The reliability of new point-of-care instruments for breath analysis in children with asthma and cystic fibrosis (CF), and healthy controls

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Research questions: Primary questions:* Are the new point-of-care instruments for the measurement of VOCs in exhaled breath feasible for use in children and adolescents aged 6 to 20 years?* Are these techniques able to differentiate between healthy…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Observational non invasive

Summary

ID

NL-OMON44692

Source
ToetsingOnline

Brief title
Breath analysis in children

Condition

- Bronchial disorders (excl neoplasms)

Synonym
asthma, cystic fibrosis (CF)

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht

Source(s) of monetary or material Support: ZonMW IMDI programma

Intervention

Keyword: asthma, cystic fibrosis (CF), exhaled breath, Volatile Organic Compounds (VOCs)

Outcome measures

Primary outcome

Exhaled nitric oxide test and exhaled breath condensate (EBC):

Fraction of exhaled nitric oxide (FeNO) will be obtained with the online NIOX analyser (Aerocrine, Solna, Sweden) according to ATS/ERS standards [12]. FeNO is currently considered as gold standard test for non-invasive measurement of lung inflammation.EBC will be collected by means of an optimised glass tube, cooled by counter-current circulating ice water, as described previously [2]. Children breathe tidally for ten minutes, while wearing a nose-clip, through a mouthpiece connected to a two-way non-rebreathing valve (Hans Rudolph Inc, series 1420, Kansas City, USA). The two-way valve and tubing to the condenser, serves as a saliva trap. After collection, EBC was rapidly frozen at -80°C using dry ice and was stored at -80ºC until analysis. Inflammatory markers and microbiome will be determined in EBC and compared to VOCs profiles as gold standard for airway inflammation.

VOCs in exhaled breath:

For analysis of VOCs the following exhaled breath techniques will be used:

* eNose Aeonose® from The eNose Company [6]

* Ion mobility Spectrometer (IMS) from Ganshorn [8]

* Gas chromatography mass spectrometry (GC-MS) from Ganshorn (gold standard

VOCs analysis)

All techniques will be randomly studied in all participants.

Procedure of exhaled VOCs techniques:

The child/adolescent will be asked to breath tidally through a mouth piece into the eNose/IMS. The duration of the procedure depends on the technique but will not exceed 5 to 10 minutes.

After a pause of 10 minutes the next technique will be performed, and so on.

The total duration of testing will be approximately 60 minutes.

Eating and exercise are prohibited within 60 minutes prior to testing. Drinking of water is allowed prior to and in between tests. Use of inhalation medication will be stopped 3 hours before measurements.

All techniques are completely non-invasive. In case of resistance of the child, the measurements will be terminated.

Outcome:

VOC profiles will be measured with all 4 techniques.

* Each technique will be evaluated in its use (child-friendliness, feasibility) and adaptations in protocol or technique will be investigated to improve measurement and feasibility in children.

* Per technique, the discriminative power of the VOC profiles between healthy children/adolescents and children/adolescents with asthma and/or CF will be

studied.

Secondary outcome

References:

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2. Klaassen EM, van de Kant KD, Jöbsis Q, van Schayck OC, Smolinska A, Dallinga JW, van Schooten FJ, den Hartog GJ, de Jongste JC, Rijkers GT, Dompeling E. Exhaled biomarkers and gene expression at preschool age improve asthma prediction at 6 years of age. Am J Respir Crit Care Med 2015;191(2):201-7.

3. Robroeks CM, van Berkel JJ, Dallinga JW, Jöbsis Q, Zimmermann LJ, Hendriks HJ, Wouters MF, van der Grinten CP, van de Kant KD, van Schooten FJ, Dompeling E. Metabolomics of volatile organic compounds in cystic fibrosis patients and controls. Pediatr Res 2010;68(1):75-80.

4. Fens N, van der Schee MP, Brinkman P, Sterk PJ. Exhaled breath analysis by electronic nose in airways disease. Established issues and key questions. Clin Exp Allergy 2013;43:705-715.

5. Van der Schee MP, Paff T, Brinkman P, van Aalderen WMC, Haarman EG, Sterk PJ. Breathomics in lung disease. Chest 2015;147(1):224-231.

6. Product information Aeonose, The eNose company: http://www.enose.nl/products/aeonose/.

7. Product information eNose, Common Invent: http://www.comon-invent.com/enose/

8. Product information Ion Mobility Spectrometer, Ganshorn:

http://www.ganshorn.nl/index.php?option=com_content&view=article&id=22&Itemid=23
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12. ATS/ERS recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide. Am J Respir Crit Care Med 2005;171:912*930.

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14. Smolinska A, Hauschild AC, Fijten RR, Dallinga JW, Baumbach J, van Schooten FJ. Current breathomics * a review on data pre-processing techniques and machine learning in metabolomics breath analysis. J Breath Res 2014;8(2): doi: 10.1088/1752-7155/8/2/027105.

Study description

Background summary

Assessing airway inflammation in young children is a challenging task. Bronchoscopy and the evaluation of bronchoalveolar lavage fluid and/or endobronchial biopsy samples is considered as the gold standard. However, these techniques are invasive (general anaesthesia is always required for bronchoscopy in children!) and therefore not suitable for routine use in children. Recently, new non-invasive techniques have been developed to assess airway inflammation for diagnostic or monitoring purposes in (preschool) children. One of these non-invasive techniques is the measurement of volatile organic compounds (VOCs) in exhaled breath. VOCs profiles have proven to accurately differentiate children with asthma from healthy children [1]. We recently demonstrated that the measurement of VOCs can accurately predict an asthma diagnosis in wheezing preschool children [2]. Furthermore, VOCs profiles can differentiate healthy children from children with Cystic Fibrosis (CF) [3], and between CF patients with and without Pseudomonas aeruginosa colonization [3]. Therefore, the measurement of VOCs in exhaled breath is a promising new non-invasive technique for assessing airway inflammation in children and adults with lung diseases.

VOCs in exhaled breath are usually measured by gas chromatography mass spectrometry technique (GC-MS), an expensive and time consuming technique. To make the analysis of VOCs more feasible in common practice, hand-held devices have been developed that are increasingly used in adult patients [4, 5].
Examples are electronic Noses (eNose) from The eNose Company (Aeonose [6]) and from Common Invent [7], and an Ion Mobility Spectrometer (IMS) from Ganshorn [8].
However, these techniques have not been studied in children, and data on feasibility in children are mostly lacking.

In this study we would like to investigate the feasibility and reliability of new point-of-care instruments for measurements of VOCs in exhaled breath in young children aged 6 to 16 years.

Study objective

Research questions:
Primary questions:
* Are the new point-of-care instruments for the measurement of VOCs in exhaled breath feasible for use in children and adolescents aged 6 to 20 years?
* Are these techniques able to differentiate between healthy children and adolescents, asthmatic children and adolescents, and children and adolescents with cystic fibrosis (CF)? e.g. will it result in different VOC profiles?

Secondary question: what is the relationship between the new point-of-care

instruments and the standard breath tests (FeNO and EBC)?

Study design

Study Design: Cross-sectional study during 60 minutes.

Study burden and risks

The burden is very limited because the study takes not more than 60 minutes and is completely non-invasive (collection of exhaled breath and a short questionnaire). The collection of exhaled breath is safe and bears no extra risks.

Children and adolescents with asthma or CF in the study may benefit as the NO test and the questionnaire may point to respiratory complaints or a respiratory infection with appropriate clinical evaluation as a consequence.

At the end, after the development of the breath test, many children with and without serious respiratory diagnoses will benefit as it will improve diagnosis and treatment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Study Population:
3 groups of children and adolescents aged 6-20 years will be randomly selected:
* 20 healthy children and adolescents
* 20 children and adolescents with asthma
* 20 children and adolescents with CF;Inclusion criteria:
* Children and adolescents aged 6 to 20 years
* Healthy group: See exclusion criteria
* Asthma group: Doctor*s diagnosed asthma
* Cystic Fibrosis group: a diagnosis of cystic fibrosis, confirmed by a sweat test or genetic analysis

Exclusion criteria

Exclusion criteria:
* Recent course of prednisone or antibiotics (< 1 month before test)
* Passive smoking
* Other chronic inflammatory disease (e.g. inflammatory bowel disease, rheumatic disease, auto-immune disease)
* Healthy children and adolescents:
* No current or history of respiratory symptoms (by using ISAAC questionnaire)
* No current or history of allergic rhinitis (by using ISAAC questionnaire)

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-03-2016
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	19-08-2015
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	03-02-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-07-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-04-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL53995.068.15