Quantitative faecal haemoglobin test (FIT) in children with gastroenterological diagnosis

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SUMMARY

Introduction

Quantitative analysis of haemoglobin (Hb) level in stool samples (FIT) using automated analysers is routinely used in colorectal screening in adults, but never been described in children diagnostics. The aim of this study is analysis of faecal Hb level in children samples in years 2010 - 2016 tested by FIT faecal blood detection OC-Sensor (Eiken).

Methods

From the total number of FIT samples analysed (n=2488) in children (age 0,1-18 years, mean 7.65, males 1232/females 1256) samples with Hb level > 100 ng/ml, i.e. 20 μg/g of stool (n=236; 9.5%) were selected. By retrospective analyse of the possible causes of FIT positivity we identified (n=170; 72%) cases with confirmed gastroenterological diagnoses. Six groups according to the most widely represented gastroenterological diagnoses were created – IBD (n=66, 38.8% of the total number of gastroenterological causes), acute gastroenteritis (n=17; 10%), gastroesophageal reflux (n=17; 10%), cow's milk protein intolerance (CMPI) (n=27; 15.8%) and anal fissures (n=17; 10%); the sixth group consists of those gastroenterological causes not elsewhere classified, marked as others (n=26; 15,3%).

Results

The median values of faecal Hb levels were in the group of IBD 102.3 μg/g (range 20.4 - 858.6 μg/g); in acute gastroenteritis 220.8 μg/g (range 23.6 - 558.8 μg/g); in CMPI 110.4 μg/g (range 22.2 - 517.6 μg/g); in gastroesophageal reflux 48.6 μg/g (range 21.6 - 291.2 μg/g); in anal fissures 370.8 μg/g (range 29.8 - 1756 μg/g); in the group of others 48.9 μg/g (range 20.4 - 396.4 μg/g).

Conclusions

Quantitative analysis of haemoglobin (Hb) level in stool samples we described in children most widely represented gastroenterological diagnoses. Evaluation of cut-off criteria values for future diagnostic procedures will follow in future studies. Supported by the Research Project RVO VFN 64165.

GASTROINTESTINAL BLEEDING IN CHILDREN

Gastrointestinal bleeding in general is in children relatively rare compared to adults, but could be potentially life-threatening condition in childhood. In pediatric age bleeding differs according to the age and different conditions/diagnoses. Due the the definition it could be upper and lower (ligamentum Treitz), acute and chronic. In addition blood in gastrointestinal tract may be present from non-GI origins (coagulopathies, odontogenic, otorhinolaryngology, others). Clinically bleeding presents as hematemesis, enteroragy, melena or occult faecal bleeding.

Most frequent reasons in different age groups are mentioned below:

Upper gastrointestinal tract bleeding in neonates: stress gastritis, hemorrhagic disease of the newborn

Lower gastrointestinal tract bleeding in neonates: necrotizing enterocolitis, inborn errors of GIT

Upper gastrointestinal tract bleeding in children aged 1 month to 1 year: esophagitis caused by GER, gastritis

Lower gastrointestinal tract bleeding in children aged 1 month to 1 year: anal fissures, intussusceptions, Cows milk protein allergy, colitis

Upper gastrointestinal tract bleeding in older children: peptic ulcers, esophageal varices result from portal hypertension, IgA vasculitis, drugs and alcohol abuse

Lower gastrointestinal tract bleeding in older children : polyps juvenile type, Meckel diverticulum, vascular lesions, IBD, Infectious diarrhea

In clinical practice, detailed clinical assessment of a child is required for therapeutic intervention, but age-specific treatment and management strategies are not the topic of this presentation. Relevant interpretation of faecal occult bleednig could help the clinicians in stratification of diagnostic approach and lead to preselection of our patients group in decission process.

OCCULT BLOOD IN THE STOOL - METHODS

FOBT - CHEMICAL METHODS FOR FECAL OCCULT BLOOD TEST

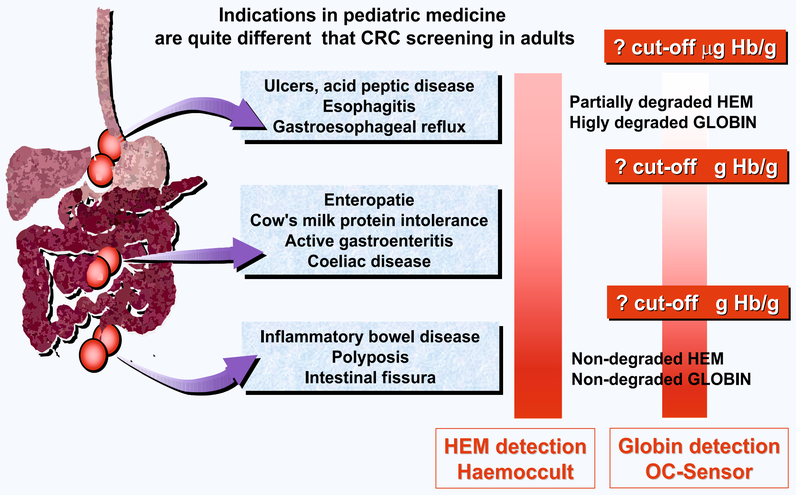
The principle of chemical tests to detect occult blood is based on the fact that haemoglobin and its derivatives react in a similar way to peroxidase enzymes– by catalyzing the transfer of an oxygen atom from the peroxide to a chromogen such as benzidine, o-toludine, guaiac or aminophenazone. Oxidation of the chromogen is indicated by the production of a blue, blue-green or pink color.

Previously used Haemoccult test changed in 2010 to OC-Sensor FIT test

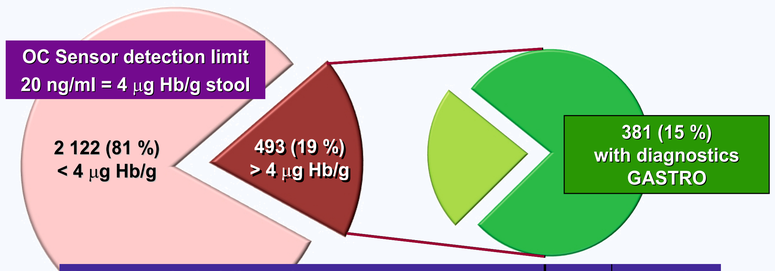
FIT - IMMUNOCHEMICAL METHODS FOR FECAL OCCULT BLOOD

Modern fecal occult blood testing is moving to an immunochemical test which is specific for human haemoglobin. This test utilizes a qualitative, sandwich dye conjugate immunoassay to selectively identify the globulin component of human haemoglobin in fecal specimens. The immunoassay uses a combination of monoclonal and polyclonal antibodies, utilizes an immunochemical chromatographic method for detection and has a high degree of analytical sensitivity.

OCCULT BLOOD IN THE STOOL - METHODS



RETROSPECTIVE ANALYSIS OF FIT TEST



Gastroenterological diagnosis	n	μg Hb/g
FIS - Fissura ani	19	333,6
IBD - Inflammatory bowel disease	94	76,7
GAS - Acute gastroenteritis	35	41,6
HSP - Henoch-Schonlein purpura with abdominal pain	23	36
CMPI - Cow's milk protein intolerance	68	14,9
GERD - Gastroesophageal reflux	59	11,6
Other gastroenterological diagnosis	83	10,8

QUANTITATIVE FIT METHOD

Haemoglobin in stool was measured using **quantitative immunochemical** method. Stool sampling was carried out following the instructions of producer.

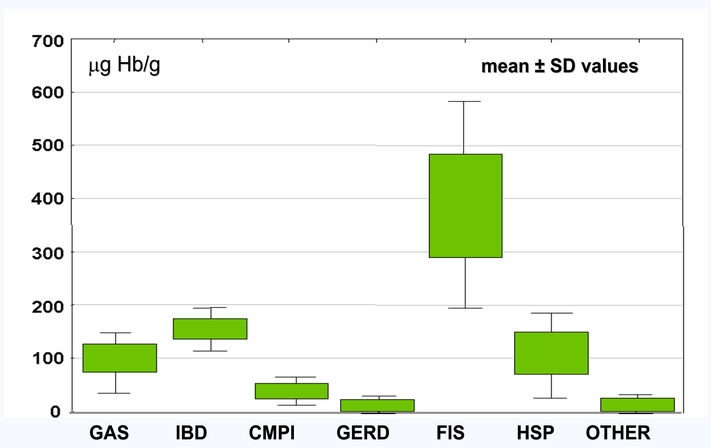
Stool was picked up by the brushing with the sampling brush on the stool surface and the immersion into the solution in test tube. This tube was kept in the temperature between 4 – 8 °C till the evaluation.

Samples were analysed continuously during a one week on the **OC Sensor-mikro®** analyser (Eiken Chemical Co., Tokyo, Japan).

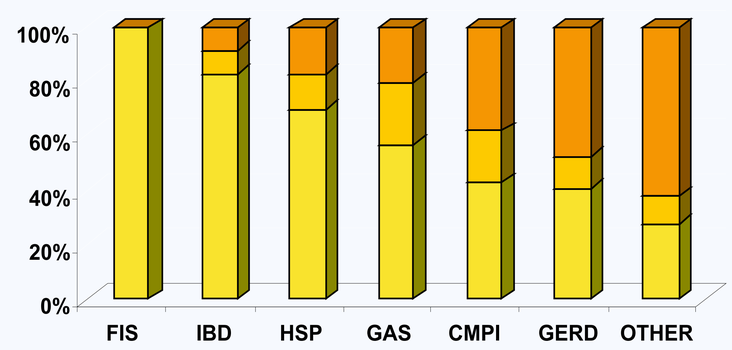
Quantitative assessment of human haemoglobin in stool (qI-FOBT) evaluates the level of human hemoglobin using polyclonal antibody against hemoglobin.

The analysis is performed using turbidimetric measurement by 600 nm in interval of measurement 0 - 2000 ng Hb/ml. In this reaction monoclonal antihuman HbA0 antibodies, which had been sentitized to latex, react with haemoglobin in the sample resulting in a latex agglutination reaction.

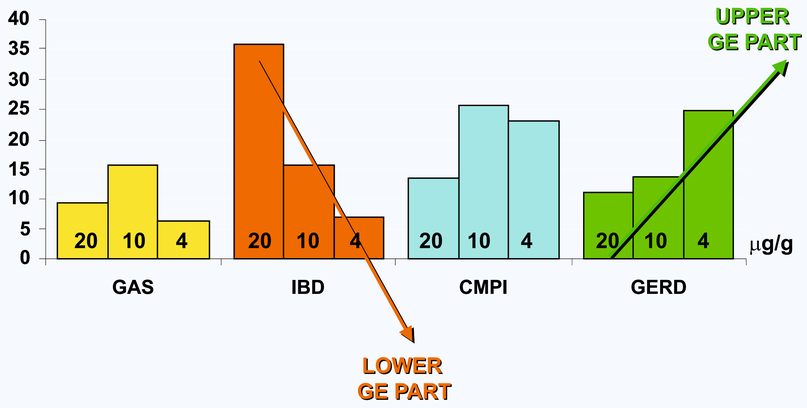
The change in optical density of the reaction solution is analyzed, optical density increases in proportion to higher concentrations of HbA0 in the sample.



Haemoglobin values (mean ± SD) in stool (μg Hb/g of stool) in 381 childrens (0 - 18 years) with gastroenterological diagnosis detected by quantitative immunochemical FIT method (OC-Sensor mikro).



Relative representation of individual diagnostic groups: Fissura ani (FIS), IBD - Inflammatory bowel disease (IBD), Henoch-Schonlein purpura with abdominal pain (HSP), Acute gastroenteritis (GAS), Cow's milk protein intolerance (CMPI), Gastroesophageal reflux (GERD), other gastroenterological diagnosis (OTHER) detected by FIT with three cut-off limits: Hb values > 20 μg Hb/g (n = 217), 10 - 20 μg Hb/g (n = 51), 4 - 10 μg Hb/g (n = 113)



Representation of individual diagnostic groups detected by FIT with three cut-off limits: Hb values > 20 μg Hb/g (n = 217), 10 - 20 μg Hb/g (n = 51), 4 - 10 μg Hb/g (n = 113) describing significant differences in upper - lower GI gradient, with two gastroenterological diagnosis - Inflammatory bowel disease (IBD) and Gastroesophageal reflux (GERD)

CONCLUSIONS

- ✓ **Previously used Haemoccult test changed in 2010 to OC-Sensor FIT test**
- ✓ **FIT positivity with the cut-off of 15 μg Hb / g faeces is defined for CRC screening in adults**
- ✓ **Indications in pediatric medicine are quite different that CRC screening in adults**
- ✓ **FIT cut-off should be different for upper and lower part of digestive system due to marked degradation of globin**
- ✓ **FIT test analytical sensitivity are 100-1000 times higher than that for previously used for Haemoccult**
- ✓ **FIT cut-off should be evaluated for every considered diagnosis**

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