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The effects of irbesartan and nebivolol on ambulatory blood pressure in patients with intradialytic hypertension.

Submission date	Recruitment status	[_] Prospectively registered
09/04/2018	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
17/04/2018	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
13/04/2018	Urological and Genital Diseases	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Hemodialysis is a process to remove waste products and excess fluid from the blood when the kidneys stop working properly. Blood pressure (BP) increase during or immediately after hemodialysis is an abnormal response and occurs in 5-15% of hemodialysis patients.
This is linked with harmful clinical outcomes and is often poorly diagnosed and controlled. The exact cause and effect background of high BP during hemodialysis are not yet fully explained and few studies have been designed to evaluate interventions for the management of this.
This study aims to evaluate the effects of a single or weekly dose of two drugs (irbesartan and nebivolol) on 24-hour BP in hemodialysis patients.

Who can participate?
Adults aged over 18 years with end-stage renal disease

What does the study involve?
Participants receive the study drugs in one of two different modes. Those in the first mode receive a single dose of the drug one hour before dialysis. Those in the second mode receive a dose once a day for a week before the evaluation. Participants are assessed at three occasions: once before any treatment has started, once after receiving the first drug, and once after receiving the second drug. The order of the drugs (nebivolol or irbesartan) is randomly decided. There is a two week period in between these two drugs where the participants do not take any drug known as a wash out period. At each assessment participants have their blood pressure measured over a 24 hour period, and have a blood sample taken before and after dialysis.

What are the possible benefits and risks of participating?
Possible benefits of the study for the patients are to identify an antihypertensive agent that is mostly appropriate for the management of their hypertension. Possible risks include side-effects of the study drugs, which are commonly used antihypertensive agents.

Where is the study run from?
1. AHEPA Hospital, Aristotle University of Thessaloniki (Greece)
2. Hippokration Hospital, Aristotle University of Thessaloniki (Greece)

When is the study starting and how long is it expected to run for?
May 2014 – April 2018

Who is funding the study?
Investigator initiated and funded - the primary investigator is supported by an annual scholarship from the Hellenic Society of Hypertension.

Who is the main contact?
Dr Athanasios Bikos (Scientific)

Contact information

Type(s)
Scientific

Contact name
Dr Athanasios Bikos

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Additional identifiers

Protocol serial number
4823/25.2.2013

Study information

Scientific Title
This study examines whether in hemodialysis patients with intradialytic hypertension (P) a single or weekly administration of irbesartan or nebivolol (I) compared to no drug administration (C) reduces peridialytic, intradialytic and ambulatory BP levels, as well as ambulatory arterial stiffness parameters (O).

Study objectives
H0:
Ambulatory BP levels in patients with intradialytic hypertension is not different after administration of irbesartan or nebivolol compared to no drug administration.

H1:
Ambulatory BP levels in patients with intradialytic hypertension is different after administration of irbesartan or nebivolol compared to no drug administration.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of the School of Medicine Aristotle University of Thessaloniki, 07/06/2016, ref: 313/7.6.2016

Study design
Pragmatic pilot multi-centre open label randomized cross-over study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Patients with end-stage renal disease on hemodialysis with intradialytic hypertension

Interventions
Each participant is evaluated on three different occasions, starting prior to a mid-week hemodialysis session (e.g. the second weekly session, Wednesday or Thursday). Participants receive the study drugs in one of two different modes. Those in the first group receive a single drug dose one hour prior to dialysis session. Those in the second group receive a once daily dose of the study drug for a whole week.
Baseline evaluation is before a standard hemodialysis session with no treatment.
After baseline evaluation, participants are randomly assigned to receive nebivolol 5 mg and subsequently irbesartan 150mg, or vice versa in a cross-over design.
On each occasion, a 24-hour ambulatory-BP-monitoring (ABPM) is performed with the use of a validated ABPM device and blood specimens are acquired for laboratory testing before and after hemodialysis.
A two-week wash-out period takes place before the initiation of the second drug in both modes of administration.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Irbesartan, Nebivolol

Primary outcome(s)
1. Ambulatory brachial BP levels are assessed with the Mobil-O-Graph NG device for ABPM at the three study-points.
2. Ambulatory central BP levels are assessed with the Mobil-O-Graph NG device for ABPM at the

three study-points.
3. Ambulatory arterial stiffness parameters (augmentation Index, augmentation pressure and pulse wave velocity) are assessed with the Mobil-O-Graph NG device for ABPM at the three study-points.

Key secondary outcome(s))
1. Plasma renin activity and aldosterone are measured at the start and the end of each hemodialysis session at the three study-points.
2. Adrenaline and noradrenaline levels are measured at the start and the end of each hemodialysis session at the three study-points.
3. Endothelin and nitric oxide levels are measured at the start and the end of each hemodialysis session at the three study-points.
4. Body weight is measured at the start and the end of each hemodialysis session at the three study-points.
5. Standard peri-dialytic BP measurements are measured at the three study-points.

Completion date
30/04/2018

Eligibility

Key inclusion criteria
1. Adult aged >18 years
2. End-stage renal disease treated with thrice-weekly maintenance hemodialysis for more than 3 months
3. Intradialytic hypertension (defined as mean intradialytic rise ≥10 mmHg in systolic BP in at least 4 over 6 consecutive hemodialysis sessions)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Existing comorbidity requiring treatment with a RAS-blocker (i.e. heart failure, acute myocardial infraction e.t.c.)
2. Existing comorbidity requiring treatment with a β-blocker (i.e. heart failure, cardiac arrhythmia, acute myocardial infarction, angina pectoris, etc.)
3. Existing specific contraindications to receive a RAS-blocker (i.e. history of hyperkalemia, angioedema, anaphylactic or allergic reaction)

4. Existing specific contraindications to receive a β-blocker (bradyarrhythmia, chronic obstructive pulmonary disease, asthma, history of anaphylactic or allergic reaction)
5. Antihypertensive treatment with RAS-blockers (angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers or renin-inhibitor) or β-blockers in a period less than one month prior to study enrollment.
6. Pre- or post-hemodialysis SBP levels <130mmHg in 4 out of 6 sessions during the two weeks of the diagnosis of intradialytic hypertension
7. Nonfunctional arteriovenous fistula in the contralateral arm of the one used as vascular access for the hemodialysis session that could interfere with proper ABPM recordings.
8. Active malignant disease or other advanced comorbidity resulting in particularly poor prognosis
9. Inability to understand and provide a written informed consent to participate in the study

Date of first enrolment
10/06/2016

Date of final enrolment
10/10/2017

Locations

Countries of recruitment
Greece

Study participating centre
AHEPA Hospital, Aristotle University of Thessaloniki
Section of Nephrology and Hypertension
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Study participating centre
Hippokration Hospital, Aristotle University of Thessaloniki
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Sponsor information

Organisation

Aristotle University of Thessaloniki School of Medicine

ROR
https://ror.org/02j61yw88

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded- the primary investigator is supported by an annual scholarship from the Hellenic Society of Hypertension

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available. The study dataset will be held in the Department of Nephrology, Aristotle University of Thessaloniki.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes