Indications for Cesarean Section in Pregnant Women with Inflammatory Bowel Disease: Results from the PIANO Registry

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BACKGROUND: Women with inflammatory bowel disease (IBD) experience high rates of cesarean section (c-section) delivery. Elective c-section is recommended for active perianal disease and should be considered in patients with deep pouch and anal stenosis to prevent perianal complications and reduce disability. All IBD patients do not require elective c-sections for these indications, yet c-section rate remains high. We aimed to determine factors associated with c-section in women with IBD, including whether pharmacologic therapy was associated with mode of delivery.

METHODS: In a multi-center prospective cohort of pregnant women with IBD, we collected demographic information, IBD disease and treatment history (unexposed, biologic therapy, immunomodulator therapy, or combination therapy), and pregnancy and labor history. Data were collected using questionnaires every trimester of pregnancy and post-partum. We evaluated c-section rates by treatment class and analyzed factors associated with c-section in each treatment class.

RESULTS: There were 1,490 women in the cohort, with 1,431 live births. A total of 618 (41.5%) underwent c-section (Table 1). The most common indications for c-section were active IBD (33%), perianal IBD (19%), elective (14%), breech or abnormal position (12%), prolonged labor (10%), fetal distress (9%), pre-term delivery (9%), augmented labor failure (5%), and pre-ecampsia (5%). Among those who had a c-section, those with an elective indication were more likely to be on biologic therapy or combination biologic and immunomodulator therapy (P = 0.05, Table 2). Those with active or severe IBD who had a c-section were more likely to be on no therapy or immunomodulator monotherapy (P = 0.02). Women who had a c-section for perianal disease were less likely to be taking biologic therapy with or without combinations immunomodulator therapy (P ≤ 0.0001). There was no association between type of drug therapy and preterm birth as an indication for cesarean section (P = 0.53). In the overall population, women on combination therapy and biologic therapy had significantly increased adjusted odds of having a c-section (OR 1.7, 95% CI 1.3-2.5 and OR 1.3, 95% CI 1.0-1.8 respectively).

CONCLUSION: In pregnant women with IBD, the most common indication for c-section was active disease. Furthermore, women who underwent c-section for active disease were much more likely to be on no therapy, instead of competing on biologic therapy. We suggest that there is an urgent need for education of patients and providers on safety of vaginal delivery in healthy IBD patients, can reduce the rate of c-section in this population.

Morbidity Due to IBD and its Influence on Health-Related Quality of Life and Virtual Social Interaction Through Facebook

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BACKGROUND: Bowel disease (BD) is a chronic condition with a relapsing and remitting clinical course. As BD symptoms manifest unpredictably over time, the present study aimed to evaluate if and how associated morbidity affected Health-related Quality of Life (HRQoL) and social interaction through Facebook (FB) among patients with BD.

METHODS: The BD Morbidity Scale (BDS), a questionnaire developed for measuring BD-related morbidity, was distributed to 185 BD patients (IBD) outpatients from Botucatu Clinical Hospital (Botucatu group) and 185 patients with IBD who are followed at other institutions in Brazil (Online group). The online group completed the same questionnaires as the Botucatu group but did so through a web link made available on patient groups on FB. Patients were excluded if they did not use FB. Disease activity was measured using the Mayo Score for Ulcerative Colitis (UC), Crohn’s Disease Activity Index (CDAI) and Harvey-Bradshaw Simple Index for Crohn’s Disease (CD) among Botucatu and Online patients respectively. FB use was measured using the questionnaire Psycho-Social Aspects of Facebook Use (PSAFU), which comprises 5 domains: compensatory use, self-presentation, socialization, addiction and virtual identity. The Inflammatory Bowel Disease Questionnaire (IBDQ) was used to measure Health-related Quality of Life. Statistical analysis: association tests, P < 0.05 and Pearson correlations.

