

# Metformin against gliclazide in patients with diabetes and heart failure

<b>Submission date</b> 29/04/2010	<b>Recruitment status</b> Stopped	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 29/04/2010	<b>Overall study status</b> Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 24/04/2019	<b>Condition category</b> Circulatory System	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**Clinical Trials Information System (CTIS)**  
2006-002812-87

**Protocol serial number**  
4836

## Study information

**Scientific Title**  
Metformin against gliclazide in patients with diabetes and heart failure: a randomised open label study

## **Acronym**

MAGPDF

## **Study objectives**

Hypothesis:

In patients with symptomatic left ventricular systolic dysfunction and type 2 diabetes, biguanide therapy compared to a sulphonylurea (Gliclazide), will improve ventricular function and vascular endothelial function.

Summary:

There are a large number of patients with both diabetes and heart failure in the UK because diabetes causes heart failure and likewise heart failure causes diabetes. Metformin and Gliclazide are two commonly prescribed diabetic medications in these patients but there is no information on which is better for the patient. In this study we will look at the effects of these two medications on the function of the heart muscle, blood vessels and symptoms in patients with diabetes and heart failure.

## **Ethics approval required**

Old ethics approval format

## **Ethics approval(s)**

Hull and East Riding Research Ethics Committee (now superseded by Leeds (West) REC), 18/07/2006, ref: 06/Q1104/98

## **Study design**

Randomised interventional treatment trial

## **Primary study design**

Interventional

## **Study type(s)**

Treatment

## **Health condition(s) or problem(s) studied**

Topic: Cardiovascular; Subtopic: Cardiovascular (all Subtopics); Disease: Cardiovascular

## **Interventions**

Follow-up:

Patients will be reviewed each month for symptom assessment using the standardised symptom questionnaire and EQ5-D. Patients will also undergo physical examination including body weight and fat composition by impedance measurement. Blood tests (non-fasting) for serum HbA1c, U&E's and blood glucose levels. Doses of the study drug (Gliclazide or Metformin) will be increased to maximum (metformin 1 g three times a day [tds] or gliclazide 160 mg twice daily [bd]) if there is inadequate diabetic control as evidenced by blood sugar readings and HbA1c levels. If this is inadequate to maintain glucose control, then agents other than a biguanide or sulphonylurea can be added to this regimen.

At 8 months all baseline tests, as described above, will be repeated and in addition the patients will undergo dobutamine stress and recovery cardiac magnetic resonance (CMR) and forearm blood flow quantification as described below. We intend to conduct dobutamine stress and recovery CMR and forearm blood flow measurements only once at 8 months (final follow-up).

We could, if requested, also do these tests at baseline but this would add an extra burden to patients and extra costs but make little further contribution to addressing the primary hypothesis of differences between treatments. The study is randomised and so the two populations should be similar, which can be assessed by comparing other baseline values.

#### CMR Methodology:

Cardiac magnetic resonance (CMR) imaging will be performed in a 1.5T Clinical Scanner (General Electric). Heart rate and blood pressure would be monitored throughout the imaging protocol.

#### Cine-CMR:

Left ventricular function and volumes will be quantified at rest and after Dobutamine stress with a breath hold gated gradient echo sequence (cine-MR). Incremental doses of dobutamine, 5 - 40 mg/kg/min, will be infused intravenously. Dobutamine infusion will be continued until patients develop symptoms of myocardial ischaemia, significant arrhythmias, or achieve target heart rate. Intravenous atropine will be used if necessary to increase heart rate. Cine-MR images will be acquired at rest and at five-minute intervals for 45 minutes during recovery following Dobutamine stress.

#### Gadolinium contrast CMR:

First pass gadolinium enhanced imaging with a saturation recovery turboflash sequence will be done for assessment of myocardial perfusion and delayed hyperenhancement (DE-CMR) with a segmented inversion-recovery fast gradient echo sequence for assessing myocardial viability. Studies will be conducted at the same time of day, approximately 4 hours after the last intake of medication and with a similar diet in the 3 days prior to scanning as assessed by a dietary diary.

