Dopamine in platelets in patients with paragangliomas/pheochromocytoma

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The purpose of the study is to determine the sensitivity of dopamine platelets levels in patients with clinically suspected or diagnosed HNPGL, abdominal PGL, and pheochromocytoma. Primary Objective: The sensitivity of dopamine levels in platelets...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neoplastic and ectopic endocrinopathies
Study type	Observational invasive

Summary

ID

NL-OMON35567

Source
ToetsingOnline

Brief title
Dopamine in platelets in patients with PGL

Condition

- Neoplastic and ectopic endocrinopathies
- Endocrine neoplasms benign

Synonym
Head and neck paraganglioma, pheochromocytoma, tumor of the adrenal medulla

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Dopamine in platelets, head and neck paraganglioma, pheochromocytoma

Outcome measures

Primary outcome

The sensitivity of platelet levels of dopamine in platelets rich plasma in

patients with HNPGL compared to the defined golden standard

Secondary outcome

Sensitivity (and specificity) in patients with suspected PGL and

pheochromocytoma compared to the golden standard

Study description

Background summary

Pheochromocytoma, sympathetic PGL and parasympathetic HNPGL are rare neuro-endocrine tumors that can synthesize and secrete catecholamines derived from neural-crest-derived chromaffin cells. The term pheochromocytoma is used for intra-adrenal PGLs, whereas similar but extra-adrenal tumors are named (extra adrenal) PGLs. Parasympathetic PGLs arise near the parasympathetic nerves in the head and neck and mediastinal region, sympathetic PGLs are symmetrically situated along the sympathetic trunk.
Pheochromocytoma and PGLs occur sporadically and in several hereditary tumor syndromes, including the pheochromocytoma-paraganglioma syndrome. This syndrome is caused by germline mutations in succinate dehydrogenase (SDH) subunit B (SDHB), subunit C (SDHC) or subunit D (SDHD) genes. About 10-30% of apparently sporadic pheochromocytomas and PGLs harbour germline SDH-gene mutations. Patients with SDHB and SDHD gene mutations have been shown to be at risk of development of multiple PGLs in the head and neck, thorax, and abdomen. Pheochromocytomas and PGLs can also occur in other familiar/hereditary syndromes. Germline mutations for these familiar syndromes may occur in the von Hippel-Lindau (VHL) gene which causes von Hippel-Lindau syndrome; the RET gene leading to multiple endocrine neoplasia (MEN) type 2 and the neurofibromatosis type 1 (NF1) gene, which is associated with von Recklinghausen*s disease.
Measurement of the plasma and urinary metabolites of catecholamines, (nor)metanephrine and 3-metoxytyramine (3-MT), is the cornerstone of for the diagnosis of a pheochromocytoma or a sympathetic PGL. However, parasympathetic

HNPGL rarely secrete catecholamines. Therefore, it is difficult to determine tumor activity biochemically and extensive imaging is necessary in the diagnostic work-up of these patients. Recently we and others have shown that dopamine secretion, measured as 3-MT in urine, can be demonstrated in 19-23% of patients with HNPGL. In these studies the urine 3-MT concentration was the most sensitive method to measure dopamine production. Measurement of 3-MT and (nor)metanephrine in urine are however affected by catecholamine-rich products in the diet, which increases the possibility of false-positive results.
Increased 3-MT may especially be expected in patients with SDHB and SDHD mutations.
The biochemical diagnosis of HNPGL could be improved if dopamine could be measured in a more sensitive way.
Free dopamine, secreted by the PGL or pheochromocytomas, is taken up from the body circulation by platelets through the dopamine transporter (DAT), and stored inside the platelets. The lifespan of platelets in the circulation is 8-10 days. In this way, platelet levels of dopamine reflect the whole 10-day dopamine metabolism.
The platelet level of dopamine could be a relatively new diagnostic parameter and has not been used before in patients with PGLs or pheochromocytomas. The platelet level of dopamine has been studied in patients with migraine and cluster headache. Plasma levels of dopamine in platelets in patients with migraine and cluster headache were higher than normal controls.
If the platelet level of dopamine is proven to be a sensitive marker for the presence of HNPGL, this is expected to be clinically useful as a tumor marker for early detection of (recurrent) disease in carriers of a mutation predisposing to PGL and pheochromocytoma, especially in patients with SDH mutations. Furthermore it would be interesting to determine dopamine in platelets before and after curative surgery of PGL and pheochromocytoma.

Study objective

The purpose of the study is to determine the sensitivity of dopamine platelets levels in patients with clinically suspected or diagnosed HNPGL, abdominal PGL, and pheochromocytoma.

Primary Objective:
The sensitivity of dopamine levels in platelets in patients with clinically suspected and/or diagnosed head HNPGL.

Secondary Objective:
The value of dopamine level in platelets in patients with PGL and pheochromocytoma.

Study design

This study is a prospective single center study.

Patients with PGLs and pheochromocytomas known at the departments of Ear Nose and Throat (ENT) and Endocrinology at the University Medical Centre Groningen are eligible for inclusion, as well as patients who are suspected of a PGL or pheochromocytoma. During routine venapuncture an additional blood volume of 20 ml is drawn. This additional blood volume will be stored at -80 0C until processing in the department of laboratory medicine.

Study burden and risks

The platelet level of dopamine is a relatively new diagnostic parameter and has not been used before in patients with PGLs. If dopamine platelet levels is a sensitive marker in patients with HNPGLs, it could be a useful marker for screening and follow-up in patients. Participating patients are not exposed to any additional risks, as the extra blood volume needed for this study is drawn during a venapuncture performed for routine blood testing.

Because of the low risk profile of this investigation, the judging Medical Ethical Committee of the Universitair Medisch Centrum of Groningen has decided that there will be a release of the insurance obligation as intended in art. 4 lid 1 of the decision obligatory assurance in medical research with humans.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
9700 RB Groningen
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
9700 RB Groningen
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. 18 years of age or older
2. Patients with diagnosed or clinically suspected PGLs and/or pheochromocytomas.
a. Diagnosis of pheochromocytoma and sympathetic PGL (golden standard):
i. Histology postoperative or;
ii. Hypertension and;
iii. Elevated plasma and/or urinary (nor)metanephrines and;
iv. Localization of pheochromocytoma with anatomical imaging (computed tomography (CT)/ Magnetic Resonance Imaging (MRI)) and functional imaging including ^{123}I-metaiodobenzylguanidin (MIBG) scintigraphy or 18F- dihydroxyphenylalanine (DOPA) positron emission tomography (PET).
b. Diagnosis of a HNPGL (golden standard):
i. Postoperative histology or;
ii. Clinical symptoms and;
iii. Localization of a HNPGL with anatomical imaging (CT/MRI) and nuclear imaging including ^{111}-In-octreotide/ ^{123}I-MIBG scintigraphy or DOPA-PET.
c. Suspected PGL:
i. Patients with a proven SDH-mutation

Exclusion criteria

1. < 18 years

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-02-2012
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	25-01-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL37513.042.11

Study results

Date completed:	26-05-2014
Actual enrolment:	122