficient to provide data to answer our study questions’ and ‘.’.

**Original Manuscript:** 109-111—page 5&6: Clinical outcome data were analyzed using ‘an intention to treat’ approach and the initial analysis examined the demographic and baseline characteristics of patients randomized to the trial.
**Answer:** ‘an “intention-to- treat” approach,’ instead ‘“an intention to treat’ approach’ between ‘Clinical outcome data were analyzed using’ and ‘the initial analysis’.
**Original Manuscript:** 111-114—page 6: For differences between groups testing of categorical data was undertaken using Fishers exact tests and T tests for continuous data, relative risks and 95 % confidence intervals were reported.

**Answer:** ‘Between-group differences in categorical data were assessed using the Fisher exact test or Mann–Whitney U test; the t test was used for continuous data.’ **Instead** ‘For differences between groups testing of categorical data was undertaken using Fishers exact tests and T tests for continuous data,’ **before** ‘relative risks and 95 % confidence intervals were reported.’; ‘Relative’ **instead** ‘relative’ **between** ‘T tests for continuous data,’ **and** ‘risks and 95%’; **Insert** ‘also’ **between** ‘95% confidence intervals were’ **and** ‘reported.’.

**Original Manuscript:** 114—page 6: Levels of significance were reported at p<0.05.

**Answer:** ‘P<’ **instead** ‘p<’ **between** ‘Levels of significance were reported at’ **and** ‘0.05’.

**Original Manuscript:** 115&116—page 6: Analysis was performed blind to study group by a study statistician.

**Answer:** ‘by a statistician who was blinded to the study group.’ **Instead** ‘blind to study group by a study statistician.’ **after** ‘Analysis was performed’.

**Original Manuscript:** 118&119—page 6: One hundred and eleven patients initially entered the study. Of these 113, sixty-five individuals did not meet study criteria, and 18 declined to participate.

**Answer:** ‘In this study, 147 participants were initially screened. Of these 147 people, 34 subjects were excluded because of the following: cancer (8 patients), multiple sclerosis (11 patients), spinal cord lesions (4 patients), traumatic brain injury (8 patients), and meningitis (3 patients). The remaining 113 patients were entered into the study. Of these 113 patients, 65 did not meet study criteria (34 patients had acute hiccups, and 31 patients had intractable hiccups), and 18 declined to participate (5 patients refused baclofen; 13 patients failed to complete treatment).’ **Instead** ‘One hundred and eleven patients initially entered the study. Of these 113, sixty-five individuals did not meet study criteria, and 18 declined to participate.’.

**Original Manuscript:** 120&121—page 6: All thirty participants completed the study and were included in the analysis (Figure 1).

**Answer:** ‘30’ **instead** ‘thirty’ **approach’** **between** ‘All’ **and** ‘participants completed the study’; **Insert** ‘final’ **between** ‘included in the’ **and** ‘analysis (Figure 1).’.

**Original Manuscript:** 121&122—page 6: Characteristics of study sample are shown in Table 1.

**Answer:** ‘The characteristics ’ **instead** ‘Characteristics’ **before** ‘of study sample are shown in Table 1.’;

**Insert** ‘the’ **between** ‘Characteristics of’ **and** ‘study sample’;
‘presented’ **instead** ‘shown’ **between** ‘study sample are’ **and** ‘in Table 1.’.

**Original Manuscript:** 122&123—page 6: The two groups did not differ significantly in the majority of socio-demographic and clinical variables investigated at the baseline. No adverse
events were documented.

**Answer:** Insert ‘At the baseline, the mean age was 60.38 ± 19.61 years in the baclofen group and 58.64 ± 18.57 years in the placebo group. The duration of hiccups was 59.24 ± 9.65 hours and 61.32 ± 10.34 hours in the baclofen group and placebo group, respectively. All patients had a history of stroke. In the baclofen group, ten and five patients had had ischemic and hemorrhagic strokes, respectively, while in the placebo group, nine and six participants had had ischemic and hemorrhagic strokes, respectively. The ischemic and hemorrhagic strokes had occurred 3.71 ± 1.28 months and 3.83 ± 1.35 months ago, respectively, in baclofen group, and 3.65 ± 1.32 months and 3.87 ± 1.39 months ago, respectively, in the placebo group. The Fugl–Meyer Assessment (FMA), modified Barthel Index (MBI), and Neurological Deficit Scale (NDS) scores were 49.56 ± 21.67, 50.97 ± 24.15, and 15.12 ± 5.89 respectively in the baclofen group, and 51.21 ± 23.11, 52.24 ± 23.53 and 13.96 ± 5.77, respectively in the placebo group.’ after ‘The two groups did not differ significantly in the majority of socio-demographic and clinical variables investigated at the baseline.’;

Delete ‘No adverse events were documented.’ after ‘The two groups did not differ significantly in the majority of socio-demographic and clinical variables investigated at the baseline.’.

**Original Manuscript:** 124—page 6: Analyses on clinical outcomes are presented in Table 2.

**Answer:** ‘An analysis of the’ instead ‘Analyses on clinical’ before ‘clinical outcomes’;

‘is’ instead ‘are’ between ‘clinical outcomes’ and ‘presented in Table 2.’.

**Original Manuscript:** 124-126—page 6: Fourteen participants in the baclofen group were cured, compared with two in placebo group (Relative Risk (RR) 7.00, 95% confidence interval (CI) 1.91-25.62, \( p=0.003 \)).

**Answer:** Insert ‘the’ between ‘compared with two in’ and ‘placebo group’;

‘(RR: 7.00, 95% CI: 1.91–25.62, \( P = 0.003 \))’ instead ‘(Relative Risk (RR) 7.00, 95% confidence interval (CI) 1.91-25.62, \( p=0.003 \))’ between ‘compared with two in placebo group’ and ‘.’.

**Original Manuscript:** 126-128—page 6: One participant in the baclofen group had improvement from persistent hiccups compared with five patients in placebo group (RR, 0.20, 95% CI 0.03-1.51, \( p=0.12 \)).

**Answer:** ‘showed’ instead ‘had’ between ‘One participant in the baclofen group’ and ‘improvement from persistent hiccups’;

‘in’ instead ‘from’ between ‘One participant in the baclofen group had improvement’ and ‘persistent hiccups’;

Insert ‘,’ between ‘persistent hiccups’ and ‘compared with five patients’;

Insert ‘the’ between ‘compared with five patients in’ and ‘placebo group’;

‘(RR: 0.20, 95% CI: 0.03–1.51, \( P = 0.12 \))’ instead ‘(RR, 0.20, 95% CI 0.03-1.51, \( p=0.12 \))’ between ‘compared with five patients in placebo group’ and ‘.’.

**Original Manuscript:** 128-130—page 6: No patient in the baclofen group had no any amelioration relieved in the symptom of persistent hiccups compared with eight in placebo group
(RR, 0.06, 95% CI 0.00-0.94, p=0.04).

**Answer:** ‘None of the patients’ instead ‘No patient’ before ‘in the baclofen group’;

Delete ‘any’ between ‘the baclofen group had no’ and ‘amelioration relieved’;

Insert ‘; ‘between ‘persistent hiccups’ and ‘compared with five patients’;

‘of the hiccups,’ instead ‘relieved in the symptom of persistent hiccups’ between ‘amelioration’ and ‘compared with eight in placebo group’;

‘patients in’ instead ‘in’ between ‘compared with eight’ and ‘placebo group’;

‘(RR: 0.06, 95% CI: 0.00–0.94, P = 0.04)’ instead ‘(RR, 0.06, 95% CI 0.00-0.94, p=0.04)’ between ‘in placebo group’ and ‘.’.

**Original Manuscript:** 130-132—page 6: Total efficacy (including persistent hiccups cured and improved) in the baclofen was differ significantly when compared that in the placebo group (RR, 2.07, 95% CI 1.22-3.51, p= 0.007).

**Answer:** ‘In addition, a significant difference in efficacy was found between the two groups (P < 0.01; Table 3).’ instead ‘Total efficacy (including persistent hiccups cured and improved) in the baclofen was differ significantly when compared that in the placebo group (RR, 2.07, 95% CI 1.22-3.51, p= 0.007).’;

Insert ‘No serious adverse events related to treatment were documented, which might be due to the short treatment duration. However, two patients in the baclofen group reported mild side effects. One patient reported mild transient drowsiness, and the other reported mild dizziness.’ after ‘Total efficacy (including persistent hiccups cured and improved) in the baclofen was differ significantly when compared that in the placebo group (RR, 2.07, 95% CI 1.22-3.51, p= 0.007).’.

