Attitudes towards antidepressants among people living with inflammatory bowel disease: An online Australia-wide survey

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KEYWORDS
Antidepressants; Attitudes; Inflammatory bowel disease; Psychotherapy

Abstract

\textbf{Background and aims:} Little research has been conducted on antidepressants (ADs) in inflammatory bowel disease (IBD) despite their widespread use and evidence that they may improve immunoregulatory activity. The present study aimed 1) To explore the use and type(s) of ADs currently prescribed to people living with IBD and to collect evidence with respect to any observed effect of ADs on the course of IBD, and 2) To explore experiences and opinions regarding the effect of ADs on IBD course and attitudes towards future trials with ADs.

\textbf{Methods:} A cross-sectional exploratory Australia-wide online survey was conducted. Numerical results of the survey were summarised using descriptive statistics and open-ended questions using a simple content analysis.

\textbf{Results:} Overall, 98 IBD respondents participated in the survey, 50% with Crohn's disease, and 79% females. Sixty five (66%) participants reported current and 46 (47%) reported past AD use. Of the current AD users, 51 (79%) reported that the symptoms ADs were prescribed for improved. Psychological well-being improved in 87% of participants. The majority of respondents observed no change in IBD activity while on ADs, however, 16 (25%) believed that ADs improved their IBD. Most (84%) respondents would recommend ADs to other people living with IBD, and 81% reported willingness to participate in clinical trials with ADs.

\textbf{Conclusions:} Future clinical trials on ADs are warranted and likely to be accepted by people living with IBD in need of mental health care; however, it is yet unknown whether ADs will have a specific impact on long-term IBD activity.

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Antidepressants in IBD

1. Introduction

IBD is a chronic relapsing condition with an unpredictable course and unclear aetiology. IBD has been associated with co-morbid mental health diagnoses,\(^1\)\(^2\)\(^3\) while stress and depression have been found to be linked with frequent disease flares.\(^5\)\(^6\) Despite this, the majority of IBD patients with symptoms of mental health disorders do not receive adequate mental health care.\(^7\)

Antidepressants (ADs) are commonly used to treat mental health symptoms secondary to a medical diagnosis but also to alleviate somatic symptoms.\(^8\) In functional gastrointestinal disorders, which share much symptomatology with IBD, antidepressants have been found helpful in managing bowel symptoms.\(^9\) In addition, studies on healthy human volunteers have demonstrated that antidepressants can improve immunoregulatory activity,\(^10\) however, very little research has been conducted on the effects of antidepressants when used in inflammatory bowel disease (IBD).

In an initial systematic review conducted by our group,\(^11\) the low quality of available studies made it impossible to determine whether there was evidence of antidepressant efficacy in IBD, despite some encouraging findings from non-controlled studies. A later review\(^12\) which summarised randomised controlled trials in animal models found a positive effect of antidepressants (i.e. desipramine and fluoxetine) on inflammation in models of gastrointestinal inflammation. In a subsequent interview study we reported that gastroenterologists commonly treat patients with IBD with antidepressants for pain, anxiety and/or depression, and insomnia.\(^13\) Gastroenterologists reported that antidepressants were particularly effective in reducing pain, gut irritability, and urgency of defecation. Furthermore, testifying to their widespread use, in a recent case note audit,\(^14\) nearly 30% of 287 included patients with IBD had used an antidepressant at some time in their life. While taking antidepressants, the majority of patients had inactive disease. The study was however retrospective in nature and could not answer the question of whether antidepressants directly improve IBD disease activity.

Finally, when patients' perspectives on the use of antidepressants and potential trials were examined in a qualitative study,\(^15\) all patients reported that antidepressants improved quality of life, with minimal side effects. Of the 15 interviewed patients currently on antidepressants, approximately 30% felt that the antidepressants had directly influenced their disease course, 60% had a generally positive attitude towards antidepressants, and 80% stated that they would be willing to participate in clinical trials. However, this latter study was conducted with only a small sample of local IBD patients, consistent with its qualitative methodology. Thus, this current study aimed: 1) To explore the use and type(s) of antidepressants currently prescribed; perceived outcome of antidepressant treatment where applicable and its relevance to IBD course; perspectives and experiences with the use of antidepressants as well as views on the interactions between antidepressant treatment and their disease course; respondents' acceptability of trials with antidepressants.

2. Materials and methods

2.1. Design

A cross-sectional exploratory online survey was conducted.

2.2. Participants

Participants were a non-clinical population recruited via print and on-line advertisement via the contact network of a national IBD patient advocacy and support group – Crohn’s and Colitis of Australia (CCA). They were invited to participate if they had a formal diagnosis of IBD and were currently or previously taking an antidepressant of any kind (since their diagnosis with IBD). Respondents were excluded from the survey if they were younger than 18 years old or had no access to Internet as the study was conducted exclusively online.

2.3. Procedure

The study was advertised through the CCA’s newsletter and website, and online advertisements via IBD Support Australia between March 2012 and April 2013. The link to the survey was included in the advertisement and interested respondents answered the survey directly through this link. SurveyMonkey\(^16\) was used as it allowed confidential access and facilitated data analysis. Study information was provided at the commencement of the survey. Respondents were also provided with the contact details of researchers in case any queries arose. Answering the questions implied informed consent.

2.4. Measurement

The survey (see Appendix 1) was anonymous.

2.5. Outcome measures

The survey outcome measures included: type, dosage of antidepressants prescribed; perceived outcome of antidepressant treatment where applicable and its relevance to IBD course; perspectives and experiences with the use of antidepressants as well as views on the interactions between antidepressant treatment and their disease course; respondents’ acceptability of trials with antidepressants.

2.6. Statistical analysis

The SurveyMonkey software facilitates data cleaning; however, despite this, data were first checked for accuracy by examining ranges. Numerical results of the survey were summarised using descriptive statistics, with means, standard deviations, median, inter-quartile ranges (IQR) and percentages presented. Open-ended questions were summarised using a simple content analysis where themes were identified and grouped together and resulting data later presented as frequencies and percentages. Sub-group differences were calculated with the chi-square test or the
Fisher’s test, with p value of less than .05 considered statistically significant.

2.7. Ethics approval

The study was approved by the Royal Adelaide Hospital Research Ethics Committee and the University of South Australia Human Research Ethics Committee in January 2012. Participants provided informed consent.

3. Results

Overall, 118 people accessed the survey. Of these, two did not give consent and another 18 provided consent but did not answer any question and thus these 20 respondents were removed from the analysis. The final sample was 98.

3.1. Demographics

The majority of participants were females, were married or in a de facto relationship, were in employment, full- or part-time, had completed at least secondary education, and had a median age of 36 years (IQR:28–44) (Table 1). The majority of respondents lived in Victoria or Queensland followed by New South Wales and South Australia (Fig. 1).

3.2. Health-related characteristics

Nearly 50% of participants had Crohn’s disease and lived with a formal IBD diagnosis for just over 9 years (Table 2). The average BMI was consistent with mild overweight and values ranged from 18 to 44. The majority (64/98) of respondents reported a co-morbid chronic condition and 63 (64%) indicated that this was a mental health condition while 16 (16%) listed another inflammatory condition such as asthma or arthritis. Over 56% of respondents reported very well controlled or mildly active IBD at the time of the survey. When asked about the biggest contributors to their perceived IBD activity the respondents indicated stress (72%), diet (51%), time of the day (14%), season of the year (10%), holidays (6%) and anxiety (3%). The most common current IBD symptom reported by the respondents was abdominal pain (over 70%) followed by diarrhoea (53%) and fatigue (45%) (Fig. 2). Males and females differed in the rates of reported fatigue, with females more commonly experiencing

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<th>Table 1 Respondents’ demographic characteristics.</th>
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<td>IBD respondents (n = 98)</td>
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<td>Marital status</td>
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<td>Age</td>
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<th>Table 2 Health-related characteristics.</th>
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<td>IBD respondents (n = 98)</td>
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<td>Other chronic illnessa</td>
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<td>Time with IBD symptoms In years</td>
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<td>Time since IBD diagnosis In years</td>
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<td>BMI</td>
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<td>Number of IBD specialists</td>
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<td>Time with a current specialist In years</td>
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<td>Number of IBD-related operations</td>
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<td>Number of IBD-related hospital admissions in the last 5 years</td>
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a Question unanswered by all 98 participants and thus results do not add up to 100%.
fatigue (39 (58%) vs. 4 (25%), p = .017). Surprisingly, more participants with well-controlled disease reported frequent bowel movements than those with active disease (p = .028).

3.3. Current IBD treatment

In terms of standard IBD treatment, 71% of participants either used 5ASA or immunomodulators (and 10% used both together), with only 12% using biological treatment such as infliximab or adalimumab. Nearly 40% of respondents reported taking pain killers for their IBD symptoms: 24 (24%) used paracetamol, 24 (24%) used codeine, 5 (5%) used oxycodone hydrochloride, 5 (5%) used ibuprofen, 3 (3%) used tramadol, and 2 (2%) used dextropropoxyphene. Fifty eight percent used alternative treatment such as vitamins, fish oil, probiotics and others (i.e. natural remedies, Chinese Medicine, Naturopathy, Acupuncture, Boswellia, L-Lysine). Overall, 37 (38%) used conventional drug therapy only, 29 (29%) used conventional plus alternative treatment, 8 (8%) used alternative treatment only, and 8 (8%) used no treatment at all for IBD.

3.4. Psychosocial aspect of IBD

Overall, 70 (71%) respondents reported that IBD had negatively affected their professional life, 71 (72%) reported that it had affected their private life, and 69 (69%) considered that it had affected their social life. Seventy (71%) respondents reported that IBD had interfered with their psychological well-being. No sex difference with respect to these variables was observed.

Of the 78 who answered the question “Have you noticed a relationship between your psychological well-being, stressful life events and disease course?” 64 (82%) believed it to be true. The respondents provided examples from their lives on stress making the disease worse, either at the time of a stressful event or shortly after. The majority of respondents perceived this relationship as bidirectional where stress causes the disease relapse or aggravates symptoms and the IBD symptoms aggravate the mental status.

When asked if they could identify a particularly stressful event in the two years preceding their IBD diagnosis, 57 (58.2%) respondents were able to identify such an event (e.g. death of a loved one, pregnancy, immigration, divorce or a relationship breakdown, sexual assault, bullying, to name the main ones).

3.5. Antidepressant use

Overall 65 (66%) participants reported current and 46 (47%) reported past antidepressant use.

3.5.1. Current antidepressant use

There were more females than males among the current antidepressant users (55 (83%) vs. 9 (56%), p = .038). Respondents reported taking an antidepressant for an average of four (SD = 3.9) years ranging from four weeks to 15 years. The most commonly used drug was reportedly sertraline followed by escitalopram and citalopram (Fig. 3). For those who provided comments, the main reasons for this treatment included depression alone (n = 25, 38%), anxiety and depression (n = 12, 18%), anxiety alone (n = 10, 15%), and postpartum depression (n = 7, 11%).

When asked whether the symptoms antidepressants were prescribed for had improved, 51 (79%) respondents said the treatment worked and the symptoms improved; 11 (17%) said the treatment had helped to a degree with some symptoms still present and two (3%) stated the treatment had not helped. Psychological well-being had improved in 87% (n = 55) of participants. The majority of respondents (39/58 – 67% – who answered this question) observed no change in disease activity while on antidepressants, while 16 (25%) reported that antidepressants had improved their IBD and 4 (7%) reported that they had worsened it. Despite these observations, the number of people reporting very well controlled and only mildly active IBD increased during antidepressant therapy from 46% at therapy initiation to
66% when ceasing them \((n = 28\) and \(n = 43\), respectively, \(\chi^2(1) = 6.29, p = .016\)) (Fig. 4).

Overall, 37 (57.8%) of the 64 respondents who answered this question reported antidepressant-related side effects, with the most commonly reported being weight gain \((n = 12)\), lethargy or drowsiness \((n = 9)\), decreased libido \((n = 4)\), dry mouth \((n = 4)\), insomnia \((n = 4)\) and many others experienced by individual respondents (e.g. increased appetite, vivid dreams, flu-like symptoms, vomiting, nausea, headache, dizziness).

Table 3 lists the respondents’ best and worst perceived aspects of antidepressant treatment. Their main advantages were restoring normality to life and improving coping, while their negative aspects were perceived reliance on them, difficulty coming off therapy, flattening of mood and associated stigma. Despite their disadvantages, the vast majority of the respondents \((51/61 = 84\%)\) would recommend antidepressants to other people living with IBD.

### 3.5.2. Past antidepressant use

Overall, 28 of the 46 past antidepressant users used antidepressants once only (one antidepressant course) and 18 respondents took antidepressants at least twice in their lifetime. The types of antidepressants used are presented in Fig. 3. Antidepressants were reportedly taken for an average of three years \((SD = 4)\), ranging from few weeks to 20 years, with a median of two years. The main reasons for past antidepressant use were similar to the indications for those on current AD therapy and included: depression alone \((n = 20, 46\%)\), anxiety and depression \((n = 9, 21\%)\), or anxiety alone \((n = 5, 12\%)\).

Table 3 Best and worst aspects of antidepressant treatment.

<table>
<thead>
<tr>
<th>Best thing about the antidepressant</th>
<th>Worst thing about the antidepressant</th>
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<tr>
<td>Settles anxiety and relaxes ((n = 12))</td>
<td>Long-term side effects, reliance on them and difficulty coming off ((n = 22))</td>
</tr>
<tr>
<td>Gives hope, makes one feel better about themselves ((n = 11))</td>
<td>Blocks my feelings, lowers motivation, reduces creativity ((n = 8))</td>
</tr>
<tr>
<td>It brought back normality to my life ((n = 10))</td>
<td>Stigma attached to its use ((n = 6))</td>
</tr>
<tr>
<td>I have better control of my feelings ((n = 10))</td>
<td>Weight gain ((n = 5))</td>
</tr>
<tr>
<td>Helps to cope with everyday life’s challenges ((n = 9))</td>
<td>Side effects in general ((n = 5))</td>
</tr>
<tr>
<td>Limited side effects ((n = 6))</td>
<td>Insomnia ((n = 4))</td>
</tr>
<tr>
<td>Helps to sleep well ((n = 3))</td>
<td>Dry mouth ((n = 4))</td>
</tr>
<tr>
<td>Improves relationships with others ((n = 2))</td>
<td>Low sex drive ((n = 3))</td>
</tr>
<tr>
<td>Tiredness ((n = 3))</td>
<td>Nausea, dizziness ((n = 3))</td>
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Figure 3 Current and past antidepressant use.

Figure 4 IBD activity and antidepressants.
When asked whether the symptom antidepressants were prescribed for had improved, 23 (56%) reported that symptoms had improved, 10 (24%) that they had improved to a degree, and eight (19%) that they had not improved. Psychological well-being reportedly had improved in 29 (71%) past antidepressant users. The majority of respondents observed no change in disease activity while on antidepressants (n = 27, 71%) while nine (24%) reported that antidepressants had improved their IBD, and two (5%) thought that antidepressants had worsened their IBD course. As per current antidepressant use, past antidepressant use was associated with improved disease activity over time (Fig. 4).

Only 25 (54%) past antidepressant users commented on side effects. Most commonly reported included lethargy and drowsiness (n = 6), low libido (n = 5), nausea and/or vomiting (n = 4) and anxiety (n = 4). Like the current antidepressant users, the majority (n = 21, 60%) of past users would recommend antidepressants to other people living with IBD.

3.5.3. Attitudes towards antidepressants (both current and past users)

Overall, 74 (75%) respondents elaborated on their attitude towards antidepressants. Antidepressants were largely accepted and found useful.

Themes identified in participant responses included: There is time and place for them (n = 21), I am ok with them, they work (n = 15), They saved my life, love them (n = 10), They are the necessary evil (n = 9), Didn’t want to take them but I would now recommend to others (n = 8), They help, but need to be accompanied by therapy/counselling (n = 6), They are a band aid for something much bigger, I don’t like them (n = 5), They are overprescribed (n = 4), I don’t tell other people due to stigma but they work (n = 3), They helped my colitis (n = 3), Not sure about them (n = 2).

3.5.4. Attitudes towards antidepressant trial (both current and past users)

When asked whether they would agree to take part in a clinical trial (if there was evidence for antidepressants to play a role in management of IBD), 60 (81.1%) responders who provided answer to this question reported willingness to participate in such a trial. No sex difference was noted. The reasons for participation included: I would do anything to feel better (n = 14), to help myself and others (n = 12), to progress understanding and control of IBD (n = 5), as they make a huge difference (n = 4), I am on them anyway (n = 2). The negative responses included: I don’t want to change the one I am on (n = 3), potential side-effects (n = 2), I live far from hospital (n = 2), I don’t want to interfere with my other IBD treatment (n = 1), problems getting off them (n = 1).

3.6. Psychotherapy use

Before their IBD was diagnosed, 33 (34%) participants had accessed some psychological services, while after their IBD diagnosis was made this number had increased to 56 (57%). Overall, users of psychological services (which mostly included cognitive–behavioural therapy (CBT)) reported satisfaction with this kind of help (n = 53, 54%), although some respondents had not found it useful (17, 17%). No sex difference in psychological services use was reported.

Overall, 50 (70%) of the respondents who tried psychotherapy reported that it had no effect on their IBD activity while 21 (30%) believed psychotherapy to have improved their IBD course.

4. Discussion

To our knowledge, this is the first survey on antidepressant use in IBD conducted to date in Australia or overseas. The main finding of the study is the overall high acceptance and positive experience of using antidepressants by these respondents, with a total of 87% of current antidepressant users reporting improved psychological well-being, 79% reporting that the symptom the antidepressant had been prescribed for improved, and 84% reporting willingness to recommend antidepressants to other people living with IBD.

This finding is important clinically since antidepressants are commonly used in IBD (with seventy-eight percent of gastroenterologists reporting treating IBD patients with antidepressants in one small but representative study13 and a lifetime use of antidepressants in IBD at around 30%14), albeit research on the role they may play in IBD management has only recently started.11–15 With a growing recognition of the brain–gut axis and the emerging interest in the importance of psycho–neuro-immunology,17 along with high rates of anxiety and depression, and limited access to psychological care worldwide, AD drugs are becoming the first line of treatment for mental health disorders in IBD. Following positive outcomes reported in studies with functional gut disorder populations,9 there is an additional hope that antidepressants will reduce pain and improve bowel symptoms and possibly offer a new pathway to reducing disease burden.

In the present study, the majority of respondents did not observe a specific benefit from antidepressants on their IBD disease activity, with just 25% reporting that antidepressants had improved the disease course. However, interestingly, when asked about how well controlled their IBD had been commencing antidepressants and at the present moment, the rate of good control of IBD increased from 46 to 66%, a trend which was also reflected in our previous case-note audit with 287 IBD patients,14 where the majority of patients taking antidepressants remained in remission or had only mild symptoms for the duration of this treatment. Similarly, the retrospective case-matched observational study by Goodhand et al.18 showed that antidepressants seem to reduce relapse rates, use of steroids, and endoscopies in the year after their introduction. Admittedly none of these studies have applied designs which enable examining causality and thus intervention studies are needed to confirm or refute the possibility that antidepressants modify the disease course in IBD. In the present study we asked participants about their willingness to participate in such trials and over 80% of the respondents expressed their interest in such studies providing reasons ranging from improving own health, to helping others and progressing understanding of IBD. This finding may mean that at least in the IBD subgroup with co-morbid mental health diagnoses, there is high interest in participating in trials with the use of antidepressants.
Further, and importantly, the group described in the present paper is unlikely to be representative of all people living with IBD. However, in IBD studies with general IBD populations rates of co-morbid depression have been reported to be around 30%, and this study participants are a likely representation of this subgroup of IBD sufferers. In particular, the majority of the study participants were prescribed antidepressants as they suffered from symptoms of anxiety and/or depression, and 57% indicated that they used psychological services after their IBD had been diagnosed. Approximately 70% reported that IBD had significantly affected their professional, private and social life and impacted on their psychological well-being. In addition, 82% reported their belief in a relationship between stress and disease course (or symptoms), with stressful events typically predating or being associated with flares. Furthermore, the most commonly reported IBD symptom was pain and 40% reported using pain killers, indicating this sample was a group with not particularly well managed symptoms. This raises a question of whether IBD sufferers with mental health symptoms are in fact people in whom the disease management is suboptimal and whether providing more adequate care would reduce both their mental and somatic symptoms. In the recent years, our group has initiated studies on providing the integrated model of care for IBD patients which have demonstrated that the model which is based on the biopsychosocial principles is likely to improve a broad spectrum of outcomes and reduce healthcare costs, with opiate use halved. Further studies on optimising usual care in IBD which would include recognition and management of mental health co-morbidities are warranted.

The limitations of the present study need to also be acknowledged. First of all, the survey relied on self-reported data and thus the results may be prone to bias. Similarly, data for past antidepressant use should be interpreted with caution as they may be prone to recall bias. In addition, participants for this survey were self-selected and recruited via the contact network of a national IBD patient advocacy group. These respondents are likely to be more aware of the role of psychological issues in IBD management and are possibly more open towards psychotherapy and/or antidepressants and thus this survey’s results may not be relevant to people who are not members of IBD patient advocacy groups or who do not typically participate in research studies. Further, as this was an online study its results may not be directly generalisable to a clinical population. However, the exclusive use of online data collection is both a strength and weakness to this study. Those people living with IBD who are computer literate are more likely to have disease related knowledge, knowledge of antidepressants and psychotherapy, and information about treatment options via internet access, and an individual’s lack of computer knowledge may or may not be related to the information and opinions an individual has about their illness. In addition, nearly 80% of participants were females meaning that the results may not be directly relevant to males. Finally, the study had some missing data particularly for open-ended questions and thus the total sample for a number of important questions was reduced. In such cases, percentages presented were of the total group who responded to a particular question.

5. Conclusion

In this study, antidepressants have been found to be accepted by IBD respondents with co-morbid mental health symptoms. Disease activity had improved in only 25% of antidepressant users however improvement in psychological well-being was reported by nearly 90% of participants. Future clinical trials on antidepressants are warranted and likely to be accepted by people living with IBD in need of mental health care, however, it is yet unknown whether antidepressants will have a significant impact on long-term disease activity.

Conflict of interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.crohns.2013.09.002.

References


