Clinical Research Information and Informed Consent

Research Project Name: Comparison of guiding sedation level by respiratory effort versus usual care in mechanically ventilated patients: A Randomized Controlled Trial.

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Affiliation : Critical care medicine, Faculty of Medicine Ramathibodi Hospital

Research Funding : None

Introduction and principle of the research

The research project is a randomized comparative study investigating the use of attempted respiratory effort versus usual care as an objective for adjusting sedative dosages in patients using ventilators. Participation in the study is voluntary, and the research aims to compare the effectiveness of attempted respiratory effort versus usual treatment in adjusting sedative dosages for critically ill patients using ventilators. The research will commence with data collection within the first 24 hours of patients being intubated with mechanical ventilators, continuing until their discharge from the hospital. A total of 162 patients are expected to participate in the study. It is anticipated that the study will span a two-year period, during which data on patients' attempted respiratory effort parameters, blood results, gas exchange, and treatment outcomes will be collected. During the measurement of respiratory effort parameter, patients may experience slight discomfort in the airways, lasting no more than 10 seconds. The expected benefits of participating in the research include obtaining appropriate measures of attempted respiratory effort to be used in adjusting sedative dosages and ensuring patient safety during ventilator use. If you choose not to participate in the research, you will continue to receive standard medical care for critically ill patients as usual.

Research Information

You have been invited to participate in the research. Please take the time to read this document, which will provide you with information about your involvement in this study. The decision to participate in this research is entirely voluntary. If you choose not to participate, it will not affect your care or any rights you may have.

Participation in this research is voluntary.

- **You have the autonomy to choose whether or not** to participate in this research.
- **You may consult with your family or healthcare provider before making a decision, and you can ask questions about the research project. The researchers will provide additional information and answer your questions until you fully understand.**
- **If you willingly decide to participate in this research, you can withdraw at any time.**
- The decision to participate in the research **must be** witnessed by a relative who will act as a confirming witness.

Research Background

Most patients in the intensive care unit often require mechanical ventilation during treatment. Even while using a ventilator, patients still need to exert a certain level of respiratory effort to maintain the coordinated functioning of the brain's respiratory control system, the respiratory nervous system, respiratory muscles, airways, and lungs. On the other hand, excessive or insufficient respiratory effort during ventilator use can have adverse effects on the overall respiratory system of patients. Specifically, the insufficiency of respiratory effort during ventilator use can lead to weakness in respiratory and airway muscles, making it difficult for patients to be weaned off the ventilator. Conversely, excessive respiratory effort can result in actions that impact the lungs and diaphragm, potentially causing them injury as if by a double-edged sword. Therefore, the crucial goal is to maintain respiratory effort at a level close to normal to prevent respiratory muscle weakness or excessive strain, which could lead to lung injury. This is a key objective in ensuring proper respiratory effort while using ventilators.

Measuring respiratory effort can be done through various methods. The chosen method for this study is the measurement of end-expiratory occlusion test using a function in the ventilator called "ΔPocc." The calculated results from this measurement help determine the respiratory muscle assistance for adjusting sedative dosages. This method can be performed at the bedside without causing side effects or serious harm to the patient. Research studies have shown that the results obtained using this method are comparable to those obtained through standard measurement methods, which can be more complex, require additional equipment, and involve potential risks during measurement.

However, since there has been no prior research on respiratory effort concerning the adjustment of sedative dosages in critically ill patients using ventilators, this study aims to analyze this relationship. The goal is to contribute to the improvement of patient care and provide guidance for future research in this field.

This research will select participants based on the following criteria:

1. Participants must be between the ages of 18 and 75 years old.
2. Patients or direct relatives who are willing to participate in the research and sign the informed consent form.
3. Individuals receiving treatment at the medical intensive care unit and semi-intensive care unit of the Department of Geriatrics, Faculty of Medicine, Ramathibodi Hospital.
4. Patients with respiratory failure require ventilator support within the first 24 hours of admission.
5. Approval from the attending physician.
6. Ability to start the research and record data within 48 hours after the patient receives ventilator assistance as mentioned above.

The total number of participants in the research is 162.

Research objection

Main Objectives:

- To compare the use of respiratory effort with usual care in adjusting sedative dosages for critically ill patients using mechanical ventilators, measured by 28 days of ventilator-free days.

Secondary Objectives:

- To study 28 days mortality and length of hospital stay.
- To study changes in gas exchange and lung mechanics at 24 and 48 hours.
- To analyze the relationship between attempted breath-holding for adjusting sedative dosages in patients and the treatment outcomes, including the amount of sedative use and side effects, in comparison to standard treatment for critically ill patients using ventilators.

Research Design

This study adopts a randomized controlled trial design and is expected to span approximately 2 years, starting from the approval granted by the Research Ethics Committee.

Research Procedure

1. You will receive a request for informed consent for research either from the patient or their direct relatives. The research procedures will be explained to ensure an understanding of the methods, benefits, and potential complications. Relatives will be asked to sign the informed consent form to participate in the research, given that patients may be in a condition where their awareness and decision-making abilities are impaired, requiring consent from relatives as the primary source.
2. You will receive treatment for respiratory failure in adults according to the standard protocol in the intensive care unit. Additionally, you/your relatives will be interviewed to gather information on two main topics, taking no more than 5 minutes, including:

- Gender, age, height, weight, and BMI
- Medical history, smoking history, and the cause of respiratory failure requiring ventilator support, as well as the date and time of admission to the intensive care or semi-intensive care unit.

3. You/your relatives will receive advice while the patient is undergoing treatment in the intensive care unit, including the necessity of using respiratory assistance equipment and adjusting ventilator settings for treatment. This includes measuring attempted breath-holding for 10 seconds for respiratory effort measurement technique, which may cause some discomfort or breathlessness.
4. The researcher will collect patient data, vital signs, gas exchange, radiographic characteristics of the lungs, blood tests before treatment, lung mechanics parameters, respiratory assistance pressure, lung compliance, and resistance. The attempted breath-holding value and Richmond Agitation-Sedation Scale will be recorded at 24 and 48 hours.
5. If you/your relatives decline to participate in the research, it will not affect the standard treatment provided.

The researcher has summarized the risks and benefits of participating in the research as follows:

Risks and uncomfortable stages of participants in the Research

During the treatment of respiratory failure, it is necessary to use breathing assistance equipment and adjust ventilator settings for treatment, including measuring the negative pressure difference during the expiration hold for 10 seconds. This may cause discomfort and a feeling of tightness. However, a thorough assessment and prompt medical treatment will be provided by specialized physicians during the treatment in the intensive care unit.

Anticipated benefits for participants in the research:

Due to the absence of bias towards the patients, which may affect the study, and the lack of research-backed evidence confirming the benefit of using respiratory effort values for adjusting sedative dosages, the researchers need to keep the measurement results confidential from the treating team. Therefore, the patients do not directly benefit from this research. However, the recent preliminary trial reports an appropriate level of respiratory effort is related to favorable clinical outcomes, leading to the potential reduction of unnecessary sedative use, decreased duration of the ICU stay, and ultimately achieving positive clinical results.

In this case, if you do not wish to participate in this research, you still have other options for medical care, as follows:

Alternative options in case you do not participate in the research:

You will receive treatment according to the standard guidelines for the specific abnormal condition that necessitates admission to the intensive care unit. This care will be provided by specialized respiratory physicians and critical care medical personnel. As this is a randomized comparative research study, the research processes are clearly defined and closely monitored by medical professionals and the treating team in the intensive care unit. Continuous monitoring and regular check-ups on vital signs are conducted throughout the study, minimizing the likelihood of research-related complications. The criteria for withdrawing from the research are specific to instances where the researcher or the immediate family member expresses a

withdrawal request during the research, or if a participant develops an adverse reaction to any sedative drugs and cannot use others.

The researcher summarizes the procedures or approaches for handling various situations that may occur during the research as follows:

Potential Situations During the Research:

Situations that may arise during the research	**Guidelines for resolution**
■ If you withdraw during the research.	You will receive treatment according to the standard guidelines for the abnormal condition that requires the patient to be admitted to the respiratory critical care unit, under the care of respiratory and critical care specialists.
■ If there is new information related to the research or your safety.	The researcher will promptly inform you, and you can decide whether to continue participating in the research or not.
■ Criteria for terminating participation.	The researcher, participants or relatives expressing the intention to withdraw during the research, or participants who are allergic to any sedative medication. As this is a randomized comparative study with controlled factors and clear research procedures, the likelihood of complications related to the research is low. The criteria for terminating participation in the research apply specifically to the researcher or direct relatives expressing the intention to withdraw during the research or participants allergic to sedative medications.

After completing the research, the physician will analyze the study results and communicate them to the medical faculty and other healthcare providers to apply the respiratory effort data to the clinical correlation in patients using ventilators. This will contribute to future research endeavors.

