Beta-blocker use is associated with a higher relapse risk of inflammatory bowel disease - a Dutch retrospective cohort study

R. A. Willemze[a], T. Bakker[a], M. Pippias[b], C.Y. Ponsioen[c], W.J. de Jonge[a]

a) Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam, The Netherlands
b) Department of Medical Informatics, Academic Medical Center, Amsterdam, The Netherlands
c) Department of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands

Contact: r.a.willemze@amc.uva.nl

Background

- Many factors may influence the disease course of inflammatory bowel disease (IBD) – like the concomitant use of medication.
- One such drug group is beta-blockers – blocking the β-adrenergic receptors – used by approximately 10% of the Dutch population. β-adrenergic receptor activation has potent anti-inflammatory effects on the myeloid compartment of the immune system.

In this pilot study, we addressed whether an association exists between the use of beta-blockers and the course of IBD, as defined by the risk of a disease relapse in patients with IBD.

Variable	**Beta-blocker** (n = 30)	**No beta-blocker** (n = 220)	**Significance**
Age [mean (standard deviation)]	64 (11.6)	49 (15.0)	**<0.001***
Male [n (%)]	13 (43.3)	91(41.4)	0.99
Follow-up in months [median (Q1-Q3)]	57 (42-75)	55 (23-105)	0.66
IBD type [n (%)]			0.60
Ulcerative colitis	19 (63.3)	121 (55.0)	
Crohn's disease	10 (33.3)	80 (36.4)	
IBD-u	1 (3.3)	19 (8.6)	
Prior IBD related surgeries [n (%)]			0.77
0	25 (83.3)	173 (78.6)	
1	2 (6.6)	28 (12.7)	
>1	3 (10)	19 (8.7)	
Prior appendectomy [n (%)]	6 (13.3)	18 (8.2)	0.05
Smoking† [n (%)]			0.95
Yes	14 (46.6)	105 (47.7)	
No	16 (53.3)	109 (49.5)	
Missing	0 (0)	6 (3)	

Table 2. Characteristics of patients using beta-blockers versus not using beta-blockers
* Significant with α = 0,05; † Smoking is defined as being a smoker in the last 20 years.

250 IBD patients had available drug prescriptions (Table 2). 30 patients (12%) used a beta-blocker (Table 3).

- IBD patients using beta-blockers: 21 relapses per 100 person-years (95% confidence interval (CI): 14.0-28.6)
- IBD patients not using beta-blockers: 29 relapses per 100 person-years (95% CI: 26.2-32.4)

Beta-blocker type	**Patients [n (%)]**
Selective β_1-blocker	22 (73%)
Non-selective β-blocker	5 (17%)
Combination	3 (10%)

Table 3. Prescribed beta-blockers

Methods

- Population-based IBD cohort of 1461 patients
- Relapses: increase in medication level (Table 1) or the start of steroids after stable medication use for at least four months
- Primary outcome: relapses per 100 person-years
- Cox proportional hazard model with shared frailty

	Medication type
Level 0	no IBD medication
Level 1	5-ASA
Level 2	thiopurines
Level 3	methotrexate
Level 4	cyclosporine, tacrolimus, anti-TNF agents

Table 1. IBD medication levels

Main Result

IBD patients using a beta-blocker had a 54% higher risk of a relapse versus IBD patients not using a beta-blocker.

		Hazard ratio	**95% CI**	**p-value**
Unadjusted	Beta-blocker use	1.26	0.88-1.80	0.21
	Frailty effect	-	-	<0.001**
Adjusted*	**Beta-blocker use**	**1.54**	**1.05-2.25**	**0.03****
	Frailty effect	-	-	<0.001**

Table 4. Output unadjusted and adjusted Cox proportional hazard model with shared frailty
* Adjusted for age and gender; ** Significant with α = 0,05

Conclusion

Our study suggest that beta-blocker use is associated with an increased relapse risk in patients with IBD. However, these results warrant confirmation in a larger cohort.
Concomitant medication use seems to be one of the factors that can influence the course of IBD and this should be acknowledged while making decisions about treatment of IBD and follow-up.