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EDITOR OF THE MONTH

PONTUS KARLING

Associate Professor

Department of Public Health and Clinical Medicine, Umeå University, Sweden

In this newsletter, highlights from articles published in PubMed in May and June 2022 are presented. In Lancet three new randomized controlled trials have been published that probably will have impact on the treatment of IBD in the following years. The studies include adalimumab versus ustekinumab for patients with Crohn's disease, risankuzimab versus placebo for patients with Crohn's disease and upadicitinib versus placebo for patients with ulcerative colitis. Furthermore, this newsletter also present data on thiopurine and anti-TNF therapy, artificial intelligence in endoscopy and on brain-gut axis interaction in IBD.

Pontus Karling

Adalimumab versus ustekinumab for patients with Crohn's disease naïve to biologics

SANDS BE, IRVING PM, HOOPS T, IZANEC JL, GAO LL, GASINK C, GREENSPAN A, ALLEZ M, DANESE S, HANAUER SB, JAIRATH V, KUEHBACHER T, LEWIS JD, LOFTUS EV JR, MIHALY E, PANACCIONE R, SCHERL E, SHCHUKINA OB, SANDBORN WJ; SEAVUE STUDY GROUP. LANCET. 2022 JUN 11;399(10342):2200-2211.

There are so far few "head to head" studies published that aim to actively compare two different biologics. Sands el al present data from a multicentre, randomized, double blind phase 3 trial comparing adalimumab with ustekinumab in patients with moderately to severely active Crohn's disease and who were naïve for biologics (Sands et al, Lancet, June 2022). Patients were required to discontinue thiopurines/ methotrexate at least 3 weeks before randomization. Oral steroids were accepted if they were on stable dose at least 3 weeks before randomization. Adalimumab induction 160 mg at 0 week, 80 mg subcutaneously at week 2 followed by 40 mg every other week was compared to ustekinumab induction 6 mg/kg on day and then 90 mg subcutaneously every eight week. Primary endpoint was clinical remission at week 52. The proportion of patients that reached primary and some secondary endpoints are shown in Table 1.

Table 1. *The proportion of patients that reach clinical and endoscopic remission in patients with Crohn randomized to either ustekinumab or adalimumab.*

	Ustekinumab (n=191)	Adalimumab (n=195)	p-value
Clinical remission at week 52	65%	61%	0.42
Corticosteroid-free remission at week 52	61%	57%	0.49
Patient related outcome (PRO)-2 symptom remission at week 52	57%	55%	0.79
Endoscopic response at week 52	42%	37%	0.35
Endoscopic remission at week 52	31%	29%	0.63

COMMENTS

This is the first clinical trial to directly and prospectively compare two approved biologic treatments for Crohn's disease. Both treatments performed equally on all outcomes, and the result of the study strengthen the argument that anti-TNF therapy should be used as the first-line biologic in Crohn's disease (based on economic reasons).

Risankizumab – a promising treatment for Crohn's disease

D'HAENS G, PANACCIONE R, BAERT F, BOSSUYT P, COLOMBEL JF, DANESE S, DUBINSKY M, FEAGAN BG, HISAMATSU T, LIM A, LINDSAY JO, LOFTUS EV JR, PANÉS J, PEYRIN-BIROULET L, RAN Z, RUBIN DT, SANDBORN WJ, SCHREIBER S, NEIMARK E, SONG A, KLIGYS K, PANG Y, PIVORUNAS V, BERG S, DUAN WR, HUANG B, KALABIC J, LIAO X, ROBINSON A, WALLACE K, FERRANTE M.LANCET. 2022 MAY 28;399(10340):2015-2030.

FERRANTE M, PANACCIONE R, BAERT F, BOSSUYT P, COLOMBEL JF, DANESE S, DUBINSKY M, FEAGAN BG, HISAMATSU T, LIM A, LINDSAY JO, LOFTUS EV JR, PANÉS J, PEYRIN-BIROULET L, RAN Z, RUBIN DT, SANDBORN WJ, SCHREIBER S, NEIMARK E, SONG A, KLIGYS K, PANG Y, PIVORUNAS V, BERG S, DUAN WR, HUANG B, KALABIC J, LIAO X, ROBINSON A, WALLACE K, D'HAENS G.LANCET. 2022 MAY 28;399(10340):2031-2046.