Your information related to this research will be kept confidential, following international research ethics standards and the Personal Data Protection Act of 2019. The dissemination of research results at conferences or in academic journals will not include personally identifiable information. However, certain groups, such as the research ethics committee, research coordinators, oversight personnel, and authorized personnel from government institutions or organizations, may request access to your data for data verification and quality assurance. This information will be presented or published in a format that does not reveal your identity.

The patient's information will be kept confidential, stored by the researcher, and destroyed three years after the research results are reported. Additionally, the research data will only be presented or published in academic settings.

Participation in this research is voluntary and does not involve any financial compensation for the participants. The participants are not required to incur any additional expenses beyond the standard treatment costs covered by their healthcare rights, such as nursing care and sedative medications.

In the case of adverse events or unwanted outcomes resulting from research participation, even though the risk is minimal, the medical supervisor will promptly notify the research team, and necessary medical treatment will be provided without additional cost to the participant.

If you have any concerns or questions about the research or your safety during participation, you can directly inquire with the researcher or contact the Department of Medicine, 7th floor, Building 1, Faculty of Medicine Ramathibodi Hospital, at 02-2011301.

You can reach out to the following individuals for additional information, to report side effects, or to discuss any unwanted events

1. Dr. Phruet Soipetkasem, MD
   Workplace: Department of Critical Care Medicine, Building 1, 7th floor Faculty of Medicine, Ramathibodi Hospital.
   Contact number: 061-2708090
2. Dr. Pongdhep Theerawit, MD, Assoc. Prof.
   Workplace: Department of Critical Care Medicine, Building 1, 7th floor Faculty of Medicine, Ramathibodi Hospital.
   Mahidol University, 270 Rama VI Road, Thung Phaya Thai, Ratchathewi, Bangkok, 10400
   Contact numbers: 02-201-1309, 081-888-1536

If you have any concerns about your rights, you can contact the Human Research Ethics Unit at the Research and Innovation Office, Research and Welfare Building, 3rd Floor, Faculty of Medicine Ramathibodi Hospital, Telephone: 02-2011544. This is to ensure that your rights, safety, and well-being are protected according to international ethical standards for human research.

Research Informed Consent Form

I, Mr./Ms./Miss ..... [Your Full Name], has decided to participate in the research study titled **" Comparison of guiding sedation level by respiratory effort versus usual care in mechanically ventilated patients: A Randomized Controlled Trial".** The objective of this study is to investigate the adjustment of sedative dosage in patients using ventilators, comparing the effort of breathing with the usual treatment. I have received information and explanations about this research, had the opportunity to ask questions, and received satisfactory answers. I have had sufficient time to read and understand the information in the participant information sheet thoroughly. Additionally, I have had enough time to decide whether to participate in this research, and **I have allowed a relative to be present as a witness to this decision.**

I understand that I can freely refuse to participate in this research, and I can withdraw from the study at any time without affecting my care or rights.

By signing this document, I do not waive any rights I may have under the law. After signing, I will receive a copy of the information and the consent form for my records.

Participant signature _____ Date/Month/Year _____
(_____)

Participant's relative signature_____ Date/Month/Year _____
(_____)

<u>Special situation</u>: In case the participant cannot read the document but understands it through listening.

"I am unable to read the document, but the researcher has read the information in the participant information sheet, and I consent to this agreement after understanding it thoroughly. I willingly sign or provide my fingerprint on this document."

Signature/Thumbprint of the participant. _____

(_____)

Date/Month/Year_____

<u>Special situation</u>: In the case of requiring consent from a direct relative of the participant.

"I, Mr./Ms./Miss..... [Name of the Relative], who is a direct relative of Mr./Ms./Miss..... [Participant's Full Name], in the capacity of.....[Relationship], have been informed about the details of the research project, as well as the benefits and risks that may occur to the research participant from the researcher, clearly and transparently, with nothing hidden or concealed. I willingly give consent for the research to be conducted in the aforementioned project. I am aware that if there are problems or questions, I can ask the researcher, and **I have the option to withdraw the research participant from this project at any time without affecting the standard treatment received by the research participant.** Additionally, the researcher will keep the participant's information confidential and will only disclose it in a summarized form when necessary for academic reasons.

Signature/Thumbprint of the relative participant. _____

(_____)

Date/Month/Year_____

Witness Certification of Non-involved Person in Research

I, the undersigned, have participated in the process of obtaining informed consent and confirm that the person requiring consent has read/explained the information to_____. The individual named above had the opportunity to ask various questions and has provided consent to participate in the research voluntarily, having been informed of the information presented in this document.

Witness signature _____ Date/Month/Year _____

(_____)

Signature of the person requesting consent_____

(_____)

Date/Month/Year_____