



Samenvatting van het proefschrift Annemieke Y. Thijssen

"Clinical, psychosocial and therapeutic aspects of Irritable Bowel Syndrome. - Results of cohort studies and a probiotic interventional trial-"

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IBS is a highly prevalent functional GI disorder with a female predominance and heterogeneous phenotype. In the current thesis we aimed to study psychosocial, central and intestinal factors as well as patients characteristics that may affect symptom scores in patients with IBS.

In chapter 2 of this thesis, we found that psychological factors as well as dysfunctional cognitions significantly affect symptom severity and quality of life (QoL) in IBS patients. IBS symptoms did improve significantly upon treatment with a probiotic when compared to placebo (chapters 3 and 4), but this effect was only seen at the end of the follow-up period (i.e. 8 weeks after the end of treatment) and only in the male population. These findings could not be explained by baseline differences in symptom scores, psychological factors or medication use. Analyses with regard to the epithelial barrier, immune markers and visceral perception did not reveal differences between the probiotic and placebo treated patients, apart from a small although significant decrease in urge perception in a subgroup of the probiotic treated patients. Further analyses in the Maastricht-IBS cohort (chapter 5), showed decreased 5-HIAA and 5-HT/5-HIAA ratio in IBS patients compared to healthy controls, in which female patients had lower concentrations than male patients. No influence was found for symptoms, anxiety and/or depression nor for medication use on plasma 5-HT, 5-HIAA or their ratio in IBS patients or subgroups with linear regression analysis. In chapter 6 we further explored possible gender differences in IBS patients, showing that female IBS patients exhibit a different disease phenotype than male IBS patients. Furthermore, female IBS patients have significantly lower fecal short chain fatty acid (SCFA) levels compared to male IBS patients, possibly pointing to a role of altered microbial activity in the supposed difference in pathophysiology between female and male IBS patients. Finally our findings in chapter 7 indicate that patients with Ulcerative colitis (UC) in remission are characterized by i) visceral hypersensitivity to rectal distension, ii) a significantly increased number of mast cells in the mucosa, activated mast cells and in close proximity of mast cells to colonic nerve endings iii) found a correlation between rectal hypersensitivity and abdominal, IBS-like symptoms and number of

mast cells in these patients. The future challenge for this group of UC-R patients is to distinguish persistent inflammation from true remission with IBS complaints.

No data were available regarding microbiota composition in the studied IBS cohorts. We believe that the intestinal microbiota may be a missing link in the pathophysiology of IBS and possibly the found gender differences. The Maastricht-IBS cohort will provide microbiota data in the future, which may provide leads for further studies gaining more detailed insight in the pathophysiology and identify groups of IBS patients for specific treatments. A combination of microbiome, SCFAs and diet analyses in IBS patients, followed prospectively with resampling over time, with evaluation of therapeutic interventions, may provide more detailed insight in the proposed underlying pathophysiologic mechanisms and may help to explain the observed gender differences. In summary, gaining more insight in the pathophysiological mechanisms of IBS remains an important goal to identify subgroups of IBS patients that could benefit from targeted interventions, taking gender and co-morbidity into account in all studies.