Interleukin (IL)-23 is an inflammatory cytokine that modulate inflammation and has been found in increase concentrations in the mucosa of patients with Crohn's disease. In Lancet two articles are presented on the treatment with a monoclonal antibody (risankizumab) to IL-23 for patients with moderate or severe Crohn's disease (D'Haens et al, Lancet, May 2022; Ferrante et al, Lancet, May 2022). Risankizumab binds to the IL-23 p19 subunit, inhibiting its interaction with the IL-23R complex and risankizumab is already approved for the treatment of psoriasis. The induction study included patients with Crohn's disease that either failed biologic or conventional therapy (ADVANCE) or patients who failed biologics (MOTIVATE). Risankizumab showed promising effect on both symptoms and objective markers such as endoscopy, hsCRP and faecal calprotectin.

A post-hoc analysis of patients with elevated concentrations of hsCRP and faecal calprotectin at baseline showed a significant decline in the treatment group at 4 and 12 weeks and higher proportion of patients who normalized these parameters at 12 weeks. The levels remained low in the maintenance study. The incidence of adverse events did not differ between risankizumab and placebo. There was a slightly increased risk for serious infections in the placebo group. Table 1 summarize the effect on symptoms and endoscopic response.

Table 1. *Proportion of patients on risankizumab 600 mg versus placebo who reached the outcomes in the induction study. NNT = Number Needed to Treat.*

Induction	Number of Patients Risankizumab 600 mg/Placebo	CDAI clinical remission at week 12	Abdominal pain and stool frequency clinical remission at week 12	Endoscopic response at week 12
ADVANCE	336/175	45% vs 25% p<0.0001 NNT 5	43% vs 22% p<0.0001 NNT 5	40% vs 12% p<0.0001 NNT 4
MOTIVATE	191/187	42% vs 20% p<0.0001 NNT 5	35% vs 19% p=0.0007 NNT 6	29% vs 11% p<0.0001 NNT 5

In the maintenance trial (FORTIFY) patients were randomized to subcutaneous risankizumab or placebo every 8 week.

Table 2 summarize the effect on symptoms and endoscopic response.

Table 2. *Proportion of patients on risankizumab 180 mg (every 8th week) versus placebo who met the outcomes in the maintenance study (FORTIFY). NNT = Number Needed to Treat*

Maintenance	Number of Patients Risankizumab 180 mg/Placebo	CDAI clinical remission at week 52	Abdominal pain and stool frequency clinical remission at week 52	Endoscopic response at week 52
FORTIFY	157/164	55% vs 41% p=0.031 NNT 7	46% vs 40% p=0.12 NNT 17	47% vs 22% p<0.0001 NNT 4

COMMENTS

These phase III trials for risankizumab perform well in comparison to previous published studies on biologics using similar design and risankizumab may challenge established treatments as a second line biologic treatment for Crohn's disease in the near future. Risankizumab did not differ to placebo in regard of safety.

Upadacitinib – an effective selective JAK1 inhibitor for ulcerative colitis

DANESE S, VERMEIRE S, ZHOU W, PANGAN AL, SIFFLEDEEN J, GREENBLOOM S, HÉBUTERNE X, D'HAENS G, NAKASE H, PANÉS J, HIGGINS PDR, JUILLERAT P, LINDSAY JO, LOFTUS EV JR, SANDBORN WJ, REINISCH W, CHEN MH, SANCHEZ GONZALEZ Y, HUANG B, XIE W, LIU J, WEINREICH MA, PANACCIONE R. LANCET. 2022 JUNE 4;399(10341):2113-2128.

Upadacitinib is an oral, selective, small molecule JAK inhibitor which mainly inhibits JAK1 in contrast to tofactinib which also inhibits JAK2 and JAK3. Due to the selective effect on JAK1 the long-term safety profile is hypothesized to be more favorable with upadacitinib in comparison to non-selective JAK inhibitors. In Lancet phase III studies on upadacitinib is newly presented (Danses et al, Lancet, June 2022). In the induction trials (UC1 and UC2) upadacitinib 45 mg once daily was compared to placebo and in the maintenance trial (UC3) upadacitinib 15 mg or 30 mg once daily was compared to placebo. The primary outcome was adapted Mayo score <3, with stool frequency score <2 and not greater than baseline, red blood score = 0, and endoscopic subscore <2 without friability. The results in UC3 were based on intention to treat. Upadactinib was superior to placebo to induce and to maintain clinical remission and endoscopic improvement/remission (Table 1 on the next side).

Adverse events in the induction and maintenance study did not differ between upadactinib and placebo. In the maintenance study the most common adverse event was worsening of ulcerative colitis (13%/7%/30% for upadactinib 15 mg/30 mg/placebo) and nasopharyngitis (12%/14%/10%). Herpes zoster was uncommon (4%/4%/0%). Adverse events leading to discontinuation were more common in the placebo group (4%/6%/11%).

Table 1. *Proportion of patients who achieve clinical remission and endoscopic improvement/remission on induction (UC1 and UC2) and maintenance (UC3) with upadacitinib and placebo. NNT = Number Needed to Treat.*

	Number of patients Upadacitinib/Placebo	Clinical remission (Adapted Mayo score)	Endoscopic improvement	Endoscopic remission
UC1 Upadactinib 45 mg week 8	319/154	26% vs 5% p<0.0001 NNT 5	36% vs 7% p<0.0001 NNT 3	14% vs 1% p<0.0001 NNT 8
UC2 Upadactinib 45 mg week 8	341/174	33% vs 4% p<0.0001 NNT 3	35% vs 8% p<0.0001 NNT 4	18% vs 2% p<0.0001 NNT 6
UC3 Upadactinib 15 mg week 52	148/149	42% vs 12% p<0.0001 NNT 3	49% vs 14% p<0.0001 NNT 3	24% vs 6% p<0.0001 NNT 6
UC3 Upadactinib 30 mg week 52	154/149	52% vs 12% p<0.0001 NNT 2.5	62% vs 14% p<0.0001 NNT 2	26% vs 6% p<0.0001 NNT 5

COMMENTS

These phase III trials with upadacitinib perform well in comparison to previous published studies on biologics and JAK inhibitors using similar design, and upadactinib may challenge established treatments as a second line treatment for ulcerative ulcerative colitis in the near future. The safety profile of upadacitinib was good.

Infliximab for IBD – Proactive therapeutic drug monitoring versus conventional treatment

FERNANDES SR, RODRIGUES IC, SERRAZINA J, BOTTO IA, BERNARDO S, GONÇALVES AR, VALENTE A, MOURA SANTOS P, CORREIA LA, MARINHO RT. SCAND J GASTROENTEROL. 2022 MAY 22:1-7.

In Lisbon, Portugal a retrospective case-control study was performed which compared proactive therapeutic drug monitoring (PTDM) with conventional treatment with infliximab in patients with IBD (Fernandez et al, Scand J Gastroenterol, May 2022). Patients received 5 mg/kg of infliximab intravenously at week 0, 2, 6 and 14, irrespective of symptoms patients in the PTDM strategy was escalated aiming at an infliximab concentration between 5-10 mg/ml. In patients with high infliximab levels (>10 mg/ml) the decision of de-escalation was decided by the attending physician. In the PTDM strategy infliximab was measured at week 14 and after every other infusion. The primary endpoint was clinical remission defined as a partial Mayo score <2 with rectal bleeding subscore <1 or patients with ulcerative colitis or a Harvey-Bradshaw index <5 for patients with Crohn's disease. Remission based on faecal calprotectin was <250 ug/g (Buhlman). Highlights of the results are presented in Table 1.

Table 1.
Proactive treatment with infliximab using therapeutic drug monitoring versus conventional infliximab treatment.

	Conventional infliximab treatment (n=70)	Proactive infliximab treatment (n=148)	p-value
Proportion of patients with: Crohns disease/ Ulcerative colitis	86%/14%	61%/39%	<0.001
Proportion of patients with perianal disease	28%	12%	0.003
Proportion of patients with immunomodulators	86%	82%	0.70
Proportion of patients naïve to anti-TNF	77%	89%	0.042
Proportion of patients in clinical remission after one year	69%	80%	0.06
Proportion of patients in remission based on faecal calprotectin after one year	47%	69%	0.03
Proportion of patients who had IBD surgery	6%	2%	0.215
Proportion of patients with any adverse outcome	40%	32%	0.285
Proportion of patients who discontinued treatment	7%	15%	0.126

COMMENTS

This study is limited by differences in baseline characteristics between the groups. There were significantly more patients with Crohn's disease, perianal disease and who were non-naïve to infliximab in the conventional group compared to the proactive group. In addition, the conventional infliximab group received treatment years before the proactive group. However, the authors present a multivariate analysis in the article and shows that the favorable remission rate based on faecal calprotectin remained significant in the proactive group compared to the conventional treatment group after adjusting for these factors. The study also included a comparison between vedoluzimab and infliximab but the differences in baseline characteristics differed even more in the patients receiving vedoluzimab compared to patients with different infliximab treatment strategy, which makes it difficult to draw any conclusions of that part of the study.

Early biologic therapy after surgery for Crohn's disease is associated with lower endoscopic recurrence

D'AMICO F, TASOPOULOU O, FIORINO G, ZILLI A, FURFARO F, ALLOCCA M, SILERI P, SPINELLI A, PEYRIN-BIROULET L, DANESE S.INFLAMM BOWEL DIS. 2022 MAY 28:IZAC110.

Up to 2 out of 3 patients with Crohn's disease need surgery due to complications (i.e. stricture, abscesses, fistulas) during their lifetime. Unfortunately, 90% of the patients have endoscopic disease recurrence after surgery and as many as 40% undergo an additional surgery within 10 years. In a retrospective study from Milan, Italy, the role of early biologic therapy after surgery for Crohn's disease was analyzed (D'Amico et al, Inflamm Bowel Dis, May 2022). The study included patients who had curative resections at baseline surgery and with at least one colonoscopy at 6-12 months after surgery. A Rutgeerts score >1 was considered to be disease relapse. Approximately one-third (30%, n=42) of the patients were under treatment with at least one biologics at baseline (the number of patients on adalimumab, infliximab, ustekinumab and vedoluzimab was 31, 13, 4 and 3). The median duration of biologic therapy at the time of the index colonoscopy was 9.8 months. At the first colonoscopy after surgery 70% showed endoscopic disease relapse. Patients not receiving biologic therapy at baseline experienced a significant higher rate of endoscopic disease relapse compared with patients receiving early postoperative therapy with biological agents (81% vs 45%; $p<0.0001$). The proportion of patients who needed hospitalization or surgery during follow-up (median follow-up 28 months) were significantly higher in patients with no biologic therapy versus biologic therapy (11% vs 0%; $p=0.018$).

COMMENTS

This study shows that regardless of risk factors, patients who have surgery for Crohn's disease, have benefits of starting or restarting biologic therapy as soon as they have past the postoperative setting.

The benefit of proactive metabolite testing in IBD patients treated with thiopurines

BARNES A, OOI SJ, LYNCH KD, PARTHASARATHY N, BISHARA M, GOUNDER M, GRAFTON R, LEACH P, BAMPTON P, SECHI A, NG W, CONNOR S, VAN LANGENBERG D, MOUNTIFIELD R, ANDREWS JM. DIG DIS SCI. 2022 JUNE 10.

The use of metabolite measurement in the treatment of patients with IBD have demonstrated inconsistent correlation between weight-based drug dosing and metabolite level. A multi-center, cross-sectional retrospective study from Australia studied the impact of proactive therapeutic drug monitoring (TDM) on long-term outcomes in patients with IBD (Barnes et al, Dig Dis Sci, June 2022). The inclusion criteria were an established diagnosis of IBD; a minimum of 4 weeks of azathioprine or 6-mercaptopurine therapy prior to baseline metabolite measurement; and documented clinical assessment at baseline and again after 12 months. A total of 541 patients were included in the analysis (median age 40 years). At baseline measurement only 40% of the patients had thiopurine metabolite levels consistent with appropriate dosing, 27% was underdosed and 16% were identified as "shunters". Overall, 62% of the patients had a change in medication based on the thiopurine TDM. Repeat TDM was available for 259 patients and the proportion of patients with therapeutic 6-TGN level (235-450 pmol/108 RBC) were significantly higher in repeated measurements compared to baseline measurement (56% vs 39%; p<0.001). Interestingly, 9 out of 10 patients (89%) with TDM were able to continue thiopurine treatment without escalation to more expensive treatments or having surgery. Table 1 show the proportion of patients on different medical therapy at baseline and after 12 months. The proportion of patients with active disease was significantly lower at 12 months compared to baseline (p<0.001).

Table 1. *Proportion of patients on different medical therapy at baseline and 12 months after start of thiopurine therapeutic drug monitoring.*

	At baseline	After 12 months
Thiopurines only	42%	31%
Thiopurines + Allopurinol	3%	13%
Thiopurines + 5-ASA	40%	30%
Thiopurines + anti TNF	15%	21%
Other IBD medical therapy	1%	4%
Surgery	-	1%
Proportion of patients in clinical remission	37%	68%

COMMENTS

This study shows that a large proportion of patients treated with thiopurines do not have adequate doses and that a half of the patients on thiopurine TDM strategy augmented their treatment partly based on metabolite levels. In consistency with the paradigm of "treating to target" a more general approach of thiopurine TDM for patients with IBD could therefore be rationale in clinical practice.

Should thiopurines be discontinued when starting anti-TNF therapy for IBD?

THOMSEN SB, UNGARO RC, ALLIN KH, ELMAHDI R, POULSEN G, ANDERSSON M, COLOMBEL JF, JESS T. ALIMENT PHARMACOL THER. 2022 MAY;55(9):1128-1138.

There have been concerns regarding an increased risk of infection and malignancy with combination therapy with anti-TNF and thiopurines. Other studies have shown that thiopurines safely could be stopped in patients in remission. In a Danish register study, the effect on either continuing or stopping thiopurines when initiating anti-TNF treatment was investigated (Thomsen et al, Aliment Pharmacol Ther, May 2022). In the analysis 979 patients who discontinued thiopurine treatment was compared to 1651 who continued thiopurine treatment. They found that patients who discontinued thiopurines when starting anti-TNF therapy had an increased risk for new corticosteroid use (adjusted HR 1.27; 95% CI 1.10-1.13-1.44) and for needing IBD-related hospitalization (adjusted HR 1.14; 95% CI 1.00-1.31). Patients who continued thiopurines did not show an increased risk of overall cancer, although the risk of non-melanoma skin cancer was increased. However, the observation time was in median less than 2 years in both groups.

COMMENTS

This study support that thiopurines should be continued when starting anti-TNF therapy in regard to effect and adverse events from IBD.

Does the mental state effect gut inflammation in patients with IBD?

GOODYEAR BG, HEIDARI F, INGRAM RJM, CORTESE F, SHARIFI N, KAPLAN GG, MA C, PANACCIONE R, SHARKEY KA, SWAIN MG.INFLAMM BOWEL DIS. 2022 MAY 19:IZAC089.

LIANG C, CHEN P, TANG Y, ZHANG C, LEI N, LUO Y, DUAN S, ZHANG Y. FRONTIERS IN PSYCHIATRY. 2022 MAY 19;13:880058.

JEDEL S, BECK T, SWANSON G, HOOD MM, VOIGT RM, GORENZ A, JAKATE S, RAEISI S, HOBFOLL S, KESHAVARZIAN A. INFLAMM BOWEL DIS. 2022 JUN 4:IZAC036.

The last month there has been several studies published that investigate the role of mood in patients with IBD. For example, Goodyear et al performed a study using multimodal brain magnetic resonance imaging (MRI) to compare IBD patients (n=35) with healthy controls (n=32) (Goodyear et al, Inflamm Bowel Dis, May 2022). Interestingly, patients with IBD showed a significantly increased activity and functional connectivity in parts of the limbic system, basal ganglia and hypothalamus, areas that are involved in cognitive and emotional processing. Patients with IBS showed a significantly increased volume in amygdala and hypothalamus, and evidence of neurodegeneration in the putamen and pallidum. Furthermore, hippocampal activity was increased in patients with active disease. The volume of the thalamus was positively correlated with CRP levels and was increased in females experiencing pain.

Venlafaxine, a serotonin and norepinephrine reuptake inhibitor (SNRI), may play a role in immunoregulation, and scientists from China presents a randomized controlled trial comparing venlafaxine 150 mg with placebo (Liang et al, Frontiers in Psychiatry, May 2022) in patients with IBD with comorbidity with anxiety/depression. In addition to improvement in anxiety/depression and quality of life, venlafaxine also showed a significant reduction in Mayo score and CDAI score compared to patients receiving placebo after 6 months of treatment. Also, there was a significantly decrease in CRP, ESR and TNF alpha levels in patients treated with venlafaxine.

Finally, in a study from Chicago, USA, an intervention with mindfulness for 8 weeks showed to have beneficial effects on patients with ulcerative colitis (Jedel et al, Inflamm Bowel Dis, June 2022). The study showed that patients who received mindfulness ▶

intervention increased the state of mindfulness and mindfulness skills and decreased perceived stress and the stress response. The mindfulness intervention also decreased the number of flares and improved the quality of life in patients with ulcerative colitis. None of the patients in the mindfulness intervention group had a flare during the 12 months study in comparison to 5 out of 23 in the control group.

COMMENTS

All these three studies emphasized that brain-gut interactions play a role in the disease behavior of patients with IBD. In patients with IBD and comorbidity with anxiety/depression, venlafaxine could be used as adjuvant therapy.

Can artificial intelligence improve surveillance colonoscopy?

YAMAMOTO S, KINUGASA H, HAMADA K, TOMIYA M, TANIMOTO T, OHTO A, TODA A, TAKEI D, MATSUBARA M, SUZUKI S, INOUE K, TANAKA T, HIRAOKA S, OKADA H, KAWAHARA Y. J GASTROENTEROL HEPATOL. 2022 AUGUST;37(8):1610-1616.

Surveillance colonoscopy is recommended in patients with ulcerative colitis with long-standing colitis. However, the evaluation of suspected dysplasia during colonoscopy is challenging because of background chronic inflammation. Recently, image recognition using a conventional neural network system based on artificial intelligence (AI) has been used in endoscopy in clinical practice. In a pilot study from Japan, the researchers tested a conventional neural network system with the purpose to improve diagnostics of dysplasia at surveillance colonoscopy for ulcerative colitis (Yamamoto el al, J Gastrenterolol Hepatol, August 2022). The system was initially trained based om images with cancer lesions, lesions with high grade dysplasia, low grade dysplasia and normal lesions. The AI system was compared to endoscopists (experts and non-experts) based on images. AI was non-inferior to experts and non-experts colonoscopists in diagnostic accuracy (Table 1).

Table 1. *The sensitivity, specificity and diagnostic accuracy for finding cancer or high-grade dysplasia based on images.*

	Expert colonoscopists	Non-expert colonoscopists	Artificial intelligence
Sensitivity	60.5%	70.5%	72.5%
Specificity	88.0%	78.8%	82.9%
Diagnostic accuracy	77.8%	75.8%	79.0%

COMMENTS

The technology or AI in endoscopy is evolving rapidly, and this study support that AI may improve surveillance colonoscopy in IBD in the near future.

Mediterranean diet in IBD

TURPIN W, DONG M, SASSON G, RAYGOZA GARAY JA, ESPIN-GARCIA O, LEE SH, NEUSTAETER A, SMITH MI, LEIBOVITZH H, GUTTMAN DS, GOETHEL A, GRIFFITHS AM, HUYNH HQ, DIELEMAN LA, PANACCIONE R, STEINHART AH, SILVERBERG MS, AUMAIS G, JACOBSON K, MACK D, MURTHY SK, MARSHALL JK, BERNSTEIN CN, ABREU MT, MOAYYEDI P, PATERSON AD; CROHN'S AND COLITIS CANADA (CCC) GENETIC, ENVIRONMENTAL, MICROBIAL (GEM) PROJECT RESEARCH CONSORTIUM, XU W, CROITORU K.GASTROENTEROLOGY. 2022 SEPTEMBER;163(3):685-698.

In a large Canadian health survey (Genetic, Enviromental, Microbial project), 2289 first degree relatives to patients with Crohn's disease were recruited (Turpin et al, Gastroenterology, September 2022). Individuals in the study was characterized based on validated food frequency questionnaire reflecting their habitual diet the last year. In all individuals, stool was investigated for microbial composition and faecal calprotectin. A diet cluster resembling the Mediterranean diet was strongly associated with a more favorable microbial composition with an increased abundance of fibre degrading bacteria such as Ruminococcus and Faecalibacterium. Faecal calprotectin levels were lower in individuals using a Mediterranean-like diet.

COMMENTS

Mediterranean diet has preventive effect on cardiovascular disease and diabetes. This study also shows that Mediterranean diet may have positive effects on microbial composition and gut inflammation.

The fertility rate in men with IBD in Sweden

DRUVEFORS E, ANDERSSON RE, HAMMAR U, LANDERHOLM K, MYRELID P. ALIMENT PHARMACOL THER. 2022 JULY;56(2):292-300

Fertility is decreased in women with IBD but fertility in men with IBD have not been studied to the same extent. Using the Swedish National Patient Register (NPR) and the Swedish Multi-Generation Register (MGR) the fertility rate (the number of children a man has fathered) was studied in patients with IBD (Druvefors et al, Aliment Pharmacol Ther, July 2022). A total of 17,627 births were linked to men with IBD, which corresponded to slightly significantly lower mean achieved parity at the end of follow-up of 1.28 (SD 1.27) compared to matched individuals from the Swedish population (mean 1.35; SD 1.26). The achieved parity at the end of follow-up was lowest in patients with Crohn's disease (mean 1.25; SD 1.29). The proportion of men with no children was significantly higher for patients with ulcerative colitis (38.4% vs 36.5%; $p<0.001$), and IBD-unspecific (39.9% vs 37.6%, $p<0.001$), whereas no statistically significant difference was seen in patients with Crohn's disease (41.5% vs 40.4%; $p<0.055$). Inclusion of socioeconomic status and multivariable analysis did not change the hazard ratio for fertility. An increasing number of bowel resection did not change fertility in patients with ulcerative colitis or Crohn's disease and perianal disease had no clear effect on male fertility. The intensity of medical treatment in patients with Crohn's disease was associated with decrease fertility rates.

COMMENTS

The result of the study shows only a modest reduction in fertility in men with IBD. This information is important to actively present and is encouraging to male patients with IBD.

Ferring Läkemedel AB • Box 4041 • 203 11 Malmö • Sweden • +46 40 691 69 00
Ferring Lægemidler A/S • Amager Strandvej 405 • 2770 Kastrup • Denmark • +45 8816 8817
Ferring Lääkkeet Oy • Bertel Jungin aukio 5 • 02600 Espoo • Finland • +358 20 7401 440
Ferring Legemidler AS • Postboks 4445 Nydalen • 0403 Oslo • Norway • +47 22 02 08 80

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