RESULTS: The Online group had more people with CD (P = 0.006) and their patients had longer duration of IBD in years (9.94 ± 8.98 vs 7.3 ± 6.81). Patients followed in the Botucatu reference center had a greater remission rate (P = 0.001 and P = 0.09, for UC and CD respectively) while the Online group had had more consultations (P < 0.0001), hospitalizations (P < 0.0001) and surgeries (P = 0.01) per year. The Online group used more biologic medications (P = 0.03). Botucatu patients had better IBDQ, in the following IBDQ domains: intestinal (P = 0.0003), systemic (P = 0.0002) and emotional (P < 0.0001). They also socialized less (P < 0.0001) on FB and presented with the lowest FB addiction rate (P < 0.0001), fewer anxious (P = 0.077) and depressive (P < 0.05) symptoms and a better body image (P = 0.02) although they had fewer patients treated with psychotherapy (P = 0.004). Considering the Online group only, patients with longer duration of IBD spent more time on self-presentation through social media (FB) (P = 0.05). Those with worse systemic IBDQ scores presented with more intense compensatory use of FB (P = 0.03). Worse emotional health was inversely associated with compensatory use of FB (P = 0.02) and addiction (P = 0.03). Among these patients, emotional burnout was related to FB use (P = 0.04). CD patients were younger at the time of diagnosis (P = 0.0003), used more biologic therapy (P < 0.0001) and had more hospitalizations (P = 0.0001) and previous surgeries (P < 0.0001). Their systemic HRQoL was negatively associated with compensatory use of FB (P = 0.0006) and the emotional aspect, with compensatory use (P = 0.008) and FB addiction (P = 0.03), while these correlations were not observed among UC Online patients.

CONCLUSION: Patients with longer duration of IBD had worse HRQoL, and interacted more through social media as disease related morbidity may affect their ability for in person social interaction. BD morbidity was inversely related to compensatory use and FB addiction among patients with longer duration of IBD. These patients also underwent consultations and medical interventions more frequently.
the 63 IBD patients, 29 (46%) had CD and 34 (54%) UC. The average age of patients with IBD was 35.6 ± 16.3 years with no significant difference between UC and CD patients. Most patients were male (60.3%). This male predominance was mainly present among patients with CD (21, 72.4%) compared to 17 (50%) males in the UC group. Of the 32 new cases of IBD, 17 (53.1%) had CD and 16 (48.1%) UC. The average age of newly diagnosed IBD patients was 38.4 ± 15.7 years. There was a statistically significant difference between the age at diagnosis in the CD group (37.4 ± 15.2 years) and the UC group (35.4 ± 16.7 years). The most common presenting symptom was bloody diarrhea (14, 42.4%) followed by abdominal discomfort/pain (10,30.3%) and then non-bloody diarrhea (5, 15.1%). Most CD patients presented with abdominal discomfort/pain (8, 47.1%) while most UC patients presented with bloody stools (9, 69.2%). Average CRP was 25.5 ± 7.5 mg/dL which was higher in CD patients (34.8 mg/dL) compared to UC patients (8.8 mg/dL). Similarly, average ESR was 22.9 ± 17.2 mm/hr, and it was higher in CD patients (28.8 mm/hr) compared to UC patients (14.1 mm/hr). Only 2 patients had a family history of IBD (6%). Only 3 patients (9.7%) had personal disease and 6 (19.4%) had extraintestinal manifestations (all of whom had arthritis).

CONCLUSION: The epidemiological trends and clinical characteristics of Lebanese patients with IBD are similar to Western populations. The next steps are to follow-up on incidence studies and determine if they mirror worldwide trends.

PO44
Designing Interventions to Elevate the Quality of IBD Care: A Systematic Review of Quality Improvement Initiatives

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BACKGROUND: Inflammatory bowel disease (IBD) care and outcomes are known to exhibit substantial geographic and inter-provider variability, suggesting quality gaps. We aimed to identify data on the design and implementation of interventions to narrow these gaps.

METHODS: A systematic review of Medline, Embase and Web of Science was performed to find reports of quality improvement (QI) interventions in IBD. The search focused on emergency room (ER) and hospital utilization and Crohn's and Colitis Foundation quality indicators on care processes, including pre-biologic testing, vaccinations, tobacco cessation, colorectal cancer (CRC) surveillance, and C. difficile infection (CDI) screening in flares. We included studies published before January 2009 and January 2020 and abstracts presented between October 2017 and January 2020 that reported on interventions in the United States and Canada for adult patients. Two authors reviewed all records and differences in inclusion were resolved by consensus.

RESULTS: The initial search identified 6257 records. 991 were duplicates and 4734 were excluded after title review. 14 new manuscripts and 11 abstracts were included after full review. Most studies used a pre/post design and reported on more than one quality indicator. Flu and pneumonia vaccination were the most studied indicators (17 references), followed by ER/hospital utilization, pre-biologic testing (hepatitis B and tuberculosis assessment) and tobacco cessation (10, 8 and 9 references, respectively). Electronic medical record (EMR)-based interventions were the most frequent, employed by 7 references, and included the use of templates and order sets. These interventions found mixed success among quality metrics but universally led to higher rates of reported vaccination. The creation of clinic protocols to evaluate and act upon patients’ vaccination history were also successful in improving vaccination rates, as were efforts to educate patients regarding vaccination. In contrast, efforts to educate physicians regarding quality IBD care led to improvements in rates of vaccination and pre-biologic testing in some cases but were not successful in improving other metrics. Utilizing support staff showed similar mixed results: the use of a scribe was linked to higher rates of vaccination, and a nursing-driven CDI testing protocol resulted in higher rates of appropriate CDI testing, but post-discharge phone calls from a pharmacist did not improve rates of 30-day readmission. Novel care models such as remote patient monitoring. Project Sonar, Qorus, and an IBD medical home, as well as the implementation of clinical care pathways, led to decreases in ER and hospital utilization but to a lesser extent. One study showed a three-point increase from the data in 2018 (6%).

CONCLUSION: The quality of IBD care can be improved with interventions that range from simple to complex. Successful interventions have employed EMR-based changes, such as templates and order sets, physicians and patient education, empowerment of support staff, and novel care models. These interventions are not universally effective, however, and prior experience should guide future QI efforts in IBD.

PO45
Effect of Etrasimod on Circulating Lymphocyte Subsets: Data From a Randomized Phase 1 Study in Inflammatory Bowel Disease

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BACKGROUND: Etrasimod, a selective sphingosine 1-phosphate (SIP) receptor 1,4,5, modulator that reduces peripheral lymphocytes and subsequently impedes their recruitment to sites of inflammation, is in development for chronic immune-mediated inflammatory diseases. Reduction in pro-inflammatory immune cells without causing broad immunosuppression is an important treatment goal in patients with these diseases. This study evaluated the effect of etrasimod on circulating lymphocyte subsets in healthy volunteers to improve understanding of its proposed mechanism of action.

METHODS: In this phase 1, single-blind (subject only) pharmacokinetic (PK) and pharmacodynamic study, 49 healthy Japanese and Caucasian men were randomized to receive once daily oral etrasimod 1 mg (n = 20), 2 mg (n = 20), or matching placebo (n = 9) from Days 1 to 7, followed by a 7-day washout and a single dose on Day 15. Absolute lymphocyte counts (ALC) were determined by complete blood count with differential. Immune cell subsets were evaluated by flow cytometry from isolated peripheral blood mononuclear cells (PBMCs) collected pre-dose on Days 1, 3, 5, 7, and 15. Change from baseline on 24 different immune cell subsets were evaluated using a mixed-effects model. Paired t-tests were computed to evaluate significant subtype modulations in etrasimod-treated groups vs placebo at Day 7.

RESULTS: Compared with placebo, etrasimod 1 and 2 mg dosed daily for 7 days resulted in similar dose dependent reductions in ALC in both ethnic groups, with total lymphocytes returning to at least 84% of baseline at Day 15. Compared with placebo, etrasimod induced reductions in mean percent change from baseline to Day 7 in total T cells, total CD4+ and CD8+ T cells, naive CD4+ and CD8+ T cells, central memory CD4+ and CD8+ T cells, effector memory CD4+ and CD8+ T cells, Th2 and Th17 cells, and total B cells. Etrasimod resulted in greater decreases in naive and central memory T cells than in effector memory T cells. Decreased immune cell subsets recovered to at least 70% of baseline on Day 15, after the 7-day washout period. No notable treatment effects were seen on monocytes, macrophages, or CD56dim NK cells. Changes in immune cell populations were similar between Japanese and Caucasian subjects. Etrasimod 1 and 2 mg once-daily dosing regimens were safe and generally well tolerated. No adverse events related to low lymphocyte values occurred.

CONCLUSION: Etrasimod affects ALC and immune cell subsets were consistent with its known mechanism of action and observations for other S1P receptor modulators. Little or no ethnic group differences in etrasimod effects on ALC and immune cell subsets were observed in this study. The effect of etrasimod on onset and offset of immune modulation is consistent with etrasimod PK, with a typical half-life of approximately 33 hours. The differential effects of etrasimod on immune cell subsets may allow for a reduction in inflammation while maintaining immune surveillance. The lymphocyte subset profile suggests that etrasimod reduces certain immune cells and behaves as a selective immunomodulator rather than as a broad immunosuppressive agent.

PO46
Though Biosimilar Infliximab Prescribing in Inflammatory Bowel Disease Has Increased, Branched Infliximab Continues to Be Prescribed More Often

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BACKGROUND: Prescribing of biosimilar infliximab in biologic-naive, inflammatory bowel disease patients, relative to the brand reference, has grown slightly over the past two years. The rate of physician acceptance of requests from pharmacies and insurance companies, to switch from the reference brand to the biosimilar infliximab, has increased at a similar rate. In a physician chart study conducted in June 2020, the majority of biologic-naive patients placed on infliximab were prescribed the reference brand despite the availability of two infliximab biosimilars. Additionally, physicians were not requested to switch the reference brand to a biosimilar in a majority of prescribing situations. A comparison study of these trends two years ago, is presented.

METHODS: An independent market analytics firm collaborated with US gastroenterologists (n = 218) to conduct a retrospective chart review of patients with inflammatory bowel disease (IBD) (n = 1,001), who were started on a biologic for the first time. Gastroenterologists submitted patient-level data via a HIPAA-compliant form which included both clinical and non-clinical data. The collaborating physicians also completed a brief survey about their practices and their opinions regarding IBD patient management. The data were collected and analyzed in June 2020. The data are then compared to a similar study with US gastroenterologists (n = 218) with a retrospective chart review of patients with inflammatory bowel disease (IBD) (n = 1,001) that was collected in 2018.

RESULTS: 26% of the patients starting on a biologic for the first time were initiated on infliximab. Of those, 73% were placed on the reference brand, while 27% were placed on a biosimilar. This represents a ten-point increase in biosimilar infliximab prescribing since the last assessment was conducted in 2018 (17%). However, the majority of infliximab prescribing is still for the reference brand. In 82% of the cases where the patient was placed on the reference brand, the physician was not contacted by a pharmacist or insurance company about using a biosimilar in place of the reference brand. This was a decrease of eight points since the last assessment in 2018 (90%). Physicians indicated that infliximab was still the preferred choice of treatment. In 52% of the cases they would have switched to a biosimilar, a nine-point increase from two years ago (43%). Rather than switch, in 39% of the request situations physicians indicated would have used to present the reference brand, a twelve-point decrease from two years ago (51%). Finally, in 9% of the request situations physicians would have chosen a non-infliximab alternative, vs switching to a biosimilar or pressing to use the reference brand, only a three-point increase from the data in 2018 (6%).

CONCLUSION: While prescribing of infliximab biosimilars has increased slightly over the past two years, use of the reference brand still occurs in the majority of patient substitution situations. Physicians’ receptivity to a requested switch to the biosimilar by a pharmacist or insurance company has increased slightly in the same timeframe.