All CMR images will be sent to a Linux-based off-line workstation for analysis. The scans will be placed in random order after the identity markers have been removed. The cine and gadolinium-enhanced CMR images will be evaluated separately by the consensus of two experienced observers.

Cine images will be used to calculate LV end-diastolic volume, end-systolic volume, ejection fraction, and myocardial mass at end-diastole with the use of analytical MRI-MASS software. Epicardial and endocardial borders of the left ventricle excluding papillary muscles and trabeculations will be traced semi-automatically in contiguous short axis slices. End-systolic volumes will be adjusted for ventricular long-axis shortening, which will be accomplished by eliminating from calculation the basal slices encompassing the left atrium at end systole.

#### Forearm blood flow measurement:

Contrast enhanced ultrasound (CEU) imaging of the forearm muscles in short-axis will be performed with intermittent ultraharmonic imaging (Sonos 5500, Philips Ultrasound) at a transmission frequency 1.3 MHz, and a mechanical index of 1.0. For CEU lipid-shelled decafluorobutane microbubbles (DMP 115, Bistol Myers Squibb) suspended in saline ( $4 \times 10^6$  ml) will be infused intravenously at 1.5 to 2.5 ml/min. CEU images will be acquired at rest (CEU-R) and after an intravenous infusion of insulin (CEU-I) for 60 minutes (1 mU/kg/min and 5 mU/kg /min). Euglycaemia will be maintained with a variable rate of 20% dextrose infusion intravenously. Heart rate, blood pressure, and blood glucose levels will be monitored every 5 to 10 minutes throughout the protocol.

Digitally acquired CEU will be analysed off-line with custom written software to quantify skeletal muscle blood volume and red blood cell velocity as described previously. Skeletal muscle blood flow reserve is then given by the ratio of blood flow measured during infusion of insulin and at rest.

Total brachial artery blood flow will be quantified by 2-D and Doppler ultrasound with a 7 MHz linear-array transducer (Sonos 5500, Philips). Brachial artery blood flow will be measured by the product of vessel cross sectional area, calculated from videocaliper measurement of the diameter and the centerline time-averaged peak velocity (cm2) determined from arterial pulsed-wave Doppler, with an angle correction of 60°.

Study entry: single randomisation only

### **Intervention Type**

Other

### **Phase**

Phase IV

### **Primary outcome(s)**

Difference in left ventricular end-systolic volume between patients randomised to metformin compared to gliclazide at 8 months

### **Key secondary outcome(s)**

Differences between the two groups in serum NT-pro BNP levels in:

1. Time to recovery of LV function after dobutamine stress
2. Insulin mediated flow reserve quantified by contrast enhanced ultrasound and markers of endothelial function
3. Average symptom score of all monthly follow-ups, which avoids undue emphasis being placed on a single time-point (patients who are withdrawn for worsening heart failure or who die will be assigned worst rank for symptom assessment at all subsequent time-points)

### **Completion date**

01/09/2010

### **Reason abandoned (if study stopped)**

Participant recruitment issue

## **Eligibility**

### **Key inclusion criteria**

1. Diabetes on oral hypoglycaemic agents (OHGA)
2. Heart failure
3. Male and female, lower age limit of 18 years

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

**Sex**

All

**Key exclusion criteria**

1. Diabetes on insulin
2. No left ventricular function (LVF)

**Date of first enrolment**

24/10/2006

**Date of final enrolment**

01/09/2010

## **Locations**

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**Department of Cardiology**

Cottingham

United Kingdom

HU16 5JQ

## **Sponsor information**

**Organisation**

Hull and East Yorkshire Hospitals NHS Trust (UK)

**ROR**

<https://ror.org/01b11x021>

## **Funder(s)**

**Funder type**

Charity

**Funder Name**

British Heart Foundation (BHF) (UK)

**Alternative Name(s)**

the\_bhf, The British Heart Foundation, BHF

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Trusts, charities, foundations (both public and private)

**Location**

United Kingdom

## Results and Publications

**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?
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes