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Perioperative use of crystalloids in patients undergoing open radical cystectomy: balanced Ringers maleate vs G5-K solution

Submission date
30/10/2013

Recruitment status
No longer recruiting

Registration date
21/11/2013

Overall study status
Completed

Last Edited
14/08/2020

Condition category
Urological and Genital Diseases

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Infections of the bladder (cystitis) can affect the bladder, kidney and the connecting tubes. Sometimes this require a cystectomy, which a surgery to remove all or part of the bladder, requiring urinary diversion (the urine is flow is changed). When patients undergo a cystectomy, they are prone to having issues with their salt and water balance. They often require hydration during the surgery and while in hospital, but the choice of what the optimal crystalloid solution (ie. The balance of water and salt) is still unclear. In addition, it has been demonstrated that the influence of salt and water balance on gastrointestinal recovery after colonic surgery is clinically relevant: patients receiving less fluid and less sodium show faster recovery of gastrointestinal function, resulting in a shorter hospitalization time. This is of crucial importance in cystectomy patients because they are at risk for postoperative constipation (not able to pass stool regularly) or ileus (buildup or blockages in the bowels). The aim of this study is so evaluate the physiology of electrolyte and water homeostasis in patients undergoing open cystectomy with urinary diversion using two different fluid regimes.

Who can participate?
Adults aged 18 and older who have cystectomy with urinary diversion

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive the Ringerfundin solution. Those in the second group receive the G5-K crystalloid solution at baseline, and during the operation. After the surgery, they receive the same type of hydration. Blood samples are taken prior to the surgery and at six hours after the surgery, as well as days one, two, three and four after the surgery.

What are the possible benefits and risks of participating?
Not provided at time of registration.

Where is the study run from?
University Hospital of Bern (Switzerland)

When is the study starting and how long is it expected to run for?
December 2013 to June 2015

Who is funding the study?
University Hospital of Bern (Switzerland)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
151/13

Study information

Scientific Title
Perioperative use of crystalloids in patients undergoing open radical cystectomy: balanced Ringers maleate vs G5-K solution - a randomized clinical trial

Study objectives
We hypothesize that an approach with glucose-potassium-based and less chloride crystalloid solution will result in a faster return of bowel function, less hypernatriemia and hyperchloremic metabolic acidosis with less frequent hyper-osmolality and a better maintained fluid balance compared to a regimen with a balanced Ringer's crystalloid solution.

On 09/06/2015 the overall trial date was changed from 31/12/2016 to 09/06/2015.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of the Canton of Bern (Kantonale Ethikkommission), Berne, Switzerland, 22/10/2013, ref: 151/13

Study design
Randomized parallel-group single-centre interventional assessor blind trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Bladder disease resulting in cystectomy and urinary diversion

Interventions
According to the randomization, an equal number of patients will be allocated to receive the Ringerfundin® solution or the G5-K crystalloid solution as baseline infusion during the whole time that an intravenous administration of fluid is necessary. The G5-K solution is already used as a baseline infusion on our intensive care unit and has been shown to be safe.

Intraoperatively: After induction of anesthesia, a concomitant norepinephrine infusion will be started at 2 µg·kg-1·h-1 until the end of surgery and the randomized crystalloid solution (Ringerfundin®, B.Braun Medical AG, Sempach), Switzerland for group 1 or the G5-K solution for group 2 (Bichsel, Interlaken, Switzerland) will be infused at a rate of 1 ml·kg-1·h-1 until the bladder has been removed, followed by 3 ml·kg-1·h-1 until the end of surgery. If hypotension is observed (mean arterial pressure (MAP) <60 mmHg), norepinephrine will be titrated to maximum 8 µg·kg-1·h-1 after an initial bolus of 10 µg. If hypotension persists; a bolus of 250 ml of randomized crystalloid solution will be given.
In both groups, a blood loss >500 ml will be substituted with an equal amount of balanced Ringer s solution (Ringerfundin®). Packed red blood cells (PRBC) will be transfused if hemoglobin values are <80 g/l (<100 g/l in patients with coronary artery disease). Additional boluses of Ringerfundin® (250 ml) will be infused as a rescue medication if a MAP <60 mmHg persists after the above mentioned correction, and in case of severe intraoperative metabolic acidosis (base excess <-5, pH <7.25) attributable to severe hypovolemia.

Postoperatively: Postoperative hydration will be identical in both groups and will consist primarily of 1500 ml of the randomized crystalloid solution per 24 hours. If the MAP is <60 mmHg after a bolus of 500 ml of balanced Ringers solution, norepinephrine will be infused up to a rate of 200 µg/h in both groups. PRBC units will be transfused according to the ASA guidelines and fresh frozen plasma units will be given if the prothrombin time is >1.5 times normal values. In both groups, patients will be allowed to drink clear fluids immediately after surgery on the intermediate care unit. A peroral liquid diet will be started on POD 1 as well as active mobilization. To enhance recovery of bowel function, the use of chewing gum will be encouraged and the subcutaneous application of neostigmine 0.5 mg will be started on POD 2. Body weight will be measured daily in the morning. Time of first flatus and first defecation will be recorded.

Time course of the study:
Admission day: After informed consent, patients undergoing open radical cystectomy with urinary diversion will be randomized, according to the concealed numbered envelopes. Preoperative blood samples will be taken (plasma samples: Na, K, Cl, Mg, HPO4, Glc, osmolality, renin, aldosterone, arginin-vasopressin, BNP; urine NGAL, Na, Cl and osmolality) and body weight documented. Patients included will be informed to note the time of the first flatus and to inform the nurses accordingly.
6 h postoperative: Blood samples will be taken (arterial blood gas analysis, plasma samples: Na, K, Cl, Mg, HPO4, Glc, osmolality, renin, aldosterone, arginine-vasopressin, BNP; urine: NGAL, Na, Cl and osmolality).
Postoperative day 1: Blood samples will be taken (arterial blood gas analysis, plasma samples: Na, K, Cl, Mg, HPO4, Glc, osmolality, renin, aldosterone, arginine-vasopressin, BNP; urine: NGAL, Na, Cl and osmolality). Body weight and assessment of flatus and defecation will be documented.
Postoperative day 2: Blood samples will be taken (arterial blood gas analysis, plasma samples: Na, K, Cl, Mg, HPO4, Glc, osmolality, renin, aldosterone, arginine-vasopressin, BNP; urine: NGAL, Na, Cl and osmolality). Body weight and assessment of flatus and defecation will be documented.
Postoperative day 3: Blood samples will be taken (arterial blood gas analysis, plasma samples: Na, K, Cl, Mg, HPO4, Glc, osmolality, renin, aldosterone, arginine vasopressin, BNP; urine samples: NGAL, Na, Cl and osmolality). Body weight and assessment of flatus and defecation will be documented.
Postoperative day 4: Blood samples will be taken (arterial blood gas analysis, plasma samples: Na, K, Cl, Mg, HPO4, Glc, osmolality, renin, aldosterone, arginine vasopressin, BNP; urine samples: NGAL, Na, Cl and osmolality). Body weight and assessment of flatus and defecation will be documented.

Added 11/09/2014: the trial is now recruiting participants.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Ringerfundin, G5-K crystalloid solution

Primary outcome measure
First defecation (return of bowel function) postoperatively

Secondary outcome measures
1. First flatus
2. Positive fluid balance (body weight difference postoperatively vs preoperatively)
3. Incidence of kidney function disorders according to the RIFLE classification
4. Difference in pH 24 h postoperatively (metabolic acidosis defined as hyperchloremia, normal anion gap, low plasma bicarbonate)
5. Changes in plasma and urine osmolality during the duration of infusion
6. Incidence of hypernatriemia during the duration of infusion
7. Incidence of hyperchloremia during the duration of infusion
8. Incidence of hypokaliemia during the duration of infusion
9. Changes in plasma renin, aldosterone, arginin vasopressin and brain natriuretic peptide (BNP) levels
10. Changes in neutrophil gelatinase-associated lipocalin (NGAL) urine values

Overall study start date
01/12/2013

Completion date
09/06/2015

Eligibility

Key inclusion criteria
1. Aged 18 years or over
2. Cystectomy with urinary diversion
3. American Society of Anaesthesiologists (ASA) classification II and III
4. Informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
44

Total final enrolment
44

Key exclusion criteria

1. Pregnant, breastfeeding women (exclusion for surgery per se)
2. Congestive heart failure [New York Heart Association (NYHA) classification ≥3]
3. Hepatic disease (prothrombin ratio <50%)
4. Significant renal dysfunction (estimated glomerular filtration rate <45 ml/min)

Date of first enrolment
14/07/2014

Date of final enrolment
26/05/2015

Locations

Countries of recruitment
Switzerland

Study participating centre
University Hospital Bern Inselspital Bern
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Sponsor information

Organisation
Bern University Hospital (Switzerland)

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/01q9sj412

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Bern University Hospital (Switzerland) - Department of Urology and Anesthesiology / Pain Treatment

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	08/07/2014		Yes	No
Results article	results	01/10/2016	14/08/2020	Yes	No