Acamprosate Improves Impulse Control Disorders in Parkinson's Disease

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ABSTRACT

Objective: To describe the effects of treatment with acamprosate on ICD in two patients with Parkinson s disease (PD), in whom reduction or discontinuation of dopamine agonist therapy did not result in improvement.

Background: Impulse control disorders (ICD) in PD are under-recognized. Many improve with reduction of PD medications, but at the expense of worsening parkinsonism, and some do not. Treatment for ICD is lacking. Acamprosate acts at glutamate receptors to treat craving for alcohol, which shares pathophysiologic similarities with ICD.

Design/Methods: Patients completed rating scales for compulsive gambling, binge eating, compulsive computer use, compulsive shopping, sweet craving, compulsive sexual behavior and punding. Patients were treated with acamprosate 333mg, 2 tablets tid for one month and repeated questionnaires without changing PD medications.

Results: A 72 year-old male with PD for 10 years, treated with rotigotine and levodopa, had a one-year history of punding behaviors, increased sexuality, and more urges to gamble that did not change with discontinuation or re-introduction of rotigotine. Following treatment with acamprosate, punding improved by 30%, compulsive sexuality by 47%, craving for sweets by 32%, and compulsive urges about gambling normalized. A 46 year-old female newly diagnosed with PD was started on ropinirole, and developed binge eating, sweet craving, and compulsive shopping within 3 months. Shopping improved after changing ropinirole to levodopa, but binge eating persisted. After acamprosate, binge eating improved by 55% and sweet craving by 11%, accompanied by an 11-lb. weight loss. Acamprosate was well-tolerated and PD symptoms did not worsen.

Conclusions/Relevance: ICD can be problematic for patients with PD and may not always resolve with discontinuation of dopamine agonists. Treatment with acamprosate can improve ICD behaviors without the need for reduction in dopaminergic medications. A larger, open-label treatment protocol of acamprosate in ICD is underway at our center, with 8 patients enrolled.

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BACKGROUND

Impulse control disorders (ICD) are increasingly recognized amongst patients with Parkinson's disease (PD), and are often associated with use of dopamine agonist (DA) medications. ICD include:

- Punding
- Pathologic gambling
- Shopping
- Computer/internet use
- Hypersexuality
- Binge Eating
- Craving for sweets
- Hedonistic homeostatic dysregulation

No definitive treatment for ICDs exists. Case reports in PD patients have suggested efficacy of psychotropic medications, but most ICDs improve with reduction in or discontinuation of the DA, or other dopaminergic medication. This may occur at the expense of worsening parkinsonian symptoms, or incur the need for initiating or increasing levodopa therapy.

Acamprosate (Campral®, Forest Laboratories, Inc.) is a medication approved for the maintenance of abstinence from alcohol in patients with alcohol dependence who have achieved sobriety. It has been shown to reduce the craving for alcohol, which may share pathophysiologic mechanisms with ICD and craving for sweets in PD.

Here we seek to describe the effects of treatment with acamprosate on ICD in patients with Parkinson s disease.

METHODS

- Patients experiencing at least one ICD completed questionnaires regarding various behaviors. A baseline score was calculated by averaging these scores.
- Questionnaires included the following:
  1) South Oaks Gambling Screen[1] (SOGS)
  2) YBOCS-Shopping Version[2] (YBOCS-SV)
  3) YBOCS-Computer Use Version (derived from YBOCS-SV)
  4) Sexual Compulsivity Scale[3] (SCS)
  5) YBOCS-Binge Eating[4] (YBOCS-BE)
  6) Sweet Craving Questionnaire (derived from the Alchohol Craving Questionnaire[5])
- Patients who scored within the abnormal range for a particular scale were treated in an open-label fashion with acamprosate 333mg, 2 tablets p.o. t.i.d. for one month.
- Patients returned at the end of one month to complete the questionnaires while on treatment with acamprosate. Pre- and post-treatment scales were compared.
- PD medications were not changed during treatment with acamprosate.

