Evaluation of a Portable Isokinetic Knee Training Device for Quadriceps Rehabilitation in Children with SMA

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1 Abstract

This study was an interventional trial with a sample size of six, involving patients with spinal muscular atrophy (SMA) who underwent a seated knee extension rehabilitation program. Participants received rehabilitation intervention using a portable isokinetic training device, and paired t-tests were employed to compare the rate of change in the primary outcome.

2 Main Text

2.1 Research Background and Significance

(1) Spinal muscular atrophy is an inherited degenerative disease that primarily affects the lower motor neurons. It is characterized by the degeneration of nerve cells originating from the spinal cord and brainstem, leading to progressive muscle weakness and atrophy in the limbs. The involvement of the lower extremities is often more severe than that of the upper extremities, and the deep tendon reflexes of the patients are significantly weakened or completely disappeared. Severe cases may lead to death due to respiratory complications. The inheritance pattern of SMA is autosomal recessive, with an incidence of about 1/10000. Based on morbidity, age, and clinical manifestation, the disease can be divided into five types. Type 0 SMA usually occurs in prenatal morbidity and usually dies within a few weeks after birth; Type I SMA is the most common, accounting for about 45%, and the morbidity age is 0 to 6 months. The survival rate of untreated type I SMA children at 20 months is only 8%. This type is one of the main causes of early hereditary death in infants; Type Ⅱ SMA accounted for about 30%. The age of morbidity was younger than 18 months. The 10-year survival rate was 82%; Type Ⅲ SMA accounts for about 15%, the morbidity is older than 18 months, the patient may survive to adulthood, and the disease progresses slowly; Type IV SMA is seen in adults. With the development of disease-modifying drugs, the motor function and prognosis of SMA patients have been significantly improved. However, the existing treatment drugs can not cure the disease, and SMA patients still need long-term rehabilitation training and care. The importance of family rehabilitation to the life of children with SMA is self-evident. By adhering to long-term standardized rehabilitation management, the progression of SMA disease can be slowed down, muscle atrophy and bone deformities can be prevented or reduced, the mental health of children can be improved, and their quality of life can be enhanced.

(2) In the process of rehabilitation, because of the advantages of isokinetic training, such as high efficiency and quantitative detection of muscle strength, patients with knee joint diseases are often recommended to use isokinetic muscle training machine for rehabilitation or postoperative functional recovery training. In addition to knee disease, it has also been used for stroke, traumatic spinal cord injury and rehabilitation training

(3) However, the scarcity of rehabilitation training resources and professional physiotherapists and the expensive use of training equipment hinder the promotion and popularization of isokinetic training. In addition, the existing commercial isokinetic training instruments such as Biodex, Cybex and IsoMed are large, heavy and high energy consumption fixed equipment. The multi-occasion rehabilitation training requirement of wearing and training at any time cannot be realized, for occasions such as home travel.

(4) From that point of view of safety, a commercial isokinetic trainer provides a large minimum impedance moment and the joint is fully rigid, Therefore, it is not suitable for rehabilitation training for people with weak muscle strength. A portable and wearable knee joint isokinetic training robot with variable joint stiffness can fit the portability and multi-scene use. Human-computer interaction flexibility requirement. With the energy regeneration technology, the problem of high energy consumption and low energy utilization efficiency can be effectively solved.

This study focused on the rehabilitation effect and evaluation of isokinetic training of lower limbs of SMA patients under the influence of stiffness. SMA patients were trained with a wearable isokinetic training robot for long-term isokinetic training to explore the effect of isokinetic training on the rehabilitation of SMA patients.

2.2 Research Objective

Under the premise of fixed angular velocity and range of motion, the objective is to observe and evaluate the long-term isokinetic rehabilitation training effect on SMA patients under the influence of their stiffness.

2.3 Study Design

2.3.1 Study Population

Inclusion Criteria:

1. Age range: 6-12 years old.
2. Diagnosed with Type II Spinal Muscular Atrophy (SMA).

Exclusion Criteria:

1. Participants with severe comorbidities, implanted medical devices preventing MRI or claustrophobia were excluded from the study;

2. Refusal to provide informed consent or inability to complete the entire study protocol, among other factors;

3. Uncontrolled hypertension (systolic blood pressure ⩾160 mmHg and/or diastolic blood pressure ⩾95 mmHg) or congestive heart failure classified as New York Heart Association (NYHA) Class III or IV;

4. Cognitively impaired or unable to comprehend the requirements of study participation.

Withdrawal Criteria：

1. The subject withdraws the informed consent form;

2. Serious violation of clinical clinical study protocol;

3. The investigator believes that it is no longer suitable to continue the clinical Experiment;

4. Death of the subject;

5. The subject was lost to follow-up.

Handling of withdrawal of subjects：

1. All participants who withdraw from the study should retain all source data and files. After the participant withdraws, the researcher should use various forms such as phone calls, emails, etc. to contact the participant as much as possible and inquire about the reasons;

2. Record the time and reason for terminating the clinical experiment in detail on the case report form;

3. The injured due to adverse events must be recorded in the case report form if it is finally judged that there is a causal relationship with the experiment device after follow-up. Participant who terminates the experiment due to adverse events must be followed up until the adverse events are resolved or stabilized.

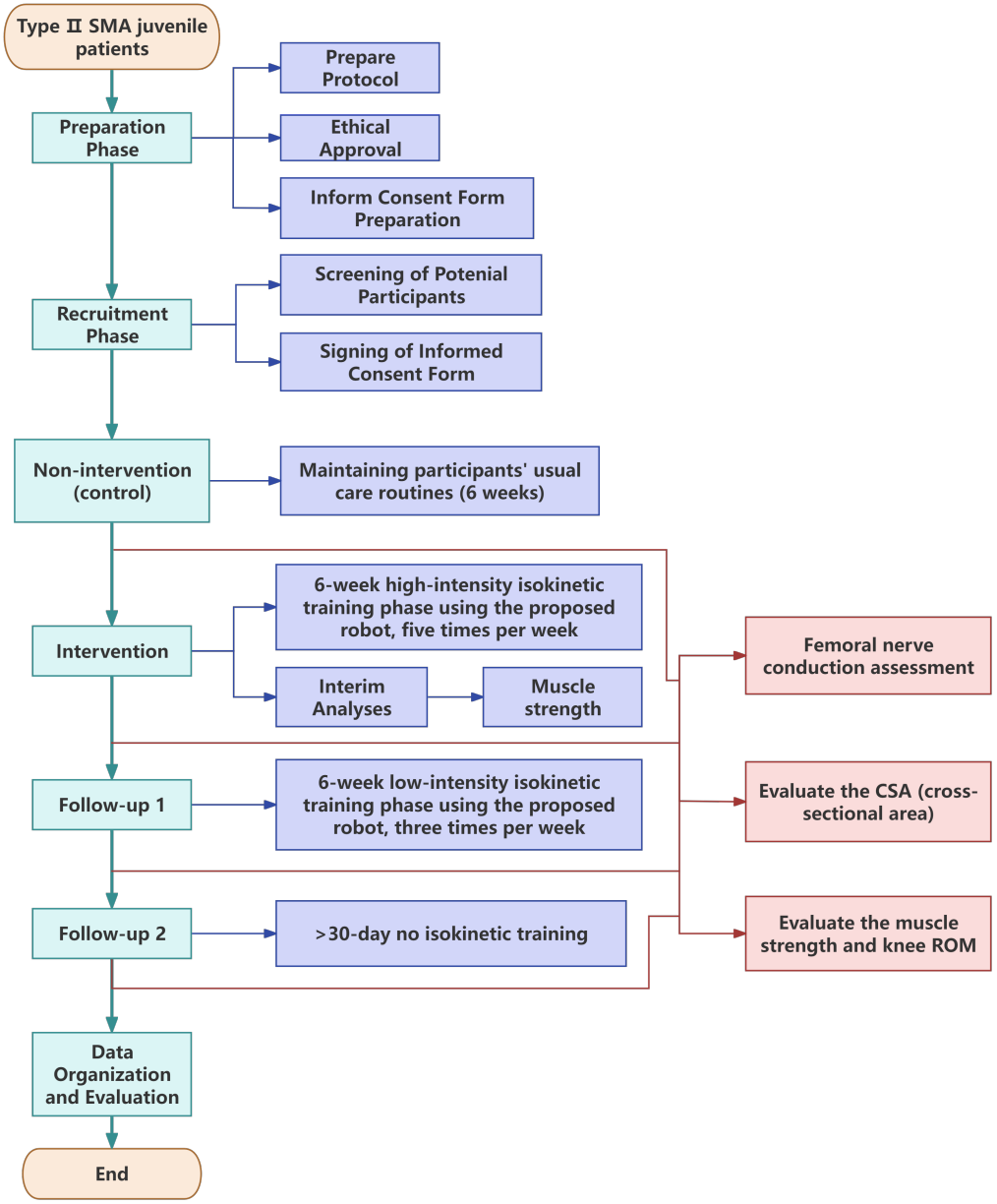
2.3.2 Random and covert grouping methods

None

2.3.3 Intervention

Study protocol：

This trial was conducted with the Department of Sports Medicine at Peking University Third Hospital providing the study site, MRI assessments, and rehabilitation protocol guidance. The Department of Neurology at Peking University Third Hospital was responsible for electromyographic evaluations. Beihang University provided the portable isokinetic training device, maintenance services, database construction, data entry, and analysis. The entire study process lasted for 5.5 months. The study flowchart is shown below：



2.3.4 Outcomes

Primary Outcomes:

Peak torque and work during isokinetic knee extension, cross-sectional area of the quadriceps and electromyographic (femoral nerve conduction) parameters.

Secondary Outcomes:

Knee range of motion, weight and height.

Safety Outcomes:

Skin temperature of the suprapatellar bursa of the knee and knee pain level.

2.3.5 Sample size

$$N = 2 * \left[\left(t_{\frac{\alpha}{2}} + t_{\beta}\right) * \frac{S}{\delta}\right]^2$$

Given that $\alpha = 0.05$ and $\beta = 0.1$, the critical values $t_{\frac{\alpha}{2}}$ and t_{β} are calculated as:

$$t_{\frac{\alpha}{2}} = 1.96,\ t_{\beta} = 1.28$$

From the Ref. [18], $S = 16.1,\ \delta = 32.3$. After calculation, we obtained

$$N > 5.21$$

Therefore, the minimum sample size $N_{min} = 6$. In this study, we recruited 6 juveniles with SMA type II.

2.4 Statically Analysis

All statistical analyses were conducted on data collected from all subjects and performed with the MATLAB R2017b (MathWorks), and Microsoft Excel. Using a paired-sample t-test to analyze the significant difference of data. We consider p-values of less than 0.05 to be statistically significant.

2.5 Safety and ethical considerations

Isokinetic training is a non-invasive rehabilitation method. A large number of clinical case studies have shown that it can improve muscle strength without serious adverse reactions, indicating that its clinical application is safe. Before carrying out this project, this robot has undergone multiple tests and validations, and its safety can be guaranteed due to its non-invasive nature and the application of flexible joints.

Possible risks during rehabilitation training with isokinetic robots include:

(1) Improper wearing of the isokinetic training device may cause discomfort in the participant's limbs.

(2) Overtraining may lead to adverse effects, including muscle soreness, joint pain,

muscle strain or sprain, and fatigue.

(3) Inappropriate posture or failure to follow medical instructions may negatively affect the rehabilitation outcome.

(4) Participants with conditions such as hypertension, hyperlipidemia, obesity, heart disease, diabetes, organ dysfunction, or venous thrombosis may be at increased risk during training.

2.5.1 Definition of Adverse Events (AE) and Serious Adverse Events (SAE)

The definition of adverse events in this experiment is: During the training period and follow-up at the end of the experiment, if the subject experiences knee joint pain without reason, or if there is daily pain but the pain worsens without reason, and there is no improvement after two weeks of the above situation, it is considered an adverse event. If given a certain amount of rest time for recovery and without affecting the observation of therapeutic effects, the experiment can continue. Serious adverse events are those that require hospitalization, extend hospitalization time, disable, affect working ability, cause permanent damage to organ function, endanger life or death, etc. during the clinical experiment. The evaluation of adverse events is divided into five levels: definitely related to training, likely related, possibly related, possibly unrelated, and definitely unrelated. The first three are counted as the incidence of adverse reactions. In case of any serious adverse event or important adverse event, no matter whether it is related to the research intervention or whether the intervention operation has been implemented, it must be reported to the clinical experiment institution and the ethics committee within 24 hours after the occurrence.

Qualification criteria for clinical experiment results:

(1) The relevant data of each subject shall be recorded in the case record form designed according to the requirements of the experiment, and the accuracy and integrity of the data shall be guaranteed, with traceability

(2) Key milestones such as the date of signing the informed consent form, the date of enrollment, and the time of each visit should pay attention to data collection to avoid missing information as much as possible.

(3) The efficacy data recorded during each visit period should be obtained by the subjects strictly following the time window specified in the protocol.

For some subjects who violate the above contents, the main researchers and statistical professionals should discuss and decide the specific treatment measures, and evaluate whether they will have a greater impact on the experiment.

2.6 Subject protection

According to relevant Chinese laws and regulations, before the start of the experiment, the researcher should make written and oral explanations to the subjects on the background, nature, significance, steps, benefits, risks, withdrawal, etc. of the study, and must obtain the informed consent signed by each subject (or the legal representative of the subject). The informed consent form should indicate the date, and the informed consent form and its copies should be kept separately by the researcher and the subjects.

2.7 Research management system

Before the start of the experiment, the experiment equipment needs to be repeatedly tested to confirm its reliability. The researchers are trained in the Sports Medicine Department of Peking University Third Hospital to be familiar with the experiment process, practical equipment, and assign specific tasks, including subject recruitment, patient guidance, communication, equipment maintenance, data recording, data entry and data processing.

2.7.1 Scheme modification

If there is no significant difference in the experiment results after the plan sample is included. Based on the existing data in this experiment, the sample size will be estimated. The experiment scheme shall be strictly followed. In case of serious adverse reactions caused by equipment defects, the experiment shall be suspended immediately, the defects shall be evaluated, and the decision as to whether the study can be continued will be subject to further ethical approval.

2.7.2 Quality Management

(1) Submit the verification plan to the ethics committee for approval.

(2) Personnel participating in this experiment shall be selected in strict accordance with the technical access requirements

(3) The researchers participating in this experiment carefully implemented the standard operating procedures for clinical verification.

(4) During the verification process, researchers monitor the correctness and completeness of the data.

(5) Researchers should fill in the case report form according to the requirements, truthfully, in detail, and carefully record all the contents of the case report form to ensure

its authenticity and reliability.

(6) All observations and findings in clinical validation should be verified to ensure the reliability of the data, ensure that all conclusions in clinical validation are derived from raw data, and have corresponding data management measures in clinical validation and data processing

2.7.3 Early termination:

In case of 1 case of serious adverse event related to product quality, the clinical experiment shall be judged as failed and the clinical experiment shall be terminated in time; Serious deviation was found in the implementation of the clinical experiment, which made it difficult to evaluate the effect of rehabilitation training. The applicant asked to terminate the trial or the administrative department asked to terminate the trial.

2.8 Organizational management

The Department of Sports Medicine of Peking University Third Hospital provides experiment sites, inspection and evaluation, and rehabilitation movement specifications. Beihang University provides portable isokinetic trainers, maintenance services, database building, data entry and analysis.

3 Reference

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Informed Consent Form

Evaluation of a Portable Isokinetic Knee Training Device for Quadriceps Rehabilitation in Children with SMA

You are invited to participate in this study because you have the conditions to be included in the study of rehabilitation effect and evaluation method of knee isokinetic training of SMA patients under the influence of stiffness. Your research doctor or researcher will provide you with a thorough explanation of the contents of the informed consent form. Please read this form carefully before making a decision on whether to participate in the study. If you are participating in another study, please inform your study doctor or researcher.

The content/nature, risks, and other important information of this study are as follows:

Yanggang Feng (Beihang University) and Fuzhen Yuan (Peking University Third Hospital) will carry out this study funded/initiated by Beihang University.

1. Why is this study conducted?

Robot assisted isokinetic rehabilitation training refers to the process of using robot technology to assist human beings in rehabilitation treatment and training, which can collect and observe various biological data of the human body, and provide help for coordinated movement of the human body. Robot can also provide movement support for patients with motor dysfunction. This type of robot will bring significant changes to human life and perception. In current robot research, robot assisted rehabilitation training is a hot topic. Due to the strong coupling and complexity of biological data related to human movement, it poses significant challenges in measurement and processing, which demands high demands for sensor measurement, data fusion processing, and control algorithms. This is also a current research difficulty. Ultimately, this project aims to clarify whether the diagnosis and treatment methods for patients with significant differentiation should be different, in order to provide evidence-based and better rehabilitation treatment methods for SMA patients and enable them to to live, work, and exercise better.

2. How many people will participate in this study?

A total of six participants will be enrolled in this study. Participants received rehabilitation intervention using a portable isokinetic training device, and paired t-tests were employed to compare the rate of change in the primary outcome.

3. Inclusion and exclusion criteria for this study:

(1) Inclusion criteria:

1) Age range: 6-12 years old.

2) Diagnosed with Type II Spinal Muscular Atrophy (SMA).

(2) Exclusion criteria:

1) Participants with severe comorbidities, implanted medical devices preventing MRI or claustrophobia were excluded from the study;

2) Refusal to provide informed consent or inability to complete the entire study protocol, among other factors;

3) Uncontrolled hypertension (systolic blood pressure ⩾160 mmHg and/or diastolic blood pressure ⩾95 mmHg) or congestive heart failure classified as New York Heart Association (NYHA) Class III or IV;

4) Cognitively impaired or unable to comprehend the requirements of study participation.

4. Study Protocol

5. Benefits of participating in this study

In this project, the symptoms related to your knee joint may be greatly relieved, and participating in this study may not directly benefit you. However, we hope that the information obtained you're your participation in this study can benefit patients with similar conditions in the future. This benefit may include the use of this robot for others with similar conditions to guide future clinical medical examinations, treatments, rehabilitation, follow-up, etc. You will receive good medical services during this period, and there may be some previously undiscovered regularity issues that may be revealed in the future. If you need, we will inform you in detail.

6. Risks associated with participating in this study

Isokinetic training is a non-invasive rehabilitation method. A large number of clinical case studies have shown that it can improve muscle strength without serious adverse reactions, indicating that its clinical application is safe. Before carrying out this project, this robot has undergone multiple tests and validations, and its safety can be guaranteed due to its non-invasive nature and the application of flexible joints.

Possible risks during rehabilitation training with isokinetic robots include:

(1) Improper wearing of the isokinetic training device may cause discomfort in the participant's limbs.

(2) Overtraining may lead to adverse effects, including muscle soreness, joint pain, muscle strain or sprain, and fatigue.

(3) Inappropriate posture or failure to follow medical instructions may negatively affect the rehabilitation outcome.

(4) Participants with conditions such as hypertension, hyperlipidemia, obesity, heart disease, diabetes, organ dysfunction, or venous thrombosis may be at increased risk during training.

7. What other medical options are available?

Under the guidance of professional healthcare professionals, we will provide you with the most suitable treatment methods based on your specific situation, including but not limited to physical therapies such as cold therapy, heat therapy, massage, and medication therapy for reducing pain or inflammation.

8.Confdentiality

Your medical records will be fully stored at Peking University Third Hospital. We will ensure the confidentiality of written materials, samples, and results related to your identity. Experimental data will be used for academic publication, but we will protect your privacy. Without your permission, no institution or individual can obtain this information. When publishing research information and data obtained from this project in scientific conferences or journals, your identity will not be disclosed. But to ensure compliance with relevant laws and regulations, your records may be reviewed. Reviewers include

relevant national management departments, the Ethics Committee of Peking University Third Hospital, and a team of Peking University Third Hospital project personnel directly involved in material collection.

9.Costs

This study does not incur any additional costs or medical insurance expenses for you. During the research period, you do not need to pay for MRI examination fees and all follow-up expenses. You can consult with the research doctor or researcher to learn more about the cost.

10.Compensation

The expenses incurred for participating in this research, such as your transportation fees, registration fees, and related examination fees, will be provided by research group.

11. Refusal to participate or withdraw

Before accepting the experiment, you need to ensure that your participation is completely voluntary. You can choose to refuse to participate or withdraw from the experiment at any stage of the experiment, and will not be discriminated against or retaliated against, and your medical treatment and rights will not be affected.

If you experience serious adverse reactions, or if your study doctor feels that continuing to participate in the study is not in your best interest, he/she will decide to withdraw you from the study. If such a situation occurs, we will notify you promptly and your research doctor will also discuss with you to provide you with other options. If the doctor thinks that the sudden interruption of the experiment will affect your health, he may ask you to have an examination in the hospital before stopping the experiment.

12. Related consultation

If you have any questions related to your own rights, or if you would like to express any dissatisfaction or concerns during your participation in this project, please contact the direct person in charge of this project at 18811728786 or 15225739671.

Disclaimer

“I have informed the subject and his/her guardian of the background, purpose, steps, risks and benefits of the experiment, and given him/her enough time to read the informed consent form, discuss with others, and answer his/her questions about the project; I have informed the subject that when encountering problems related to the project, he/she can contact the Sports Medicine Department of Peking University Third Hospital or the School of Mechanical Engineering and Automation of Beihang University at any time, and when encountering problems related to his/her own rights/interests, he/she can contact the Research Ethics General Office of Peking University Third Hospital at any time, and provide accurate contact information; I have informed the subject and his/her guardian that he/she can withdraw from the study at any time without any reason; I have informed the subject that they will receive a copy of this informed consent form, which includes my and his/her signatures”

Signature of researchers who obtained informed consent: Contact number:

Informed consent statement

"I have been informed of the background, purpose, steps, risks and benefits of the experiment. I have enough time and opportunity to ask questions, and I am very satisfied with the answers to the questions. I have also been told who to contact when I have questions, complaints, concerns, or want further information. I have read this informed consent form and agreed to participate in the project. I know that I can withdraw from the study at any time without any reason. I was told that I will get a copy of this informed consent form, which contains the signatures of me and the researcher."

Participant signature: Contact number: Date: