

A Double-Blind, Randomized Control Trial of Rapidly Infused High Strong Ion Difference Fluid versus Hartmann's solution on Acid-Base Status in Sepsis and Septic Shock Patients in the Emergency Department Hospital Pulau Pinang

Protocol number: ED-HPP-1701 (15th Jan 2017)
NCT number: NCT03530046

PARTICIPANT INFORMATION SHEET AND INFORMED CONSENT FORM

1. **Title of study:** A Double-Blind, Randomized Control Trial of Rapidly Infused High Strong Ion Difference (SID) Fluid versus Hartmann's Solution on Acid-Base Status in Sepsis and Septic Shock Patients in the Emergency Department Hospital Pulau Pinang
2. **Name of investigator and institution:**
 - i. Yeoh Chun Chiat, Emergency Physician Trainee, Emergency Department, Hospital Pulau Pinang.
 - ii. Teo Aik Howe, Consultant Emergency Physician, Emergency Department, Hospital Pulau Pinang
 - iii. Sasi Kumar A/L Sappanie, Senior Medical Officer, Emergency Department, Hospital Pulau Pinang.
 - iv. Sherene Tan Su Ann, Pharmacist, Pharmacy Department, Hospital Pulau Pinang.
 - v. Abdul Muhaimin bin Noor Azhar, Emergency Physician and Lecturer, Emergency Department, University of Malaya
3. **Name of sponsor:** Self funded.

4. Introduction:

You are invited to participate in a research study because you are suspected to have a severe infection in your body that requires a high volume of fluid to bring up your blood pressure. The details of the research trial are described in this document. It is important that you understand why the research is being done and what it will involve. Please take your time to read through and consider this information carefully before you decide if you are willing to participate. Ask the study staff if anything is unclear or if you like more information. After you are properly satisfied that you understand this study, and that you wish to participate, you must sign this informed consent form. To participate in this study, you may be required to provide your doctor with information on your health history; you may harm yourself if you are not truthful with the information provided.

Your participation in this study is voluntary. You do not have to be in this study if you do not want to. You may also refuse to answer any questions you do not want to answer. If you volunteer to be in this study, you may withdraw from it at any time. If you withdraw, any data collected from you up to your withdrawal will still be used for the study. Your refusal to participate or withdrawal will not affect any medical or health benefits to which you are otherwise entitled.

This study has been approved by the Medical Research and Ethics Committee, Ministry of Health Malaysia.

5. What is the purpose of the study?

The purpose of this study is to review the different types of fluid for the treatment of resuscitation in bloodstream infection or shock patients. This research is necessary to determine whether, among patients with severe bloodstream infection or shock who needs

initial high volume of fluid to bring up the blood pressure, the use of high strong ion difference (SID) intravenous solution (one half-normal saline with addition of 75mEq/L sodium bicarbonate, SID = 75 mEq/L) as an early fluid choice, when compared with Hartmann's solution (SID = 28 mEq/L) is associated with greater change of your body acidic pH and low bicarbonate level towards normal body pH and bicarbonate level. According to literatures, correction of your body pH and bicarbonate level will result in better clinical outcomes. At the same time, this research will also be able to determine other associated clinical outcomes such as the mean difference in lactate level (which is a mineral present in high level if your body is severely infected), 30-day-mortality, development of lung congestion with fluid, the mean length stay in hospital and the incidence of acute kidney injury.

A total of 162 subjects like you will be participating in this study. The whole study will last about 1 year and your participation will be up to 30 days.

6. What kind of study products will I receive?

If you agree to participate in the study, the doctor may need to perform some tests and examinations to determine if you are suitable for the study. If you are deemed suitable, you will be randomly (by chance, like flipping a coin) assigned to one of the treatment groups below. You have equal chance of being assigned to each of the groups. Neither you nor the doctor will know which group you are assigned to but in case of emergencies, this information is available to your doctor.

The study products do not contain porcine, bovine or animal components.

Group 1 will receive the investigational regime which is 30ml/kg of IVD half-normal saline with addition of 75mEq/L sodium bicarbonate

Group 2 will receive 30ml/kg of IVD Hartmann's Solution.

7. What will happen if I decide to take part?

Approximately 5mls (about 1 teaspoon) of blood sample in total will be taken from you.

First 2.5mls (about ½ teaspoon) of blood sample for analysis of minerals in your body fluid, venous blood gas measurement at baseline before the initiation of study fluid (part of standard treatment).

When 30ml/kg of study fluid is administered or at 2 hours (whichever comes first), another 0.5mls (1/5 tea spoon) of blood sample for venous blood gas measurement will be taken (part of standard treatment).

Patients will subsequently be followed up in the ward for another 2mls (about 2/5 teaspoon) of blood sample within 48 hour (additional for study) and for all-cause mortality in 30 days (no blood taking).

At least one trained staff member will be available throughout the intervention period.

8. When will I receive the trial product and how should it be kept?

You will be given the study product only during the treatment period in the emergency department.

9. What are my responsibilities when taking part in this study?

It is important that you answer all of the questions asked by the study staff honestly and completely. If your condition or circumstances change during the study, you must tell the study doctor. There may be certain medications that you cannot take while participating in this study. The doctor will discuss those medications with you.

It is very important that your study doctor be informed very rapidly of any eventual changes to your health during your participation in the study. For your own security, it is important that you follow your study doctor's instructions throughout the entire duration of the study.

10. What kind of treatment will I receive after my participation in the trial?

No study product will be given to you at the end of your participation in the study. Whether you complete the study or withdraw early, your doctor will discuss the best alternatives for your future treatment with you.

11. What are the potential risks and side effects of being in this study?

All patients will receive the standard care of treatment by the physicians in emergency department. The rate of infusion, time of initiating antibiotics, medications needed for resuscitation will not be interfered by commencement of study fluid. There may be a chance of causing slight bruises or swelling during blood taking or study fluid entering into the surrounding tissues during administration. Supportive management will be given to minimize the damage should the risks occur. From the previous literatures, both study fluids are proven to be safe and beneficial to patients. High strong ion difference (SID) fluid is hypothesized to normalise the acidic blood pH faster and to the greater extend as compared to Hartmann's solution.

The effect of the study product on an unborn child is not known. Notify your study doctor immediately if you think that you or your partner is pregnant during the study. If you are pregnant, the study therapy will be discontinued immediately and you will be removed from the study.

Please ask your study doctor if you need more information on risks and side effects. The trial staff will inform you in a timely manner about any new findings or changes about the study product which may affect your health or willingness to continue in this study. Where necessary, you may be asked to reconsent to participate.

12. What are the benefits of being in this study?

There may or may not be any benefits to you. Information obtained from this study will help improve the treatment or management of other participants with the same disease or condition.

13. What if I am injured during this study?

Every effort will be taken by the study doctor to prevent any harm or injury due to this trial. If you are injured as a result of being in this study, you should contact your study doctor. An immediate medical therapy will be made available to you at your study hospital.

Regardless of this, if you wish to complain about any aspect of the way you have been approached or treated during the course of this study, the normal Health Service Complaint mechanism may be available to you.

By signing this form you have not given up any of your legal rights that you otherwise would have as a participant in a research.

14. What are my alternatives if I do not participate in this study?

You do not have to participate in this study to get treatment for your disease or condition. All patients will receive the standard care of treatment by the physicians in emergency department. The study doctor will discuss in more details the benefits and risks of those treatments with you.

15. Who is funding the research?

This study is an investigator-initiated study and thus, it is not sponsored by any companies. All other drugs and procedures that are not required by the study but are part of your routine medical care will have to be paid by you or your insurance.

16. Can the research or my participation be terminated early?

The study doctor may due to concerns for your safety, stop the study or your participation at any time. If the study is stopped early for any reason you will be informed and arrangements made for your future care. You may be asked to attend a final follow-up visit.

17. Will my medical information be kept private?

All your information obtained in this study will be kept and handled in a confidential manner, in accordance with applicable laws and/or regulations. When publishing or presenting the study results, your identity will not be revealed without your expressed consent. Individuals involved in this study and in your medical care, qualified monitors and auditors, governmental or regulatory authorities may inspect and copy your medical records, where appropriate and necessary.

Your blood sample will be sent to the laboratory in Hospital Pulau Pinang for testing. If this is required, your blood sample will be coded and information that can identify you will be removed. Only your study doctor and study staff will be able to link the code with you.

Data from the study will be archived and may be transmitted outside the country for the purpose of analysis, but your identity will not be revealed at any time.

With your permission/request, your family doctor may be informed of your participation in the study.

18. Will I be informed of the study findings?

You will not be informed of the study findings.

19. Will be given any prorated payment for reimbursement?

No payment will be given for reimbursement.

20. Who should I call if I have questions?

If you have any questions about the study or if you think you have a study related injury and you want information about treatment, please contact the study doctor, **Dr Yeoh Chun Chiat** at telephone number **019-9316939**.

If you have any questions about your rights as a participant in this study, please contact: The Secretary, Medical Research & Ethics Committee, Ministry of Health Malaysia, at telephone number 03-2287 4032.

INFORMED CONSENT FORM**A Double-Blind, Randomized Controlled Trial of Rapidly Infused High Strong Ion Difference (SID) Fluid versus Hartmann's Solution on Acid-Base Status in Sepsis and Septic Shock Patients in the Emergency Department Hospital Pulau Pinang**

By signing below I confirm the following:

- I have been given oral and written information for the above study and have read and understood the information given.
- I have had sufficient time to consider participation in the study and have had the opportunity to ask questions and all my questions have been answered satisfactorily.
- I understand that my participation is voluntary and I can at anytime free withdraw from the study without giving a reason and this will in no way affect my future treatment. I am not taking part in any other research study at this time. I understand the risks and benefits, and I freely give my informed consent to participate under the conditions stated. I understand that I must follow the study doctor's (investigator's) instructions related to my participation in the study.
- I understand that study staff, qualified monitors and auditors, and governmental or regulatory authorities, have direct access to my medical record in order to make sure that the study is conducted correctly and the data are recorded correctly. All personal details will be treated as STRICTLY CONFIDENTIAL
- I will receive a copy of this subject information/informed consent form signed and dated to bring home.
- I agree/disagree* for my family doctor to be informed of my participation in this study.
(*delete which is not applicable)

Subject/Representative:

Signature:

I/C number:

Name:

Date:

Investigator conducting informed consent:

Signature:

I/C number:

Name:

Date:

Impartial witness: *(Required if subject is illiterate and contents of participant information sheet is orally communicated to subject)*

Signature:

I/C number:

Name:

Date: