

HISTAMINE INTOLERANCE AND MICROBIOTA CHANGES IN PATIENTS WITH PAINFUL BLADDER SYNDROME / INTERSTITIAL CYSTITIS

Hypothesis / aims of study

The cause of Painful Bladder Syndrome / Interstitial Cystitis is currently unknown. Histamine seems to play a major role in IC as neurogenic inflammation is one of the hypothesis of IC. Antihistamines are also part of the guideline recommendations, foods high in histamine (e.g. Shorter-Moldwin Food Sensitivity Questionnaire) aggravate IC symptoms. Within this retrospective case collection the role of histamine overload in the gut and vagina is highlighted.

Study design, materials and methods

Between September 2012 and March 2016 a total of 71 women (range 19-75 years, mean age 48 years) were surveyed. Histamine in fecal samples was measured with a commercially available ELISA kit (LDN Labor Diagnostika Nord GmbH & Co. KG, Nordhorn, Germany). The results were compared to an age-matched control group of 57 healthy women. Additionally, vaginal swabs were analysed for histamine producing bacteria of the Enterococcus and Enterobacteriaceae family. Furthermore a complete gut microbiota analyses was done in all women.

Results

In 50 of the 71 analysed women elevated histamine levels were found in fecal samples. In 37 out of the 50 women with the elevated histamine level the presence of Enterococcus ssp. and / or Enterobacteriaceae in vaginal swabs was also detected. In 8 women only the presence of Enterococcus ssp. and / or Enterobacteriaceae was found. Only 4 women did neither show elevated histamine levels nor the presence of histamine producing bacteria in vaginal swabs. Moreover concerning gut microbiota in most of the patients the protective microbiota (lactobacilli and bifidobacteria) was also diminished.

Interpretation of results

There are parallels between IC and histamine intolerance: prevalence of 1%, 80% female and middle aged, symptom improvement in pregnancy because of a 500 fold higher level of the diamine oxidase (histamine eliminating enzyme). Histamine intolerance is a poorly described disease which can present with a variety of symptoms like e.g. migraine, irritable bowel syndrome, urticaria, tachykardia, nasal congestion and perhaps also IC? Histamine can increase intestinal permeability causing a leaky gut which prompts the body to initiate immune reactions causing autoimmune diseases. Irritable bowel syndrome and autoimmune diseases are both comorbidities of IC.

Concluding message

In irritable bowel syndrome it has been demonstrated that abdominal pain correlates with activated mast cells in proximity to colonic nerves which leads to the hypothesis of a neural-mediated crosstalk between colon and bladder afferents. Moreover histamine alone as shown in mice can also cause pelvic pain. Another consequence of the leaky gut is a toll-like receptor (TLR)-4 inflammatory response leading per se to pain. That TLR-4 plays a role in pain has been recently demonstrated in IC patients by the MAPP research group.

Pre- and probiotics could be a new therapeutic approach for IC as they can repair the gut layer and can influence toll-like-receptors.

References

1. Barbara et al, Gastroenterology 2004; 126: 693-702
2. Rudick et al, PloS ONE 2008; 3: e2096
3. Schrepf et al, Pain 2014 Sep; 155(9):1755-61

Disclosures

Funding: none **Clinical Trial:** No **Subjects:** HUMAN **Ethics not Req'd:** retrospective case collection **Helsinki not Req'd:** retrospective case collection **Informed Consent:** No