Power Calculations in Randomised Controlled Trials of Inflammatory Bowel Disease

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BACKGROUND: Sample size estimation is a vitally important calculation to make when designing a trial. How many patients are needed to see a difference? This question is frequently the subject of heated debate in the scientific community. The sample size estimation is a key component of the study design and must be completed before the study begins.

METHODS: We investigated the sample size estimation for the treatment of IBD in patients of any age and interventions for either induction or maintenance of remission against placebo, which has been used in previous studies. The relevant data was extracted, and the studies were grouped according to the intervention used. We recalculated sample size and the achieved difference, as well as minimum sample sizes needed in the future.

RESULTS: A total of 105 trials were included. There was a large discrepancy between the estimated figure for the minimal clinically important difference for use in calculations and the actual differences seen. The minimum sample sizes to use in future trials were proposed based on the calculations made from actual observed clinical differences from previous studies.

CONCLUSION: A third of intervention studies in IBD within the last 25 years are underpowered, with large variations in the calculation of sample sizes. The resource containing sample size estimates constructed on the published evidence base is required for future researchers and key stakeholders within the IBD trial field.

Measuring Patient-Reported Outcomes in Crohn’s Disease Patients During the Outbreak of COVID-19

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BACKGROUND: There are no data regarding the application of Patient-Reported Outcome (PRO) measures under the COVID-19 pandemic. The aim of the present study was to use a specific PRO measurement for CD patients during the COVID-19 pandemic.

METHODS: We interviewed 67 consecutive CD patients during the COVID-19 quarantine. We measured PROs using an adapted questionnaire that consists of a structured questionnaire evaluating 2 major domains: “symptoms” and “impacts.” In the “symptoms” domain, 4 sub-domains were evaluated, namely: “gastrointestinal,” “pain and discomfort,” “nutritional-related” and “energy-related.” In the “impacts” domain, 6 sub-domains were evaluated: “emotional,” “daily performance,” “lifestyle and activities,” “social functioning” and “diary.”

RESULTS: A total of 67 patients were interviewed. Mean age was 43.0 ± 14.7 years, 58.2% of patients were male. Mean disease duration was 12.4 ± 9.1 years, a history of perianal disease was present in 49.3% of patients, and 41.8% had previous bowel resection. There were no statistical differences in any of the 4 symptoms subdomains (p = 0.51), “pain and discomfort” (p = 0.08), “nutritional-related” (p = 0.97), and “energy-related” (p = 0.70) when we compared active CD patients and patients in deep remission. There were no statistical differences in 4 of 6 subdomains (“daily performance” (p = 0.13), lifestyle and activities (p = 0.89), “social functioning” (p = 0.97), “dietary” (p = 0.34)). Two out of 6 “impacts” sub-domain were significantly reduced in patients with clinical activity compared to patients in deep remission [Emotional (p = 0.04) and additional QoL (p = 0.001)].

CONCLUSION: The application of PRO measures in IBD patients demonstrated a negative impact on the emotional aspects and QoL quality of life during COVID-19 outbreak.

Tofacitinib and Ileal Pouch Anal Anastomosis. A Single-Center Case Series

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BACKGROUND: Tofacitinib is an emerging off label option for patients with moderate to severe ulcerative colitis (UC). However, data about the postoperative complications after ileal pouch anal anastomosis (IPAA), and the long-term pouch function after using tofacitinib is scarce. This study aims to describe postoperative complications and pouch function for patients with UC who had prior exposure to tofacitinib preoperatively.

METHODS: After institutional review board approval, electronic medical records were reviewed for patients with UC treated with tofacitinib postoperatively. Demographics, anesthetic variables, postoperative complications, and long-term pouch function were evaluated.

RESULTS: A total of 13 patients were included. Of them, 10 (76.9%) were male, 1 (7.7%) current smokers, and 3 (23.1%) had prior exposure to tofacitinib. The median age at diagnosis was 23 years (IQR 21.5 – 34) and the median duration of UC was 10 years (IQR 4 – 17.5). All patients had previously failed tumour necrosis factor-alpha inhibitors and steroids while 11 (85%) patients failed aminosalicylate and 7 (54%) failed thiopurines. The most common dose used for tofacitinib prior to colectomy was 10 mg twice per day (86%) and most patients had three-stage operation 11 (85%). No 90-day postoperative Clavien Dindo class III or IV complications were reported, no intra-abdominal sepsis, no other infectious complications, and no mortality. At a median follow up of 4 months (IQR 3.2 – 10.3), 3 (23.1%) patients had pouchitis, of whom 1 had a prior history of PSC and liver transplantation. Only 1 out of the 3 patients who had pouchitis needed a permanent stoma, the other 2 were managed medically. One of these patients also had chronic fistulizing ileitis.

CONCLUSION: No major postoperative complications were reported after IPAA for patients who were treated with tofacitinib. From a surgical standpoint, tofacitinib was not associated with surgical complications in our small cohort of medically refractory UC patients. Pouch function was similar to expected in this patient population. Larger scale studies with longer follow up are needed to confirm these findings.
BACKGROUND: Crohn’s disease (CD) patients present characteristic abnormalities in the meso-entropic adipose tissue (MAT) near the affected intestinal area. The MAT is thickened and wraps around the bowel circumference. Recent evidence indicates that this tissue plays a role in storing memory immune cells and potentially supporting antigen-driven immune responses. Therefore, the potential of immune cells to identify the microRNA (miRNA) profile of CD patients is of interest, as a means of an RNA sequencing (RNAseq) analysis and to further perform a biological validation of the results comparing to controls (CTR).

METHODS: For this purpose, 25 patients with active ileocolic CD who underwent surgery were included in the study. The control group consisted of 15 patients operated on for other diseases, except inflammatory bowel diseases. The in silico analysis of the modulated miRNA was performed by Targetscan and the enrichment of the metabolic pathways through the DAVID platform. The biological validation of the transcripts was performed by RT-qPCR analysis. The data were analyzed using the nonparametric Mann-Whitney Test. Univariate and multivariate analysis were performed based on the Cox regression model for correlations between gene expressions and the disease recurrence after surgery. The level of significance was set at P < 0.05. The study was approved by the Research Ethics Committee.

RESULTS: RNAseq identified a significant increase in miR-650 expression in the MAT of the CD group compared to the CTR (P = 0.03; 95% CI: 0.03). Among the 227 downregulated genes, 25 were identified as miR-650 target genes of this enriched pathway. The biological validation by RT-qPCR confirmed significant increased miR-650 expression in the MAT of CD compared to the CTR (P = 0.05), besides decreased levels of GPT2 (P = 0.02) and ALDHHA1 (P = 0.005) target genes. Moreover, Cox regression analysis showed that the miR-650 levels in the MAT of CD patients strongly correlated with the post-operative disease recurrence in the first 36 postoperative months (Hazard Ratio = 6.85; Confidence Interval 95%; P = 0.006).

CONCLUSION: For this time, the modulation of miR-650 and its target genes (ALDH4A1 and GPT2) were validated in the MAT of CD patients. Indeed, the miR-650 levels correlated to a higher risk of postoperative disease recurrence. Although a larger multicenter prospective study is needed, these findings may constitute a potential tool to guide the clinical management after surgical resection.


REFERENCES

P063
Prophylaxis of Hepatitis B Reconviction and Inflammatory Bowel Disease: A case report
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BACKGROUND: The risk of opportunistic infections is increasing with the progressive use of immunosuppressants and biological therapy in IBD treatment. In this scenario, screening for hepatitis B virus (HBV) is important in order to prevent viral reconviction.

METHODS: CASE REPORT. A 48 year old female with longstanding ulcerative colitis (diagnosed in 2010) was submitted to total colectomy presented with ileovaginal fistula, a day with mucous in stool and blood, diffuse abdominal pain, tenesmus, and urgent evacuation. Laboratory tests showed leukocytosis without left shift, normal platelets and liver tests. Flexible sigmoidoscopy showed a severe disease activity (Mayo score 3) in the rectum and sigmoid. The patient was admitted to our hospital and received IV corticosteroids without response, and then azathioprine. The patient underwent laparotomy. Hydrazine and anti-HBs Ag were positive. In admission, HBV DNA was detected (225 IU/mL). Other labs were consistent with chronic hepatitis B (Anti-HBeAg positive, HBeAg negative, Anti-HBsAg positive). Abdominal ultrasonography and ultrasound were normal. Considering the serological profile and the use of high-dose corticosteroids, inﬂammatory, and anastomotic, Entrectin 0.5 mg/d was initiated.

RESULTS: HBV produces stable cccDNA mini-chromosomes in infected hepatocytes, that can be present even after the loss of the HBs Ag and seroconversion to anti-HBs. cccDNA serves as a matrix for reconviction even in patients with a remote history of hepatitis B. This fact explains the impossibility of HBV infection evaluation. Viral reconviction in chronic inactive patients is defined as a 2-log increase in HBV-DNA. The use of prophylaxis must be based on the patient’s epidemiological profile and the risk of drugs used and their potential for viral reactivation. Higher doses than 20 mg/d of prednisone for 4 weeks or more are considered of moderate risk but the use of immunosuppressants or biological therapy increase this risk (high risk). Antiaflurines must be ceased, not associated with viral reactivation, unlike what occurs with the sole use of immunflurines. Antimalarial prophylaxis should be done with nucleoside analogues (NA) with high potency (Entrectin, Trimethoprim Dicloxacil Fumarate or Tenofovir Alafenamide). Lamivudine and other NAs are not recommended because of the risk of selection of resistant strains, but it can be used if it is the only option. Prophylaxis should be maintained for 6–12 months after the suspension of the immunomodulator agent. Pre-emptive therapy with an antiviral can be performed in moderate risk patients with easy access to viral load dosage, transaminases and serology.

CONCLUSION: Screening for HBV infection should be a routine in IBD patients mainly at diagnosis, as HBV reactivation can occur in the context of immunosuppressive therapy. As this risk depends on host factors, virological factors, and type and degree of immunosuppression, prophylactic strategies must be individualized.

P064
Manometric Study and the Role of the Perianal Disease and the Clinical Activity in Anorectal Dysfunction in Crohn’s Disease
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BACKGROUND: There is still evidence that the pre-surgical approach before CD surgery is needed, these results can present with radiologic findings seen in Crohn’s disease including fistula formation stenosis, ulceration, and anastomosis. It behoves us to consider alternative diagnoses if the presentation is atypical for IBD or symptoms fail to respond as expected.

RESULTS: Of the 56 patients evaluated, 53.6% are male, with a mean age of 41.4 years (SD: 12.4). According to the Montreal Classification, most patients have non-penetrating/non-stenosing disease (61.5%). Perianal disease, was present in 44.2% of the patients. Most patients were in remission, according to the Harvey-Bradshaw Index. Among the functional complaints, the most common is fecal incontinence (38%), followed by a sensation of obstructed/incomplete evacuation (36%) and fecal urgency (29%). When patients with anorectal functional complaints (fistula incontinence, incomplete/obstructed evacuation, fecal urgency and tenesmus) were compared with patients without anorectal functional complaints, statistically significant differences were found in relation to perianal disease. On the other hand, a statistically significant difference was found when we compared the patients with any anorectal functional complaint (fistula incontinence, incomplete/obstructed evacuation, fecal urgency and tenesmus) with the patient without any complaints to relation to index activity of the disease and fecal consistency.

CONCLUSION: Our results suggest that functional complaints in patients with Crohn’s disease are more related to disease activity and fecal consistency, among other factors, than structural and functional anti-retro-perianal abnormality, including those caused by perianal involvement of the disease. Therefore, the control of the disease activity probably is critical for the management of this functional symptom.

P065
Clinical Aspects of Pediatric Inflammatory Bowel Disease – A Multicentric Study From Brazil
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