**Original Manuscript:** 134&135—page 6: Our study provides data to warrant further evaluation of baclofen in stroke patients with persistent hiccups.

**Answer:** ‘indicating that’ instead ‘to warrant’ between ‘Our study provides data’ and ‘further evaluation’;

Insert ‘is warranted’ between ‘further evaluation of baclofen’ and ‘in stroke patients with persistent hiccups.’.

**Original Manuscript:** 135&136—page 6: Clinical outcomes identify trends in cessation of persistent hiccups within intervention period; however numbers were small with wide confidence intervals.

**Answer:** ‘Analysis of the clinical’ instead ‘Clinical’ before ‘outcomes’;

‘identified’ instead ‘identify’ between ‘outcomes’ and ‘trends in cessation of persistent hiccups’;

Insert ‘the’ between ‘identify trends in’ and ‘cessation of persistent hiccups’;

Insert ‘the’ between ‘persistent hiccups within’ and ‘intervention period’;

‘however, the numbers were too small,’ instead ‘however numbers were small’ between ‘persistent hiccups within intervention period;’ and ‘with wide confidence intervals.’.

**Original Manuscript:** 137&138—page 6&7: The study demonstrated acceptability by subjects with baclofen, randomization and participation in the trial.

**Answer.** Insert ‘the’ between ‘The study demonstrated’ and ‘acceptability’;
‘of baclofen by the subjects, randomization,’ instead ‘by subjects with baclofen, randomization’ between ‘The study demonstrated acceptability’ and ‘and participation in the trial.’

**Original Manuscript:** 138—page 7: Compliance and follow-up were all acceptable.
**Answer:** ‘also’ instead ‘all’ between ‘Compliance and follow-up were’ and ‘acceptable’.

**Original Manuscript:** 138&140—page 7: Recruitment was slower than planned, with barriers to recruitment included the low prevalence of persistent hiccups from stroke patients, and recruitment at one hospital site.
**Answer:** ‘and’ instead ‘with’ between ‘Recruitment was slower than planned,’ and ‘barriers to recruitment’;
‘among’ instead ‘from’ between ‘low prevalence of persistent hiccups’ and ‘stroke patients’;
Delete ‘,’ between ‘stroke patients’ and ‘and recruitment’;
‘a single’ instead ‘one’ between ‘recruitment at’ and ‘hospital site.’

**Original Manuscript:** 141&142—page 7: Our results suggest baclofen 10 mg three times daily was an acceptable dose and concur with findings by Mirijello [13].
**Answer:** ‘that 10 mg baclofen’ instead ‘baclofen 10 mg’ between ‘Our results suggest’ and ‘three times daily’;
Insert ‘,’ between ‘an acceptable dose’ and ‘and concur with findings’;
Insert ‘the’ between ‘and concur with’ and ‘findings’;
‘of’ instead ‘by’ between ‘low prevalence of persistent hiccups’ and ‘stroke patients’;
Delete ‘,’ between ‘concur with findings’ and ‘Mirijello [13].’

**Original Manuscript:** 142&143—page 7: Both studies found that persistent hiccups successfully treated with baclofen and had no significant side effects.
**Answer:** Insert ‘have’ between ‘Both studies’ and ‘found’;
Insert ‘can be’ between ‘persistent hiccups’ and ‘successfully’;
‘without any’ instead ‘and had no’ between ‘treated with baclofen’ and ‘significant side effects.’

**Original Manuscript:** 143&144—page 7: Our study highlighted the need for further research.
**Answer:** Insert ‘on the topic’ between ‘Our study highlighted the need for further research’ and ‘.’

