Cardiac sympathetic activity in 22q11 deletion syndrome.

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The objective of this study is to investigate cardiac sympathetic ativity in subjects with 22q11DS and the effect of catecholamine depletion.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON35870

Source
ToetsingOnline

Brief title
Cardiac sympathetic activity in 22q11 deletion syndrome.

Condition

- Other condition
- Cardiac arrhythmias
- Endocrine disorders congenital

Synonym
cardiac nerve activity, cardiac sympathetic innervation

Health condition

cardiale sympathische activiteit

Research involving
Human

Sponsors and support

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

Intervention

Keyword: 123I-MIBG, 22q11 deletion syndrome, cardiology, sympathetic innervation

Outcome measures

Primary outcome

Difference in cardiac sympathetic activity as assessed with 123I-MIBG between

subject with 22q11DS and healthy subjects, with and without cathecholamine

depletion.

Secondary outcome

not applicable

Study description

Background summary

The cathecholamines dopamine and noradrenaline share a common precursor in the form of tyrosine. The conversion of tyrosine to dopamine/noradrenaline can be decreased by the administration of alpha methylparatyrosine (AMPT), a reversible tyrosine hydroxylase inhibitor. Administration of AMPT results in lower concentrations of catecholamines in blood and urine. A deletion in chromosome 22q11is frequently observed. This 22q11 deletion syndrome (22q11DS) is characterised by a variable clinical phenotype with congenital heart, facial abnormalities and behaviour problems. The gene responsible for the enzyme catechol-O-methyl-transferase (COMT) lies in this deletion. COMT is one of several enzymes that degrade catecholamines. Subjects with 22q11DS have only one COMT gene and this may cause a disturbed degradation of catecholamines compared with controls. After administration of AMPT dopamine metabolism is more decreased in subjects with 22q11DS compared with healthy subjects. As COMT is also involved in the degradation of noradrenaline it can be assumed that the concentration of noradrenaline will decrease after admnistration of AMPT in subjects with 22q11DS. This is important because there is a clear association between a raised concentration of noradrenaline and heart arrhythmias. There

are several case reports suggesting that in people with 22q11DS there is a relation between arrhythmias and an increased concentration of noradrenaline. A recent publication describes a higher occurrence of sudden dead in a larger cohort of patients with 22q11DS compared to controls. However, there is the knowledge on cardiac sympathetic activity in these subjects is limited. Cardiac sympathetic activity can be non-invasively visualised with 123I-meta-iodobenzylguanidine (123I-MIBG) scintigraphy. In this study we assume that increased serum concentration noradrenaline will result in increased cardiac sympathetic activity. It is expect that by depletion of cathecholamines with AMPT the concentration of noradrenaline will decrease resulting in a normalised sympathetic activity. The importance of this research lies in the relation between raised cardiac sympathetic activity and possible fatal arrhythmias. To what extent a raised cardiac sympathetic activity in 22q11DS is associated with an increased risk on (fatal) arrhythmia is unknown.

Study objective

The objective of this study is to investigate cardiac sympathetic ativity in subjects with 22q11DS and the effect of catecholamine depletion.

Study design

Catecholamine depletion will be achieved by administration of the reversible tyrosine hydroxylase inhibitor *-methylparatyrosine (AMPT). All subjects will be given both AMPT and a placebo on two separte days. All subjects are blinded for administration of AMPT/placebo. Before receiving any tablets, blood examples will be collected and questionaires will be taken. After the administration of the last tablet a second blood exemple will be collected and questionaires will be taken again. The 123I-MIBG scans will be preformed 15 minutes and 4 hours after the last administration of AMPT/placebo.

Study burden and risks

- Possible side effects of AMPT are fatigue, rigidity (extrapyramidale symptoms), restlessness and dysphoria. All side effects are reversibel.
- The amount of radiation that the subjects of our study are exposed to is within the international limits. However, within the same year, subjects, as participants to any other study, can not be exposed to additional radiation.
- To our knowledge no side effects have been reported of the administered MIBG.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

patients with the 22q11 deletion syndrome, confirmed by genetic analysis

Exclusion criteria

- Congenital hart disease
- Use of medication that might influence dopamine and norepinephrine concentrations
- Pregnancy
- Known allergy to iodine

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-12-2012
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL36224.018.11