Midodrine for the Early Liberation of Vasopressor Support in the ICU (LIBERATE Multi-Site)

ClinicalTrials.gov Identifier: NCT05058612

Recruitment Status : Recruiting

First Posted : September 28, 2021

Last Update Posted : September 28, 2021

See **Contacts and Locations**

Sponsor:

University of Alberta

Collaborators:

University Hospital Foundation

Institute of Health Economics, Canada

Alberta Health Services

Information provided by (Responsible Party):

University of Alberta

Study Description

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Brief Summary:

Vasopressors are medications that are given intravenously to increase the blood pressure of patients with illnesses that cause dangerous blood pressure drops. When a doctor prescribes a vasopressor, they ask that the dose be adjusted to achieve a specific blood pressure. This kind of medical support with intravenous (IV) vasopressors are usual treatments in intensive care unit (ICU) settings. Oral vasopressors, such as midodrine, have been historically used to maintain blood pressure in non-critically ill patients. In this study, the investigators will be using midodrine to reduce the need for IV vasopressors as blood pressure improves during the stay in the ICU.

The LIBERATE multi-site study will continue the work of the pilot study to evaluate the role of midodrine for patients with low blood pressure in the ICU.

Condition or disease	Intervention/treatment	Phase
Vasoplegia	Drug: Midodrine Drug: Placebo	Phase 4

Detailed Description:

Purpose: Resuscitation and hemodynamic support with intravenous (IV) vasopressors is a prime indication of treatment in intensive care unit (ICU) settings. Hemodynamic support is typically provided with intravenous (IV) vasopressors. However, these have been shown to have significant negative effects including increased central venous catheter line associated infections, venous thromboembolic disease, impaired mobility and gastrointestinal injury and ischemia. Oral vasopressors, such as midodrine, have been historically used for hemodynamic support in non-critically ill patients, but their study in patients as IV pressor sparing therapy has been limited.

Hypothesis: to evaluate the expanded role of midodrine for any vasoplegic patients in the ICU.

Justification: In 2018, there were 1,613 admissions to the adult general systems ICU (GSICU) at the University of Alberta Hospital (UAH). Patients were sick, with a mean Acute Physiology and Chronic Health Evaluation II (APACHE) score of 21.3, with 36.4% requiring vasopressors on admission, accounting for 1942 patient-days (data from eCritical TRACER database). In the environment strained healthcare resources and limited ICU capacity, the ability to safely wean patients from IV vasopressors with transition to oral hemodynamic supporting agents would greatly improve how patients navigate through the healthcare system. This in turn will improve patient-centered case.

Primary Objective:

To compare the effect of enteral midodrine vs. placebo in critically ill patients with vasoplegia receiving continuous IV vasopressor therapy on ICU length of stay.

Secondary Objectives: To compare the effect of enteral midodrine vs. placebo on: Total and post-hospital length of stay, Duration of IV vasopressor support, 90-day all-cause mortality, Rates of ICU re-admission, Rate of re-initiation of IV vasopressors.

Tertiary Objectives: To determine the health economic effects of the usage of midodrine vs placebo on: ICU costs, Hospital costs, Total healthcare costs, Cost-effectiveness.

Safety Endpoints: Adverse drug reactions, Serious adverse drug reactions, Suspected unexpected serious adverse reactions.

Research Method/Procedures: The LIBERATE Trial is a multi center, concealed-allocation parallel-group blinded randomized controlled trial. Patients will be randomly assigned to midodrine (enteral, 10mg every 8h) or placebo (microcrystalline cellulose) for the duration of their IV vasopressor therapy and 24h following the discontinuation of their IV vasopressor therapy. The recruitment target is 350 patients (i.e., 175 patients per arm) with full follow-up.

Study Design

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Study Type :

Interventional (Clinical Trial)

Estimated Enrollment :

350 participants

Allocation:

Randomized

Intervention Model:

Parallel Assignment

Masking:

Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)

Primary Purpose:

Treatment

Official Title:

Midodrine for the Early Liberation From Vasopressor Support in the ICU - The LIBERATE Multi-Site Study

Actual Study Start Date :

March 22, 2021

Estimated Primary Completion Date :

December 2023

Estimated Study Completion Date :

March 2024

Resource links provided by the National Library of Medicine

Drug Information available for: Midodrine Midodrine hydrochloride

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: Midodrine Midodrine 10 mg PO/NG q8h	Drug: Midodrine 10 mg PO/NG q8h
Placebo Comparator: Placebo Microcrystalline cellulose PO/NG q8h	Drug: Placebo Microcrystalline cellulose PO/NG 18h

Outcome Measures

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Primary Outcome Measures :

1. ICU length of stay [Time Frame: 1 year]

   The total duration of patient stay in ICU

Secondary Outcome Measures :

1. Total and post-ICU length of stay [Time Frame: 1 year]

   The total duration of patient stay in hospital and the duration of hospital stay after ICU discharge

2. Duration of vasopressor support [Time Frame: 1 year]

   Duration of intravenous vasopressor support

3. Mortality [Time Frame: up to 90 days]

   All cause mortality within 90 days of study recruitment

4. ICU readmission [Time Frame: 1 year]

   Rate of ICU re-admissions during the index hospitalization

5. Re-initiation of vasopressors [Time Frame: 1 tear]

   Rate of re-initiation of intravenous vasopressors during ICU stay

6. ICU costs [Time Frame: 1 year]

   Total cost of ICU stay

7. Hospital costs [Time Frame: 1 year]

   Total cost of hospital stay

8. Total health care costs [Time Frame: 1 year]

   Total healthcare costs

9. Cost effectiveness [Time Frame: 1 year]

   Incremental costs and effectiveness based on ICU lengths of stay and average daily ICU costs

Eligibility Criteria

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Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:

18 Years and older (Adult, Older Adult)

Sexes Eligible for Study:

All

Accepts Healthy Volunteers:

Yes

Criteria

Inclusion Criteria:

- Age > 18 years
- Ongoing vasopressor support
- Decreasing vasopressor dose(s)

Exclusion Criteria:

- Greater than 24 hours from peak vasopressor dose
- Contraindication to enteral medications
- Previously received midodrine in last 7 days
- Expected death or anticipated withdrawal of life-sustaining therapies in next 24 hours
- Pregnancy
- Known allergy to midodrine

Contacts and Locations

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Information from the National Library of Medicine

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Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT05058612***

Contacts

Contact: Dawn Opgenorth, RN 780 492-4698 dawno@ualberta.ca

Contact: Oleksa **Rewa**, MD 780 492-6621 rewa@ualberta.ca

Locations

Canada, Alberta

University of Alberta Hospital **Recruiting**

Edmonton, Alberta, Canada, T5R 0T1

Contact: Dawn Opgenorth, RN 780 492-4698 dawno@ualberta.ca

Contact: Oleksa **Rewa**, MD 780 492-6621 rewa@ualberta.ca

Sponsors and Collaborators

University of Alberta

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Alberta Health Services

Investigators

Principal Investigator: Oleksa **Rewa**, MD University of Alberta

More Information

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Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Opgenorth D, Baig N, Fiest K, Karvellas C, Kutsogiannis J, Lau V, Macintyre E, Senaratne J, Slemko J, Sligl W, Wang X, Bagshaw SM, Rewa OG. LIBERATE: a study protocol for midodrine for the early liberation from vasopressor support in the intensive care unit (LIBERATE): protocol for a randomized controlled trial. Trials. 2022 Mar 4;23(1):194. doi: 10.1186/s13063-022-06115-0.

Responsible Party:

University of Alberta

ClinicalTrials.gov Identifier:

NCT05058612 History of Changes

Other Study ID Numbers:

Pro00112293

First Posted:

September 28, 2021 Key Record Dates

Last Update Posted:

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Last Verified:

September 2021

Studies a U.S. FDA-regulated Drug Product:

No

Studies a U.S. FDA-regulated Device Product:

No

Keywords provided by University of Alberta:

critical care medicine
intensive care
shock
midodrine

Additional relevant MeSH terms:

Vasoplegia
Vascular Diseases
Cardiovascular Diseases
Postoperative Complications
Pathologic Processes
Midodrine
Sympathomimetics
Autonomic Agents
Peripheral Nervous System Agents
Physiological Effects of Drugs
Vasoconstrictor Agents
Adrenergic alpha-1 Receptor Agonists
Adrenergic alpha-Agonists
Adrenergic Agonists
Adrenergic Agents
Neurotransmitter Agents
Molecular Mechanisms of Pharmacological Action