

Piima- ja gluteenitalumatus erinevate haiguste korral

Lidén M, Kristjánsson G, Valtysdóttir S, Venge P, Hällgren R. Cow's milk protein sensitivity assessed by the mucosal patch technique is related to irritable bowel syndrome in patients with primary Sjögren's syndrome. *Clin Exp Allergy*. 2008 Jun;38(6):929-35.

Limaskesta *patch*- tehnikaga hinnatud lehmapiima valgule tundlikkus on seotud IBSündroomiga primaarse Sjögreni sündroomi korral

Patsiendid primaarse Sjögreni sündroomiga (pSS) kogevad gastrointestinaalseid (GI) ehk mao-sooletrakti sümptome, mida on seostatud sageli lisaks esineva tsöliaakiahaigusega (CD). Meie leidsime, et neil esineb sageli ka IBS- taolisi sümptome, ning allergiat ravimitele. On oletatud toiduallergia esinemist IBS korral.

Uuringu eesmärk oli uurida limaskesta vastust lehmapiima valgule pSS korral ja seoseid võimaliku reaktiivsusega lehmapiimale sellel sündroomi puhul. 21-l pSS ja 18-l tervel isikul teostati rektaalne väljakutse lehmapiimaga. 15t pärast hinnati NO tootmist ja MPO vabastamist kui limaskesta põletikulise reaktsiooni markereid, kasutades limaskesta patch - (*mucosal patch*) tehnikat. 8 patsienti 21-st pSS-ga omasid kindlat mukosaalse NO sünteesi suurenemist ja MPO luumenisse vabastamist pärast rektaalset väljakutset lehmapiimaga. Piimatundlikkus ei olnud seotud IgG/IgA antikehadega piimavalgule. IBS sümptoomid RomeIII kriteeriumite järgi olid täidetud 13-l patsiendil. **Kõik, kes olid tundlikud piimale, kannatasid IBS all.** Väike avatud uuring raporteeris soolesümptomide paranemist piimavaba dieediga piimale tundlike isikute puhul.

JÄRELDUS: mukosaalne põletikuline vastus lehmapiimale esineb 38%-l pSS-ga patsiendil ja on märk piimale tundlikkusest. IBS taolised sümptoomid on tavalised pSS korral ja seotud piimatalumatusega.

Patients with primary Sjögren's syndrome (pSS) are reported to have a variety of gastrointestinal symptoms partly attributed to an overrepresentation of celiac disease. We have observed that irritable bowel syndrome (IBS)-like symptoms are frequent complaints in this patient group. Allergic manifestations to various drugs are also common in pSS. A role of food allergy in IBS has been proposed. This study is aimed at evaluating the mucosal response to rectal challenge with cow's milk protein (CM) in patients with pSS and relates possible CM reactivity to their intestinal symptoms. A rectal challenge with CM was performed in 21 patients with pSS and 18 healthy controls. Fifteen hours after challenge the mucosal production of nitric oxide (NO) and the release of myeloperoxidase (MPO) as signs of mucosal inflammatory reaction were measured using the mucosal patch technique. Eight out of 21 patients with pSS had a definite increase of mucosal NO synthesis and the luminal release of MPO after rectal CM challenge. This sign of milk sensitivity was not linked to IgG/IgA antibodies to milk proteins. The symptoms for IBS according to Rome III criteria were fulfilled in 13 patients. All patients who were CM sensitive suffered from IBS. In a small open study, patients reactive to CM reported an improvement of intestinal symptoms on a CM-free diet. A rectal mucosal inflammatory response after CM challenge is seen in 38% of patients with pSS as a sign of CM sensitivity. IBS-like symptoms were common in pSS, linked to CM sensitivity.

Smerud HK, Fellström B, Hällgren R, Osagie S, Venge P, Kristjánsson G. Gluten sensitivity in patients with IgA nephropathy. *Nephrol Dial Transplant*. 2009 Aug;24(8):2476-81.

Gluteenitundlikkus IgA nefropaatia korral.

IgA nefropaatia korral esineb tsöliaakiahaigust (CD) sagedamini kui tervetel. On püstitatud hüpoteese, et gluteenisarnased toiduantigeenid võivad olla haaratud IgAN ehk IgA nefropaatia puhkemisse. Võrdlesime tervete ja IgAN patsientide põletikulisi reaktsioone limaskesta patch-tehnika abil gluteenile.

Gluteenreaktiivsus (MPO ja/või NO tõusu) gluteenile leiti 8-l 27-st IgAN patsiendil, kusjuures HLA-DQ2 ja DQ8 ei olnud neil tõusnud ja CD üldine esinemus oli IgAN grupis sama, mis üldelanikkonnas. Seerumi IgA AGA vastus oli tõusnud 9-l IgAN patsiendil ja see ei korreleerunud gluteenitundlikkusega, mida mõõdeti NO ja/või MPO-ga. Spetsiifilist seerumi IgG AGA vastust leiti ainult ühel patsiendil. Kudede transglutaminaasi ja endomüüsiumivastased antikehi ei leitud ühelgi juhul.

Umbes kolmandikul IgAN patsientidel oli suurem pärasoole limaskesta tundlikkus gluteenile, kuid ilma tsöliaakiahaiguse tunnusteta. Me hüpoteesime, et selline subkliiniline põletik gluteenile võib olla kaasatud IgAN alagrupi patsientide patogeneesi.

Coeliac disease is more frequent in IgA nephropathy (IgAN) patients compared to the healthy population. Several hypotheses postulate that food antigens like gluten may be involved in the onset of IgAN. In this study, we used a recently developed mucosal patch technique to evaluate the rectal mucosal inflammatory reaction to gluten in patients with IgAN (n = 27) compared to healthy subjects (n = 18). The rectal mucosal production of nitric oxide (NO) and release of myeloperoxidase (MPO) and eosinophil cationic protein (ECP) were measured. Serum samples were analysed for IgA and IgG antigliadin antibodies (AGA), IgA antibodies against tissue transglutaminase and IgA endomysium antibodies. Gluten reactivity, defined as increase in MPO and/or NO after gluten exposure, was observed in 8 of 27 IgAN patients. The prevalence of HLA-DQ2 and DQ8 was not increased among gluten-sensitive patients, and the total prevalence among IgAN patients was the same as for the normal population. An elevated serum IgA AGA response was seen in 9 of 27 IgAN patients. The increase in IgA AGA did not correlate with the gluten sensitivity as measured by NO and/or MPO. A specific serum IgG AGA response was seen in one patient only. Antibodies against tissue transglutaminase and endomysium were not observed. It is concluded that approximately one-third of our IgAN patients have a rectal mucosal sensitivity to gluten, but without signs of coeliac disease, and we hypothesize that such sub-clinical inflammation to gluten might be involved in the pathogenesis of IgAN in a subgroup of patients.

Lidén M, Kristjánsson G, Valtysdóttir S, Venge P, Hällgren R. Self-reported food intolerance and mucosal reactivity after rectal food protein challenge in patients with rheumatoid arthritis. *Scand J Rheumatol*. 2010 Aug;39(4):292-8

Iseendal avastatud toidu talumatus ja limaskesta reaktiivsus rektaalsele valgu väljakutsetestile reumatoidartriidiga patsientidel

Mitmetes uuringutes on raporteeritud toidu seoseid reumatoidartriidiga (RA). Uurisime inimeste endi poolt registreeritud toidureaktsioone. Teine eesmärk oli seostada neid tähelepanekuid piima ja nisu osas limaskesta muutustega (kasutades rektaalselt väljakutset nende valkudega). **27% RA isikutest viitavad mingile toidu talumatusele, eriti lehmapiima, liha ja nisugluteeni talumatusele.** Tugev limaskesta reaktsioon piimale leiti **11%1 patsientidest**, mõõdukalt tõusnud mukosaalne reaktsioon **lehmapiimale ja gluteenile** leiti

22%-l ja 33%-l vastavalt. Seost ei leitud aga enda poolt kogetud piimale ja gluteenile vastuseks tekkinud negatiivsete reaktsioonide ja limaskesta reaktiivsuse vahel.

Enda poolt kogetud toidutalumatuse sagedus RA korral on umbes sama mis üldises elanikkonnas. Mukosaalne reaktiivsus piimale ja gluteenile esineb teatud grupil RA haigetel ning pole seotud tajutava talumatusega.

A dietary link to rheumatoid arthritis (RA) has been suspected and an influence on arthritic symptoms by different diets has been reported. Our primary aim was to record the self-experienced adverse food reactions in patients with RA. A secondary aim was to relate self-experienced adverse reactions to dairy produce and wheat to the local mucosal reactivity observed after rectal challenge with cow's milk protein (CM) and wheat gluten. A questionnaire about self-experienced adverse reaction to food was sent to 347 RA patients. Rectal challenge with CM and gluten was performed in 27 of these patients and in healthy controls (n = 18). After a 15-h challenge the mucosal production of nitric oxide (NO) and the mucosal release of myeloperoxidase (MPO) and eosinophil cationic protein (ECP) were measured by using the mucosal patch technique. Twenty-seven per cent of the RA patients reported food intolerance (FI) to various foods, and in particular to CM, meat, and wheat gluten. Strong mucosal reactivity to CM was observed in 11% of the patients. Moderately increased mucosal reactivity to CM and gluten was found in 22% and 33%, respectively, of the patients. No relationship was found between self-experienced adverse reactions to CM or gluten and mucosal reactivity to these proteins. Perceived FI is reported frequently by RA patients, with a prevalence similar to that reported previously in the general population. Mucosal reactivity to CM and gluten is seen in a minor fraction of RA patients and is not related to the frequently perceived intolerance to these proteins.

L. Peters, J. R. Biesiekierski, G. W. Yelland, J. G. Muir, P. R. Gibson. Gluten May Cause Depression in Subjects With Non-Coeliac Gluten Sensitivity Alimentary Pharmacology & Therapeutics, Randomised Clinical Trial, An Exploratory Clinical Study. Alimant Pharmacol Ther. 2014;39(10):1104-1112.

Gluteen võib põhjustada depressiooni mittetsöliaakilise gluteenitundlikkuse korral, juhuvalikuga kliiniline uurimus

Praegused tõendid viitavad sellele, et paljudel iseendal mittetsöliaakilist gluteenitalumatust (NCGS) diagnoosinud patseintidel jäävad mao-sooletrakti (GI gastrointestinaalsed) sümptoomid alles ka pärast gluteenivaba dieeti, kuid nad jätkavad dieediga, sest tunnevad ennast paremini. Uuringu eesmärk oli näidata, et gluteeni toime võib olla ka vaimsele seisundile, mitte ainult GI sümptoomidele. 22 isikut vanuses 24–62 a (viis meest) ärritatud soole sündroomiga ja ilma tsöliaakiata võeti kaksikpimedasse uuringusse (3 päeva said patsiendid juhuslikult toiduga väljakutseid, millele järgnes 3 väljakutsetevaba päeva, enne kui nad lülitati ümber uuele dieedile). Väljakutseks oli gluteenivabale toidule lisatud gluteen (16 g/pv), nisu (16 g/pv) või platseebo. Lõpp-punktides hinnati ka *vaimset seisundit Spielberger State Trait Personality Inventory (STPI)* küsimustikuga, uuriti kortisooli sekretsiooni ja GI sümptoome. Gluteeni, mitte nisu tarbimine oli seotud kõrgema üldise STPI seisundiga depressiooni skoorides võrreldes placeeboga, Teiste STPI joonte puhul ei olnud erinevusi, ka kortisooli tootmises ei olnud erinevusi erinevate väljakutsete puhul. GI sümptoomid tekkisid kõikide väljakutsete puhul sarnaselt. Järeldus: lühiajaline gluteeni manustamine tekitab depressiooni sümptoome, mõjutamata teisi emotsioone, gluteenispetsiifilist mao-sooletrakti sümptoomide tekitamist ei leitud. See võib selgitada, miks kliendid ennast sellisel dieedil olles paremini tunnevad.

Current evidence suggests that many patients with self-reported non-coeliac gluten sensitivity (NCGS) retain gastrointestinal symptoms on a gluten-free diet (GFD) but continue to restrict gluten as they report 'feeling better'. **Aim.** To investigate the notion that a major effect of gluten in those with is on mental state and not necessarily on gastrointestinal symptoms. Twenty-two subjects (24–62 years, five male) with irritable bowel syndrome who had coeliac disease excluded but were symptomatically controlled on a GFD, undertook a double-blind cross-over study. Participants randomly received one of three dietary challenges for 3 days, followed by a minimum 3-day washout before crossing over to the next diet. Challenge gluten-free food was supplemented with gluten (16 g/day), whey (16 g/day) or not supplemented (placebo). End-points included mental state as assessed by the Spielberger State Trait Personality Inventory (STPI), cortisol secretion and gastrointestinal symptoms. **Results.** Gluten ingestion was associated with higher overall STPI state depression scores compared to placebo [$M = 2.03$, 95% CI (0.55–3.51), $P = 0.010$] but not whey [$M = 1.48$, 95% CI (–0.14 to 3.10), $P = 0.07$]. No differences were found for other STPI state indices or for any STPI trait measures. No difference in cortisol secretion was identified between challenges. Gastrointestinal symptoms were induced similarly across all dietary challenges. **Conclusions.** Short-term exposure to gluten specifically induced current feelings of depression with no effect on other indices or on emotional disposition. Gluten-specific induction of gastrointestinal symptoms was not identified. Such findings might explain why patients with non-coeliac gluten sensitivity feel better on a gluten-free diet despite the continuation of gastrointestinal symptoms.

Novembre E, Vierucci A. Milk allergy/intolerance and atopic dermatitis in infancy and childhood. *Allergy*. 2001;56 Suppl 67:105-8.

Piima allergia/talumatus ja atoopiline dermatiit imiku- ja lapseas

Ebasoovitavad reaktsioonid piimavalgule viitavad piimaallergiale/talumatussele (CMPA/CMPI *cow's milk allergy, cow's milk intolerance*), sest sümptomide alusel ei ole neid seisundeid võimalik eristada ning pole olemas ühte laboratoorset testi, mis neid diagnoosiks, vajalik on korrektne provokatsioonitest.

Atoopiline dermatiit (AD) on kõige tavalisem CMPA/CMPI sümptom, kolmandikul ADga lastest on CMPA/CMPI diagnoos eliminatsiooni dieedi või väljakutse testi alusel ja 40-50% alla 1-aastastest lastest CMPA/CMPI-ga omavad AD-d. Paljud lapsed omandavad täieliku taluvuse mõne aastaga, kuid need, kellel jääb talumatus püsima, omavad sagedamini perekondlikku atoopilise haiguse ajalugu ja nendel lisanduvad väga sageli teised allergilised haigused nagu riniit või astma ning mitmesed toidutalumatused. Simultaanne allergilise taluvuse arenemine ühes organis ja talumatuse arenemine teises organis viitab geneetiliste, immunoloogiliste ja keskkondlike faktorite keerulisele rollile AD jt atoopiliste haiguste tekkes.

Adverse reactions to cow's milk proteins are usually indicated as cow's milk allergy/intolerance (CMPA/CMPI) because no differentiation is possible on the basis of symptoms, and there is no reliable single laboratory test available for the diagnosis of CMPA or CMPI. Elimination and challenge tests for cow's milk proteins using strict, well-defined diagnostic criteria are required for the diagnosis of CMPA/CMPI. Atopic dermatitis (AD) is one of the most common symptoms of CMPA/CMPI. Approximately one third of AD children have a diagnosis of CMPA/CMPI according to elimination diet and challenge tests, and about 40-50% of children < 1 year of age with CMPA/CMPI have AD. Many children with AD and CMPA/CMPI develop a complete tolerance to CMP in a few years. Children with persisting forms of CMPA/CMPI have a more frequent history of familial atopic disease, change in CMPA/CMPI manifestations over time and very high frequency of multiple food intolerance and allergic diseases. Many children who outgrow their AD develop other allergic diseases, such as rhinitis or asthma. The simultaneous development of allergic tolerance in one organ and the intolerance or atopic disease in another organ suggest that genetic, immunologic and environmental factors play a complex role in the natural history of AD and other atopic diseases.

Armisen M, Vidal C, López-Rosés L, Rodríguez V, Bartolomé B. Eosinophilic esophagitis due to allergy to sheep and goat milk proteins. *Rev Esp Enferm Dig*. 2008 Jan;100(1):53-6. [Article in Spanish]

Eosinofiilne ösofagiit lamba- ja kitsepiimavalgu allergia tõttu

Eosinofiilne ösofagiit on põletikuline söögitoru haigus, mille puhul esineb eosinofiilsete lümfotsüütide infiltratsioon limaskestas. See on täiskasvanutel ebatavaline, sümptomideks on neelamishäire ja toidu poolt mõjutatus. Kirjeldatakse meest, kellel esines pikaaegne vahelduv düsfaagia pärast teatud tüüpi kitse- ja lambajuustu tarbimist ning tarbis seetõttu ibuprofeeni. Biopsia andis eosinofiilse infiltratsiooni ja allergiatestid näitasid IgE antikehi kitse- ja lambapiimale. Kohalik steroidravi fluticasoniga ja nende piimatoodete elimineerimine viis sümptomide täieliku kadumiseni. 4 kuu pärast ei olnud ka biopsias enam eosinofiile.

Eosinophilic esophagitis is an inflammatory disease of the esophagus characterized by the presence of high numbers of eosinophils in the esophageal mucosal layer (> 20 high-power field). It is uncommon in adults but in such cases intermittent dysphagia and food impaction are the most common presenting symptoms. We report the case of a male with long-standing intermittent dysphagia after eating selected goat and sheep cheese types, who required medical help following the impaction of an ibuprofen pill in the esophagus. A biopsy demonstrated the presence of eosinophilic inflammation, and allergy testing showed specific IgE against proteins in the milk of goats and sheep. Topical steroid therapy with oral fluticasone, and the elimination of these dairy products from the diet induced complete symptom resolution, and biopsy specimens taken 4 months later showed no eosinophils.