ISRCTN16586164 https://doi.org/10.1186/ISRCTN16586164

PLUTO: A randomised clinical trial comparing PlasmaLyte fluid to standard care for children receiving a kidney transplant

Submission date
20/12/2019

Recruitment status
No longer recruiting

Registration date
10/01/2020

Overall study status
Completed

Last Edited
14/12/2023

Condition category
Injury, Occupational Diseases, Poisoning

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
In the first few days after a kidney transplant, many children develop dangerous changes in the amount of salt and water in the bloodstream. This is because doctors give very large volumes of artificial fluids into the veins to keep the new kidney working. If the main salt in the blood (sodium) falls too far, serious problems including brain damage and even death can occur. Because of this, blood samples are taken every 2-4 hours for the first day after the transplant operation to check sodium levels and change them if necessary.
This research aims to compare the standard fluid used after the transplant operation with an alternative that may reduce dangerous changes in salt (sodium) levels and help the transplanted kidney to work better.
The alternative fluid is called PlasmaLyte. It matches the normal composition of blood more closely than standard fluid. PlasmaLyte is already used in other sick children, including those in intensive care units. Although there are good reasons to believe that PlasmaLyte may be a safer choice of fluid for children after kidney transplant, there is no evidence comparing PlasmaLyte with standard fluid for children.

Who can participate?
Patients aged under 18 years receiving a kidney transplant

What does the study involve?
This research will work out which of the two fluids is better by looking at children's kidney transplants in the UK, half using standard fluid and half using PlasmaLyte. The choice of fluid will be made randomly by a computer. No additional blood samples will be required. Children who participate in the study will continue to have all the usual care that they would otherwise receive.

What are the possible benefits and risks of participating?
This research has the potential to improve the treatment and outcomes of children and young people receiving kidney transplants. Plasma-Lyte may reduce the risk of developing abnormalities in salt (sodium) levels after a transplant operation. Plasma-Lyte may also help the transplanted kidney to work better, but at present, we do not know if this will be the case. The

PLUTO study will help to find out whether Plasma-Lyte is better than current standard care. There are few risks to taking part in this study (above the risk of kidney transplantation). Abnormal levels of salts and minerals in the bloodstream can be experienced by children and young people receiving any fluid. We do not expect these to be more common with Plasma-Lyte but will monitor all children's blood levels closely to check for this.

Where is the study run from?
1. NHS Blood and Transplant Clinical Trials Unit, UK
2. Belfast City Hospital, UK
3. Birmingham Women's and Children's NHS Foundation Trust, UK
4. University Hospitals Bristol NHS Foundation Trust, UK
5. Great Ormond Street Hospital, UK
6. Guy's and St Thomas' NHS Foundation Trust, UK
7. Leeds Teaching Hospitals NHS Trust, UK
8. Manchester University NHS Foundation Trust, UK
9. The Newcastle Upon Tyne Hospitals NHS Foundation Trust, UK
10. Nottingham University Hospitals NHS Trust, UK

When is the study starting and how long is it expected to run for?
February 2020 to November 2022

Who is funding the study?
National Institute for Health Research (NIHR), UK

Who is the main contact?
Fotini Kaloyirou (public)
PLUTO@nhsbt.nhs.uk
Dr Wesley Hayes (scientific)
wesley.hayes@gosh.nhs.uk

Contact information

Type(s)
Public

Contact name
Ms Fotini Kaloyirou

ORCID ID
https://orcid.org/0000-0001-7290-6934

Contact details
NHSBT Clinical Trials Unit
Long Road
Cambridge
United Kingdom
CB2 0PT
+44 (0)7385 388072
fotini.kaloyirou@nhsbt.nhs.uk

Type(s)

Scientific

Contact name
Dr Wesley Hayes

Contact details
Great Ormond Street Hospital
London
United Kingdom
WC1N 3JH
+44 (0)7522217511
wesley.hayes@gosh.nhs.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2019-003025-22

Integrated Research Application System (IRAS)
270431

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
18IA31; CPMS 43031; IRAS 270431

Study information

Scientific Title
PlasmaLyte Usage and assessment of kidney Transplant Outcomes in children: the PLUTO trial

Acronym
PLUTO

Study objectives
To determine whether the incidence of abnormal and potentially dangerous plasma electrolyte levels in paediatric kidney transplant recipients will be different with the use of Plasma-Lyte-148 compared to intravenous fluid with current standard composition

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/12/2019, London Central Research Ethics Committee (Health Research Authority, Skipton House, 80 London Road, London, SE1 6LH; +44 (0)207 104 8208; NRESCommittee.London-Central@nhs.net), ref: 19/LO/1866

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Prevention of hyponatremia in children undergoing kidney transplant

Interventions
SCREENING
All paediatric patients awaiting kidney transplantation will be screened for participation in PLUTO. Data will be collected on the Patient Log. Also as part of this study, a Qualitative Sub-Study will be undertaken to find out more about patients/families opinions of the screening and consent process. To facilitate this, all patients/families who are given the study information sheet will also be given a short questionnaire to complete (whether or not they decide to participate).
The screening data will be regularly reviewed by the Trial Management Group, as well as feedback from the process evaluation.

RANDOMISATION
Informed consent will take place during the pre-transplant preparation period, which typically takes several months. This will allow adequate time for patients and families to consider participating in the study. Randomisation will take place on the day of the transplant (after study consent is re-confirmed verbally by a member of the clinical or Research Team). Participants will be randomised using an online randomisation service, called SealedEnvelope, and given a unique Randomisation Number. The treatment allocation will also be provided and communicated to all relevant members of the clinical care team at that site.

TREATMENT
The study treatment is Plasma-Lyte 148 (+/- 5% glucose). This will be compared to standard intravenous fluid therapy. Standard therapy varies across the participating sites, which will be accounted for in the trial analysis. The fluid will be administered as required throughout the operation and for 72 hours afterwards as per routine clinical care.

FOLLOW-UP OF PARTICIPANTS
Patients will be reviewed as per standard clinical care. Data will be collected for the trial (e.g. results of blood tests taken as part of standard clinical care). A symptom assessment will be carried out once daily (for 3 days) for headaches, nausea, vomiting and seizures. A proportion of the follow-up data will be obtained the routinely collected data (on the UK Transplant Registry, which is held by NHS Blood and Transplant). No additional study visits or blood tests outside routine clinical care will be required for the trial.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)

Plasma-Lyte 148 & Glucose 5% w/v

Primary outcome(s)
Acute hyponatraemia in the first 72 hours post-transplant (defined as plasma sodium concentration < 135mmol/l)

Key secondary outcome(s))
1. Symptoms of acute hyponatraemia (nausea, vomiting, headache, seizures) within the first 72 hours post-transplant
2. The degree of fluid overload experienced (defined as proportional increase in patient weight between pre-transplant weight and maximum weight in the 72 hours post-transplant weight)
3. Time to discharge from hospital (measured from transplant operation start time ("knife to skin")), measured in days
4. Transplant kidney function at 1, 3, 7 and 90 days (using creatinine-based univariate Schwartz formula(24) to determine eGFR)
5. Other electrolyte abnormalities within the first 72 hours post-transplantation:
5.1. Hypernatraemia (defined as plasma sodium concentration > 145mmol/l)
5.2. Hyperkalaemia (defined as plasma potassium concentration > 5.5mmol/L)
5.3. Hypokalaemia (defined as plasma potassium concentration < 3.5mmol/L)
5.4 Non anion-gap acidosis (defined as plasma bicarbonate < 20mmol/L and anion gap < 20mmol/L)
5.5. Hyperglycaemia (defined as random blood glucose > 5.5 mmol/L)
5.6. Hypomagnesaemia (defined as plasma magnesium concentration < 0.7 mmol/L)
5.7. Hyperchloraemia (defined as plasma chloride concentration > 107mmol/L)
5.8. Excessive rate of reduction in plasma sodium concentration (defined as >1mmol/L/hour averaged over 6 hours)
5.9. Excessive magnitude of reduction in plasma sodium concentration (defined as > 10mmol/L from pre-transplant level)
6. Maximum and minimum systolic blood pressure (normalised to age and height percentile) sustained on 3 repeated values on each day, for 3 days post-transplant
7. Number of changes in intravenous fluid composition and rationale for change within the first 72 hours post-transplant

Completion date
17/11/2022

Eligibility

Key inclusion criteria
1. Children expected to be under 18 years of age at the time of transplantation
2. Children undergoing preparation for living or deceased donor kidney only transplantation, or active on the deceased donor transplant waiting list for a kidney only transplant at participating UK paediatric transplant centres either pre-emptively (not currently receiving dialysis) or patients on dialysis

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Upper age limit
18 years

Sex
All

Total final enrolment
144

Key exclusion criteria
1. Multi-organ transplant recipients

Date of first enrolment
03/02/2020

Date of final enrolment
09/08/2022

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Study participating centre
NHS Blood and Transplant Clinical Trials Unit (lead centre)
Long Road
Cambridge
United Kingdom
CB2 0PT

Study participating centre
Belfast City Hospital
51 Lisburn Road
Belfast
United Kingdom
BT9 7AB

Study participating centre

Birmingham Women's and Children's NHS Foundation Trust
Steelhouse Lane
Birmingham
United Kingdom
B4 6NH

Study participating centre
University Hospitals Bristol NHS Foundation Trust
Trust Headquarters
Marlborough Street
Bristol
United Kingdom
BS1 3NU

Study participating centre
Great Ormond Street Hospital
Great Ormond Street
London
United Kingdom
WC1N 3JH

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre
Leeds Teaching Hospitals NHS Trust
St. James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Manchester University NHS Foundation Trust
Cobbett House
Oxford Road
Manchester

United Kingdom
M13 9WL

Study participating centre
The Newcastle Upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Sponsor information

Organisation
Great Ormond Street Hospital for Children NHS Foundation Trust

ROR
https://ror.org/03zydm450

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: NIHR200512

Funder Name
National Institute for Health Research (NIHR) (UK)

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from the PLUTO Trial Manager (PLUTO@nhsbt.nhs.uk) or the PLUTO Chief Investigator Dr Wesley Hayes (wesley.hayes@gosh.nhs.uk).
The type of data: full dataset, anonymised.
When the data will become available and for how long: no later than 18 months after the last participant has been recruited.
By what access criteria data will be shared including with whom: submit a request to the CI/Trial Manager for review by the Sponsor. A full Data Sharing Request form will be required.
For what types of analyses, and by what mechanism: to be agreed before data is shared
Whether consent from participants was obtained: full informed consent obtained
Comments on data anonymisation: data will be anonymised prior to sharing
Any ethical or legal restrictions: none
Any other comments: a contract is mandatory before any data is shared with a third party

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		31/10/2023	05/12/2023	Yes	No
Protocol article	protocol	14/03/2022	25/03/2022	Yes	No
HRA research summary			28/06/2023	No	No
Statistical Analysis Plan	version 1.1	20/12/2022	14/12/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes