Spanish and Irish study of lithium toxicity and extracorporeal removal (SILITOX Study)

First published: 15/02/2023

Last updated: 15/07/2024

Study Finalised

Administrative details

EU PAS number

EUPAS103542

Study ID

103543

DARWIN EU® study

No

Study countries

Ireland

Spain

Study description

Lithium's narrow therapeutic index continues to make it a difficult drug to manage, and its potential toxicity a major concern when indicated. The goals of

treatment of lithium poisoning are to prevent death and to avoid lithium irreversible neurotoxicity syndrome (SILENT). Treatment of lithium toxicity includes fluid therapy to correct hypovolaemia and increase renal elimination of lithium (even in states of euvolemia), digestive decontamination in certain circumstances, and haemodialysis in cases of severe toxicity. Haemodialysis is the treatment of choice for severe lithium toxicity, as it is easily dialysable due to its low molecular weight, negligible protein binding and small volume of distribution. According to the recommendations of the EXTRIP workgroup the decision on when to use extracorporeal therapy should take into account Li+, renal function, the patient's clinical situation (symptoms of lithium toxicity) and the availability of extracorporeal therapy. Although this treatment and its indications are well defined, the degree of application of these renal replacement therapies remains controversial. In this context, a retrospective observational multicentre international study is proposed to evaluate the degree of adherence to the current EXTRIP recommendations regarding renal replacement therapies in the treatment of lithium poisoning, as well as to determine predictors of mortality and hospital stay at 30 days and the incidence of the development of irreversible lithium neurotoxicity (SILENT) at ICU discharge, hospital discharge and at 60 days.

Study status

Finalised

Research institutions and networks

Institutions

Clinical Pharmacology Service, Puerta de Hierro-Majadahonda University Hospital (HUPHM)

Spain

First published: 26/12/2012

Last updated: 20/08/2024

Institution | Educational Institution | Hospital/Clinic/Other health care facility

Clinical Pharmacology Service, Puerta de Hierro-Majadahonda University Hospital (HUPHM)

Spain

First published: 26/12/2012

Last updated: 20/08/2024

Institution | Educational Institution | Hospital/Clinic/Other health care facility

Hospital Universitario Son Espases Spain, Hospital Clinic de Barcelona Spain, Hospital Sant Joan Despí Spain, Hospital del Mar Spain, Hospital Universitario Dr. Josep Trueta Spain, Mater Misericordiae University Hospital Ireland

Contact details

Study institution contact

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Primary lead investigator

Belen Ruiz-Antoran

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 13/02/2023

Actual: 13/02/2023

Study start date

Planned: 01/03/2023

Actual: 14/02/2023

Data analysis start date

Planned: 01/06/2023

Actual: 14/02/2023

Date of interim report, if expected

Planned: 01/08/2023

Actual: 14/02/2023

Date of final study report
Planned: 01/10/2023

Actual: 14/02/2023

Sources of funding

- Other

More details on funding

The study is not funded

Study protocol

SILITOX Study Protocol 07_feb_2023.pdf (247.69 KB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Other

If ‘other’, further details on the scope of the study

To compare the degree of adherence to current recommendations (EXTRIP criteria) on the management of lithium poisoning

Data collection methods:

Secondary use of data

Main study objective:

To compare the degree of adherence to current recommendations (EXTRIP criteria) on the management of lithium poisoning in the participating centres. Others objectives: - To determine the effectiveness of renal replacement techniques - To quantify the incidence of patients with SILENT - To describe different clinical or analytical predictors of severity

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Multicentre retrospective observational international study

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(N05AN) Lithium

Lithium

Medical condition to be studied

Toxicity to various agents

Population studied

Short description of the study population

Patients aged 18 years or older diagnosed with lithium poisoning identified from 2012 to 2022.

Age groups

- Adults (18 to < 46 years)
- Adults (46 to < 65 years)
- Adults (65 to < 75 years)
- Adults (75 to < 85 years)
- Adults (85 years and over)

Special population of interest

Other

Special population of interest, other

Patients with lithium poisoning

Estimated number of subjects

150

Study design details

Outcomes

Variables to establish adherence to EXTRIP recommendations. - Percentage of patients treated with RRT meeting EXTRIP criteria. - Percentage of patients treated with RRT who do not meet the EXTRIP criteria. - Percentage of patients not treated with RRT meeting EXTRIP criteria. - Percentage of patients not treated with RRT who do not meet the EXTRIP criteria. -Percentage of patients developing SILENT at 60 days follow-up. -Percentage of patients who die by day 30. -Percentage of patients discharged by day 30. -Percentage of patients with symptoms suggestive of SILENT at discharge from ICU and/or hospital. -Total days of stay in ICU/ of hospital stay.

Data analysis plan

Descriptive analysis will be performed for all study variables, with appropriate analyses depending on the nature of each of the variables: The incidence in exposed (cohort treated with renal replacement therapy) and unexposed (untreated cohort) individuals will be calculated for each of the effectiveness variables listed above.) From these, measures of association will be calculated for each of the variables: relative risk (RR), absolute risk reduction (ARR) and relative risk reduction (RRR), with their 95% CIs. Different hypothesis tests will be applied depending on the nature of the variable. These tests are: Fisher's

exact test for categorical variables, Student's t-test for continuous variables and Mann-Whitney U-test for ordinal variables. Logistic regression models will be used to identify predictors of non-response and serious adverse events. Multivariate stepwise logistic regression analysis will be used to identify any independent baseline predictors.

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data sources (types)

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No