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The effectiveness of dapagliflozin versus furosemide in controlling blood pressure in resistant hypertension with subclinical fluid retention in chronic kidney disease

Submission date
28/12/2023

Recruitment status
No longer recruiting

Registration date
12/01/2024

Overall study status
Completed

Last Edited
06/11/2024

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
Chronic kidney disease (CKD) poses a significant health challenge, often accompanied by uncontrolled blood pressure (hypertension) that is difficult to manage. This study aims to address this issue by comparing the effectiveness of two medications, dapagliflozin and furosemide, in individuals with CKD and resistant hypertension. Dapagliflozin is known for its ability to lower blood pressure and promote urine excretion by affecting kidney function. Furosemide, a commonly used diuretic, is also prescribed to manage fluid retention and blood pressure.

Who can participate?
Patients aged 18 years and over with chronic kidney disease before undergoing kidney replacement therapy, who also have a condition of resistant hypertension.

What does the study involve?
Participants undergo interviews, echocardiograms and bioimpedance spectroscopy (BIS), and receive dietary advice to limit their salt intake to less than 2 g per day. They are randomly allocated to two groups to be treated with either dapagliflozin or furosemide. Blood samples and data are collected over a 6-month period. Body fluid status is measured using BIS monthly during the first 3 months and at 6 months. Echocardiogram and laboratory tests are carried out at 6 months.

What are the possible benefits and risks of participating?
The anticipated benefits include potential reductions in blood pressure, slowing the progression of kidney impairment, and lowering the risk of heart disease. However, some participants may experience hypovolemia (low body fluid volume) if the treatment is not followed according to guidelines or if there is an occurrence of drug allergies.

Where is the study run from?
Bhumibol Adulyadej Hospital (Thailand)

When is the study starting and how long is it expected to run for?
September 2023 to August 2024

Who is funding the study?
Bhumibol Adulyadej Hospital (Thailand)

Who is the main contact?
Natchaya Songsilp, muk.natchaya@gmail.com

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRB8866

Study information

Scientific Title
Efficacy of dapagliflozin compared to furosemide for controlling blood pressure in resistant hypertension with subclinical fluid retention in chronic kidney disease

Study objectives
Current study hypothesis as of 29/10/2024:
There is currently no comparative study of SGLT2i and furosemide use in patients with chronic kidney disease (CKD) and resistant hypertension, so a comparison of both medications for reducing high blood pressure was conducted.

Previous study hypothesis as of 12/04/2024:
There is currently no comparative study of SGLT2i and furosemide use in patients with chronic kidney disease (CKD) and uncontrolled hypertension, so a comparison of both medications for reducing high blood pressure was conducted.

Previous study hypothesis:
There is currently no comparative study of SGLT2i and furosemide use in patients with chronic kidney disease (CKD) and resistant hypertension, so a comparison of both medications for reducing high blood pressure was conducted.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 19/10/2023, The Institutional Review Board of Bhumibol Adulyadej Hospital, Directorate of Medical Service, Royal Thai Air Force (171 Phaholyothin road, Khlong Thanon, SaImai, Bangkok, 10220, Thailand; +66 25347255; bhumibolhospital@rtaf.mi.th), ref: 8866

Study design
Single-center non-inferior prospective randomized open-label study

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 to request a patient information sheet

Health condition(s) or problem(s) studied
Resistant hypertension with subclinical fluid retention in chronic kidney disease

Interventions
1. Select participants for the research based on inclusion and exclusion criteria.
2. Inform patients about the study and obtain their informed consent to participate.
3. Gather baseline data through interviews, echocardiogram, bioimpedance spectroscopy (BIS), and provide dietary advice to limit salt intake to less than 2 g per day.

4. Randomly assign patients into two groups by block of four randomization.
5. Conduct the experiment by administering 10 mg of dapagliflozin per day to the experimental group, and provide an initial dose of 20 mg/day of furosemide to the control group, adjusting the dosage based on BIS assessments.
6. Perform blood sampling, collect variables related to the research outcomes, and record data over a 6-month period.
7. Assess body fluid status using BIS monthly during the first 3 months and at 6 months.
8. Evaluate outcomes at the 6-month mark through Echocardiogram and laboratory tests.
9. Analyze the obtained results statistically.

Intervention Type
Drug

Pharmaceutical study type(s)
Bioequivalence

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Dapagliflozin, furosemide

Primary outcome measure
Blood pressure is measured using sphygmomanometer at baseline and 6 months

Secondary outcome measures
Current secondary outcome measures as of 12/04/2024:
1. Urine volume is measured by patient 24-hour urine volume collection at baseline and 6 months
2. LV mass index is measured using Echocardiogram at baseline and 6 months
3. Total body water is measured using bioimpedance at baseline and 6 months
4. Intracellular water is measured using bioimpedance at baseline and 6 months
5. Extracellular water is measured using bioimpedance at baseline and 6 months
6. Extracellular water/total body water is measured using bioimpedance at baseline and 6 months
7. Hospitalization for heart failure reported outcome using an IPD data at 6 months
8. NT-pro BNP level is measured using laboratory blood test at baseline and 6 months
9. eGFR is measured using laboratory blood test at baseline and 6 months
10. Serum sodium is measured using laboratory blood test at baseline and 6 months
11. Urine albumin creatinine ratio is measured using laboratory urine test at baseline and 6 months
12. Urine sodium is measured using laboratory urine test at baseline and 6 months
12. Body weight is measured using weighing at the hospital at baseline and 6 months

Previous secondary outcome measures:
1. Urine volume is measured by patient 24-hour urine volume collection at baseline and 6 months
2. LV mass index is measured using Echocardiogram at baseline and 6 months
3. Total body water is measured using bioimpedance at baseline and 6 months
4. Intracellular water is measured using bioimpedance at baseline and 6 months
5. Extracellular water is measured using bioimpedance at baseline and 6 months
6. Extracellular water/total body water is measured using bioimpedance at baseline and 6 months

7. Death from any cause reported outcome using an IPD data at 6 months
8. Fatal or nonfatal myocardial infarction reported outcome using an IPD data at 6 months
9. Hospitalization for heart failure reported outcome using an IPD data at 6 months
10. NT-pro BNP level is measured using laboratory blood test at baseline and 6 months
11. eGFR is measured using laboratory blood test at baseline and 6 months
12. Serum sodium is measured using laboratory blood test at baseline and 6 months
13. Serum urine albumin creatinine ratio is measured using laboratory urine test at baseline and 6 months
14. Body weight is measured using weighing at the hospital at baseline and 6 months

Overall study start date
01/09/2023

Completion date
15/08/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 29/10/2024:

1. Age from 18 years old
2. Chronic kidney disease (GFR-EPI 20-60 ml/min/1.73m²)
3. Resistant hypertension with fluid retention detected by bioimpedance

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Previous inclusion criteria as of 12/04/2024:

1. Age from 18 years old
2. Chronic kidney disease (GFR-EPI 20-60 ml/min/1.73m²)
3. Uncontrolled hypertension with fluid retention detected by bioimpedance

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Previous inclusion criteria:

1. Age from 18 years old
2. Chronic kidney disease (GFR-EPI 20-60 ml/min/1.73m²)
3. Resistant hypertension

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit

90 Years

Sex
Both

Target number of participants
30

Total final enrolment
16

Key exclusion criteria
Current exclusion criteria as of 29/10/2024:

1. Patient receiving diuretics or SGLT2i
2. Resistant HT with euvolemic status
3. Life expectancy <12 months (principal investigator's judgement)
4. Living-donor transplant scheduled within the next 12 months
5. Cardiovascular disease (dilated cardiomyopathy, valvular heart disease)
6. Active infection
7. Current active malignancy
8. Known HIV or active hepatitis B or C
9. Chronic liver disease and/or screening alanine transaminase or aspartate transaminase above 3 times the upper limit of the normal range
10. Pregnancy or breastfeeding
11. Subject has any kind of disorder that compromises their ability to informed consent and/or to comply with study procedures

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1. Patient receiving diuretics or SGLT2i
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10. Pregnancy or breastfeeding
11. Subject has any kind of disorder that compromises their ability to informed consent and/or to comply with study procedures

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Previous exclusion criteria:

1. Life expectancy less than 12 months
2. Living-donor transplant scheduled within the next 12 months
3. Cardiovascular disease (dilated cardiomyopathy, valvular heart disease)
4. Active infection
5. Current active malignancy
6. Known HIV or active hepatitis B or C
7. Chronic liver disease and/or screening alanine transaminase or aspartate transaminase above 3 times the upper limit of the normal range
8. Pregnancy or breastfeeding
9. Subject has any kind of disorder that compromises their ability to informed consent and/or to comply with study procedures

Date of first enrolment
18/01/2024

Date of final enrolment
11/02/2024

Locations

Countries of recruitment
Thailand

Study participating centre
Bhumibol Adulyadej Hospital
171 Phaholyothin Road
Khlong Thanon
SaImai
Bangkok
Thailand
10220

Sponsor information

Organisation
Bhumibol Adulyadej Hospital

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Sponsor type
Hospital/treatment centre

Website
https://bhumibolhospital.rtaf.mi.th/

ROR
https://ror.org/041e85345

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Bhumibol Adulyadej Hospital

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
18/04/2025

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request from Natchaya Songsilp (muk.natchaya@gmail.com).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file			12/04/2024	No	No
Other unpublished results			06/11/2024	No	No