

Introduction:

Fatigue is highly prevalent in patients with IBD, yet effective treatments are lacking. Modafinil is a central nervous system stimulant, which can be used off-licence in depression. Modafinil improves fatigue by increasing available dopamine in the brain and is safe with long-term use. However, its role in IBD has not been studied.

Methods:

In our specialist bowel hospital, adults with IBD and severe fatigue (IBD Fatigue Assessment Scale [IBD-FAS] Score >10/20) were referred to a Consultant Psychiatrist. In the absence of any contraindications or cautions to its use, patients were offered modafinil. The dose offered was 100mg twice daily (8am and midday) and titrated up to 400mg a day if required. If there was poor response to 400mg/day, we offered augmentation with aripiprazole 2.5mg/day. Any prescribed antidepressants were continued alongside modafinil. Patients were advised that treatment may be required long-term to sustain benefit. Follow-up was at 3 months, at which time the IBD-FAS was repeated. Change from baseline IBD-FAS score was measured using a paired t-test. We also measured adverse events.

Results:

Of 44 patients offered modafinil, 36 (81.8%) agreed to start. Mean age was 35.8 (8.8) years. Overall, 26 patients (72.2%) had Crohn's disease, 9 (25.0%) had ulcerative colitis and 1 (2.8%) had unspecified IBD; 23 (63.9%) were currently treated with biologic therapy; 20 (55.6%) had been treated with multiple biologics and 20 (55.6%) had previous bowel resection. At baseline, 28 (77.8%) were receiving antidepressant treatment and 19 (52.8%) had treatment-resistant depression (non-response to 2 or more treatments).

In terms of transient side-effects, 2 patients (5.6%) reported self-limiting headache, 1 (2.8%) transient dizziness, 1 (2.8%) occasional palpitations and 1 (2.8%) loss of appetite. Three patients (8.3%) discontinued due to adverse effects (2 headache and 1 worsening depression), though 2 of these were unable to tolerate at least 3 psychotropic medications previously. Of the 33 patients who continued modafinil, 4 (12.1%) required only 100mg/day, 20 (60.6%) 200mg/day total and 8 (24.2%) required 300-400mg per day. Of the 33 who remained on treatment, 3 (9.1%) required augmentation with aripiprazole.

Following treatment, mean IBD-FAS score improved from 16.2 (2.0) at baseline to 9.5 (3.5) at follow-up (mean 41.4% reduction, paired t-test $p < 0.001$). Of the 36 patients originally treated, 23 (63.9%) were no longer in the severe fatigue range after treatment with modafinil.

Conclusions:

In this prospective service evaluation, modafinil was observed to improve fatigue by 41.4% overall, even in a cohort with predominantly refractory IBD and refractory depression. Our findings suggest that deficiency of brain dopamine may be a key pathway to IBD fatigue. Clinical trials of modafinil and other dopaminergic medications for IBD fatigue are warranted.