

# Palmitoylethanolamide intake and systemic endothelial function in ocular hypertensive patients

<b>Submission date</b> 05/09/2011	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 19/09/2011	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 21/04/2017	<b>Condition category</b> Eye Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Glaucoma is an eye condition where the optic nerve, which connects the eye to the brain, becomes damaged, leading to loss of vision if not detected and treated early on. It is caused by several different factors, the most important is increased pressure in the eye (ocular hypertension), but endothelial dysfunction, where the endothelium (inner lining) of blood vessels fails to function normally, may prevent the proper distribution of blood in the eye, contributing to the damage. Changing endothelial function may help to improve the blood supply to the optic nerve and prevent patients with ocular hypertension from developing glaucoma. Palmitoylethanolamide (PEA) is a substance that is involved in the eye tissues and blood vessels so could play a role in the treatment of ocular hypertension and glaucoma patients. The aim of this study is to assess the action of PEA on the blood vessels of ocular hypertensive patients.

### Who can participate?

Patients aged under 65 with ocular hypertension, and healthy volunteers

### What does the study involve?

Participants are asked to give a small sample of blood and their height, weight and blood pressure are measured. They undergo an eye examination including an eye pressure test, optic nerve assessment, and a blood vessel assessment. Participants are randomly allocated to take either PEA or a matching placebo (dummy) tablet twice a day for a period of 90 days under medical supervision to monitor possible side effects. There is then a 2-month break, after which each participant switches to the other treatment for a further 3 months. All participants' blood vessels are assessed before and after each treatment period and are compared with the blood vessels of the healthy volunteers.

### What are the possible benefits and risks of participating?

PEA may improve blood vessel function in ocular hypertensive patients

Where is the study run from?  
University of Bologna (Italy)

When is the study starting and how long is it expected to run for?  
September 2010 to July 2011

Who is funding the study?  
University of Bologna (Italy)

Who is the main contact?  
Dr Mauro Cellini  
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## Contact information

**Type(s)**  
Scientific

**Contact name**  
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## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**  
C/2009/U/DISP

## Study information

**Scientific Title**  
Palmitoylethanolamide intake and systemic endothelial function in ocular hypertensive patients: a single centre, randomized double blind, placebo controlled cross-over study

**Study objectives**  
Glaucoma is a multi-factorial optic neuropathy of unknown aetiology in which the increased intraocular pressure is the most important risk factor, but also ischaemia, vascular dysregulation, vasospasm and endothelial dysfunction, may prevent the physiological regulation of ocular

blood flow, determining modifications in the optic nerve head supply, contributing to the damage of the ganglion cells.

Therapeutically, therefore, both reducing intra ocular pressure (IOP) and improving ocular blood flow may be considered as treatment options both in glaucoma and ocular hypertension. It is feasible that ameliorating endothelial function may contribute to improve optic nerve head blood supply and to reducing susceptibility of Orthotopic heart transplantation (OHT) patients to develop glaucoma or of glaucoma patients to progress more rapidly.

Palmitoylethanolamide belongs to the endocannabinoid system and it is implicated in the physiology of different human systems, included ocular tissues and vascular system where seems to exert, among others, an important role in the endothelial protection in the rat so it could play a main role in the treatment of glaucoma or OHT patients.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Local Ethics Committee of the S. Orsola-Malpighi Hospital, Bologna, 05/09/2010, ref: C/2009/U/DISP

### **Study design**

Single centre randomized double blind placebo controlled cross-over study

### **Primary study design**

Interventional

### **Secondary study design**

Randomised cross over 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**

Ocular hypertension

### **Interventions**

Treatment arms: 20 OHT patients randomly assigned to assume a 300 mg oral tablet of palmitoylethanolamide (PEA) two times a day for three months and after two months of wash out switched to treatment with placebo. The others 20 OHT patients randomly assigned to assume placebo and after two months of wash out switched to treatment with palmitoylethanolamide (PEA).

All patients underwent:

1. Ophthalmologic examination including visual acuity and applanation IOP assessment
2. Corneal thickness evaluation with a Tomey SP3000 pachymeter (Tomey Corp., Nagoya, Japan)
4. Biomicroscopy of the anterior and posterior segment with automatic measurement of the C/D area ratio of the optic nerve head with Stratus OCT3 (Zeiss-Humphrey, Dublin, CA).
5. Standard achromatic perimetry (SAP) with a Humphrey Field Analyzer-SITA program (Zeiss-Humphrey, San Leandro, CA)
6. Blood sampling to assess lipid profile and fasting serum glucose.
7. Body mass index calculation
8. Systolic and diastolic blood pressure measurement
9. Assessment of the flow-mediated vasodilatation (FMD) with a Philips ENVISOR echographic machine (Philips Medical Systems, Best, The Netherlands); FMD was calculated as the percentage change in brachial artery diameter in response to reactive hyperemia:  
$$\text{FMD} = [(\text{VD}_{\text{Hyperemia}} - \text{VD}_{\text{Baseline}}) / \text{VD}_{\text{Baseline}}] \times 100\%$$
  
VD= Vessel Diameter

## **Intervention Type**

Drug

## **Phase**

Not Applicable

## **Drug/device/biological/vaccine name(s)**

Palmitoylethanolamide

## **Primary outcome measure**

1. FMD values in OHT patients compared with controls at baseline
2. FMD values in OHT patients randomly assigned to assume Palmitoylethanolamide or placebo for 3 months
3. FMD values in OHT patients after 2 month washout period
4. FMD values in OHT patients after they switched to the other treatment for further 3 months

## **Secondary outcome measures**

Effect of palmitoylethanolamide vs placebo on the endothelial function of OHT patients at baseline, after treatment and wash-out

## **Overall study start date**

28/09/2010

## **Completion date**

10/07/2011

# **Eligibility**

## **Key inclusion criteria**

1. 40 patients aged < 65 years (mean 56.8±8.1)
2. Baseline IOP ≥ 22 mm/Hg, on at least two measurements (mean 23.11±0.93)
3. Open anterior chamber angle at gonioscopy, cup/disc ratio < 0.4
4. Normal visual field (VF) (MD <3 dB and PSD < 2.5 dB) and corneal central thickness within

normal values

5. 40 healthy control subjects aged matched (mean  $56.2 \pm 10.4$ )

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

Mixed

### **Age group**

Adult

### **Sex**

Both

### **Target number of participants**

40 OHT patients and 40 healthy controls subjects

### **Key exclusion criteria**

1. Cardiovascular disease
2. Diabetes, hypertension, hypercholesterolemia
3. Vasoactive medications

### **Date of first enrolment**

28/09/2010

### **Date of final enrolment**

10/07/2011

## **Locations**

### **Countries of recruitment**

Italy

### **Study participating centre**

Via Palagi 9

Bologna

Italy

40138

## **Sponsor information**

### **Organisation**

University of Bologna (Italy)

### **Sponsor details**

Ophthalmology Service

Via Palagi 9

Bologna  
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40138

**Sponsor type**

University/education

**Website**

<http://www.eng.unibo.it/PortaleEn/default.htm>

**ROR**

<https://ror.org/01111rn36>

## **Funder(s)**

**Funder type**

University/education

**Funder Name**

Università di Bologna

**Alternative Name(s)**

University of Bologna, UNIBO

**Funding Body Type**

Government organisation

**Funding Body Subtype**

Local government

**Location**

Italy

## **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?
<a href="#">Results article</a>	results	01/02/2013		Yes	No