**Original Manuscript:** 144-147—page 7: Findings from the practitioner interviews may not represent the views of all clinicians at the host institution or be considered representative of practitioner elsewhere; however our findings indicate a supportive research culture for this topic of study.
**Answer:** ‘physician’ instead ‘practitioner’ between ‘Findings from the’ and ‘interviews’;
‘physician’ instead ‘practitioner’ between ‘be considered representative of’ and ‘elsewhere;’;
Insert '; between 'however' and 'our findings';

Insert a new paragraph ‘The side effects were generally well tolerated in this study. No serious adverse events were recorded, and only two patients reported mild side effects. One patient reported mild transient drowsiness, and the other reported mild dizziness. This low incidence of adverse effects might attributable to the short duration of the study.’ after ‘Findings from the practician interviews may not represent the views of all clinicians at the host institution or be considered representative of practician elsewhere; however our findings indicate a supportive research culture for this topic of study.’.

Original Manuscript: 148&149—page 7: Firstly, the trial was randomized thereby reducing selection bias.
Answer: ‘First,’ instead ‘Firstly,’ before ‘the trial was randomized thereby reducing selection bias.’.

Original Manuscript: 149-151—page 7: Secondly, though there is no consensus of dose to the acceptable intervention of administering baclofen for persistent hiccups, this study suggests that our intervention was in the therapeutic range.
Answer: ‘Second, although’ instead ‘Secondly, though’ before ‘there is no consensus of dose’;
‘on the optimal dose of baclofen’ instead ‘of dose to the acceptable intervention of administering baclofen’ between ‘there is no consensus’ and ‘for persistent hiccups’;
‘our findings suggest that the dose used in this study was in’ instead ‘this study suggests that our intervention was in’ between ‘Secondly, though there is no consensus of dose to the acceptable intervention of administering baclofen for persistent hiccups,’ and ‘the therapeutic range.’.

Original Manuscript: 151&152—page 7: However, the main limitation of the present study was its size, which should be interpreted with caution.
Answer: ‘is’ instead ‘was’ between ‘limitation of the present study’ and ‘its size’;
‘and our findings should therefore’ instead ‘which should’ between ‘However, the main limitation of the present study was its size,’ and ‘be interpreted with caution.’.

Original Manuscript: 153&154—page 7: The findings will influence future decisions concerning resource and planning for a future trial.
Answer: Insert ‘of this study’ between ‘The findings’ and ‘will influence future decisions’;
‘resources’ instead ‘resource’ between ‘future decisions concerning’ and ‘and planning for a future trial’;
‘trials’ instead ‘a future trial’ between ‘The findings will influence future decisions concerning resource and planning for’ and ‘.’

Original Manuscript: 154-156—page 7: We consider that randomization is acceptable, and we will explore if the window for eligibility could be extended, an appropriate sample size has been determined allowing for attrition.
Answer: Insert ‘the’ between ‘We consider that’ and ‘randomization is acceptable,’;
‘was’ instead ‘is’ between ‘We consider that randomization’ and ‘acceptable,’;
‘can’ instead ‘could’ between ‘and we will explore if the window for eligibility’ and ‘be extended,’;
‘instead’ ‘after’ ‘the window for eligibility could be extended’;
‘An’ instead ‘an’ ‘the window for eligibility could be extended,’ and ‘appropriate sample size’;
‘to allow’ instead ‘allowing’ between ‘an appropriate sample size has been determined’ and ‘for attrition.’.

Original Manuscript: 156&157—page 7: Therefore, further studies with larger numbers of patients receiving baclofen are needed to verify the results of this study.
Answer: ‘required’ instead ‘needed’ between ‘larger numbers of patients receiving baclofen are’ and ‘to verify the results of this study.’.

Original Manuscript: 158-160—page 7: Conclusions
The results of this study provide evidence to support the hypothesis that baclofen may be of some use in treating persistent hiccups. However, larger studies are warranted.
Answer: Insert ‘Abbreviations
RR: relative risk; CI: confidence interval; ChiCTR: Chinese Clinical Trials Register; FMA: Fugl–Meyer Assessment; MBI: modified Barthel Index; NDS: Neurological Deficit Scale.’

after ‘Conclusions
The results of this study provide evidence to support the hypothesis that baclofen may be of some use in treating persistent hiccups. However, larger studies are warranted.’.

Answer: ‘Cochrane Database Syst Rev’ instead ‘Cochrane Database of Systematic Reviews’ between ‘Massage therapy for preventing pressure ulcers.’ and ‘2013; (5): CD010518.’.

Insert 'Figure 1. Flow chart of participants through the trial.' after '20. Johanson GA, Brooks GP: Initial scale development: sample size for pilot studies. Educ Psychol Meas 2010, 70(3):394-400.'

Original Manuscript: 217-240—page 10-Table 1:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baeolofen (n=15)</th>
<th>Placebo (n=15)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (SD)</td>
<td>60.38 (19.61)</td>
<td>58.64 (18.57)</td>
<td>0.78</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8 (53.33%)</td>
<td>9 (60.00%)</td>
<td>0.71</td>
</tr>
<tr>
<td>Female</td>
<td>7 (47.67%)</td>
<td>6 (40.00%)</td>
<td>0.71</td>
</tr>
<tr>
<td>Married</td>
<td>15 (100%)</td>
<td>14 (93.33%)</td>
<td>0.47</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yellow</td>
<td>14 (93.33%)</td>
<td>13 (86.66%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0.00%)</td>
<td>1 (6.67%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Not recorded</td>
<td>1 (6.67%)</td>
<td>1 (6.67%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>2 (13.33%)</td>
<td>1 (6.67%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Unemployed</td>
<td>1 (6.67%)</td>
<td>1 (6.67%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Retired</td>
<td>12 (80.00%)</td>
<td>13 (86.66%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completed high school</td>
<td>12 (80.00%)</td>
<td>13 (86.66%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Completed tertiary education</td>
<td>3 (20.00%)</td>
<td>2 (13.34%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Duration of hiccups (hours)</td>
<td>59.24 (9.65)</td>
<td>61.32 (10.34)</td>
<td>0.51</td>
</tr>
<tr>
<td>Underlying disease</td>
<td>Stroke</td>
<td>15 (100%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Answer:
Table 1. Baseline characteristics of participants at trial entry

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baclofen (n = 15)</td>
<td>Placebo (n = 15)</td>
</tr>
<tr>
<td>Age</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>60.38 (19.61)</td>
<td>58.64 (18.57)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8 (53.33%)</td>
<td>9 (60.00%)</td>
</tr>
<tr>
<td>Female</td>
<td>7 (47.67%)</td>
<td>6 (40.00%)</td>
</tr>
<tr>
<td>Married</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Han Chinese</td>
<td>14 (93.33%)</td>
<td>13 (86.60%)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0.0%)</td>
<td>1 (6.67%)</td>
</tr>
<tr>
<td>Not recorded</td>
<td>1 (6.67%)</td>
<td>1 (6.67%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>2 (13.33%)</td>
<td>1 (6.67%)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>1 (6.67%)</td>
<td>1 (6.67%)</td>
</tr>
<tr>
<td>Retired</td>
<td>12 (80.00%)</td>
<td>13 (86.60%)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completed high school</td>
<td>12 (80.00%)</td>
<td>13 (86.60%)</td>
</tr>
<tr>
<td>Completed tertiary education</td>
<td>3 (20.00%)</td>
<td>2 (13.34%)</td>
</tr>
<tr>
<td>Duration of hiccups (h)</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>59.24 (9.65)</td>
<td>61.32 (10.34)</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>10 (66.67%)</td>
<td>9 (60.00%)</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>5 (33.33%)</td>
<td>6 (40.00%)</td>
</tr>
<tr>
<td>Duration of stroke (m)</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Ischemia</td>
<td>3.71 (1.28)</td>
<td>3.65 (1.32)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>3.83 (1.35)</td>
<td>3.87 (1.39)</td>
</tr>
<tr>
<td>Severity of stroke</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>FMA</td>
<td>49.56 (21.67)</td>
<td>51.21 (23.11)</td>
</tr>
<tr>
<td>MBI</td>
<td>50.97 (24.15)</td>
<td>52.24 (23.53)</td>
</tr>
<tr>
<td>NDS</td>
<td>15.12 (5.89)</td>
<td>13.96 (5.77)</td>
</tr>
</tbody>
</table>

Note: h-hours; m-months; FMA-Fugl-Meyer Assessment; MBI-Modified Barthel Index; NDS-Neurological Defect Scale.

Table 1. Baseline Characteristics of Participants at Trial Entry

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baclofen (n=15)</td>
<td>Placebo (n=15)</td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>60.38 (19.61)</td>
<td>58.64 (18.57)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8 (53.33%)</td>
<td>9 (60.00%)</td>
</tr>
<tr>
<td>Female</td>
<td>7 (47.67%)</td>
<td>6 (40.00%)</td>
</tr>
<tr>
<td>Married</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yellow</td>
<td>14 (93.33%)</td>
<td>13 (86.60%)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0.0%)</td>
<td>1 (6.67%)</td>
</tr>
<tr>
<td>Not recorded</td>
<td>1 (6.67%)</td>
<td>1 (6.67%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>2 (13.33%)</td>
<td>1 (6.67%)</td>
</tr>
<tr>
<td>Retired</td>
<td>12 (80.00%)</td>
<td>13 (86.60%)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completed high school</td>
<td>12 (80.00%)</td>
<td>13 (86.60%)</td>
</tr>
<tr>
<td>Completed tertiary education</td>
<td>3 (20.00%)</td>
<td>2 (13.34%)</td>
</tr>
<tr>
<td>Duration of hiccups (h)</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>59.24 (9.65)</td>
<td>61.32 (10.34)</td>
</tr>
<tr>
<td>Underlying disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>15 (100%)</td>
<td>15 (100%)</td>
</tr>
</tbody>
</table>

instead
**Original Manuscript:** 241-248—page 10-Table 2:

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Baclofen (n=15)</th>
<th>Placebo (n=15)</th>
<th>Relative Risk (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hiccup cessation</td>
<td>14</td>
<td>2</td>
<td>7.00 (1.91-25.62)</td>
<td>0.003</td>
</tr>
<tr>
<td>Improvement</td>
<td>1</td>
<td>5</td>
<td>0.20 (0.03-1.51)</td>
<td>0.12</td>
</tr>
<tr>
<td>Null and void</td>
<td>0</td>
<td>8</td>
<td>0.06 (0.00-0.94)</td>
<td>0.04</td>
</tr>
<tr>
<td>Total efficacy</td>
<td>15</td>
<td>7</td>
<td>2.07 (1.22-3.51)</td>
<td>0.007</td>
</tr>
<tr>
<td>Side effects</td>
<td>None</td>
<td>None</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Answer:**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Baclofen (n = 15)</th>
<th>Placebo (n = 15)</th>
<th>Relative risk (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hiccup cessation</td>
<td>14</td>
<td>2</td>
<td>7.00 (1.91–25.62)</td>
<td>0.003</td>
</tr>
<tr>
<td>Improvement</td>
<td>1</td>
<td>5</td>
<td>0.20 (0.03–1.51)</td>
<td>0.12</td>
</tr>
<tr>
<td>No effect</td>
<td>0</td>
<td>8</td>
<td>0.06 (0.00–0.94)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

**Instead**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Baclofen (n=15)</th>
<th>Placebo (n=15)</th>
<th>Relative Risk (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hiccup cessation</td>
<td>14</td>
<td>2</td>
<td>7.00 (1.91-25.62)</td>
<td>0.003</td>
</tr>
<tr>
<td>Improvement</td>
<td>1</td>
<td>5</td>
<td>0.20 (0.03-1.51)</td>
<td>0.12</td>
</tr>
<tr>
<td>Null and void</td>
<td>0</td>
<td>8</td>
<td>0.06 (0.00-0.94)</td>
<td>0.04</td>
</tr>
<tr>
<td>Total efficacy</td>
<td>15</td>
<td>7</td>
<td>2.07 (1.22-3.51)</td>
<td>0.007</td>
</tr>
<tr>
<td>Side effects</td>
<td>None</td>
<td>None</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Insert**

**Table 3. Comparison of efficacy between the two groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>Total patients</th>
<th>Hiccup cessation</th>
<th>Improvement</th>
<th>No effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baclofen</td>
<td>15</td>
<td>14</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Placebo</td>
<td>15</td>
<td>2</td>
<td>5</td>
<td>8</td>
</tr>
</tbody>
</table>

Difference in efficacy between the two groups, \( P < 0.01 \).

*after Table 2*

**Original Manuscript:** 250-260—page 11-Figure 1:
Figure 1: Flow of participants through the trial.

**Answer:**

Figure 1: Flow chart of participants through the trial.

*instead*
Figure 1 Flow of participants through the trial.