RESULTS

Patient 1

- 72 year-old male with PD for 10 years, treated with rotigotine and levodopa.
- In the previous 1 year, he had developed punding behaviors (cleaning/tidying up, sorting and filing papers, repairing and dismantling household tools), increased demands for sex, impulsive shopping (tools and gadgets despite lack of need), and increased urges to gamble.
- No subjective change in these behaviors on or off rotigotine.
- At baseline, he had elevated scores on SCS, CQ, and Punding.
- Treatment with acamprosate was associated with reduction in time spent on punding behaviors and decreased irritability associated with punding, decreased demands for sex, and less craving for sweets.

Patient 2

- 46 year-old female newly diagnosed with PD and treated with ropinirole.
- Developed excessive eating (mostly sweet foods), craving for sweets, and compulsive shopping within 3 months.
- Shopping improved after changing ropinirole to levodopa, but binge eating and sweet craving persisted.
- At baseline, she had elevated scores on YBOCS-SV and CQ.
- Treatment with acamprosate was associated with better mental control over eating and sweet craving, and an 11-lb. weight loss.

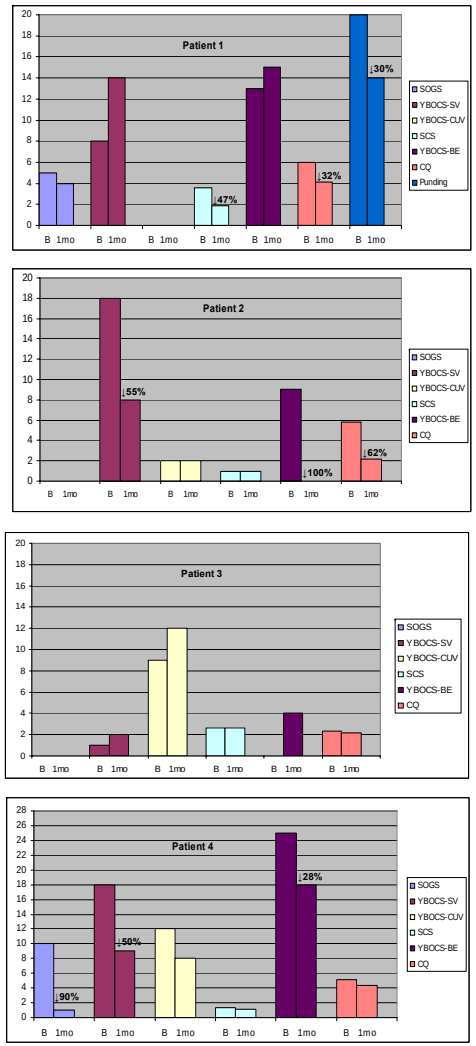
Patient 3

- 58 year-old male with PD for 6 years, treated with pramipexole.
- Since developing PD, he developed increased sexual thoughts and desires that were straining his marriage.
- At baseline, he had an elevated SCS score.
- No subjective changes noted with acamprosate.

Patient 4

- 68 year-old male with PD for 2 years, treated with pramipexole.
- In the last year, he reported the insidious onset of increased desires to go gambling, increased desire for sweets, and eating past feelings of satiety, associated with a 33-lb. weight gain.
- At baseline, he had elevated scores on SOGS, YBOCS-SV, and YBOCS-BE.
- Treatment with acamprosate was associated with feelings of better control over gambling and eating, but no weight loss.

RESULTS - continued



Adverse effects:

Only Patient 2 experienced side effects attributable to acamprosate during the treatment period. She developed explosive diarrhea that improved significantly by changing the timings of her concomitant medications. Acamprosate dosage and timings were not changed. Diarrhea is known side effect of acamprosate.

CONCLUSIONS

ICD has been likened to drug craving and addiction, which in turn is thought to be influenced by glutamate and dopamine levels in the nucleus accumbens.

- The NAcc and other limibic areas are enriched with D2 and D3 receptors[6], a fact which may underlie the pathophysiology of ICD in patients exposed to dopamine agonists.

Acamprosate has a complex mechanism of action that includes partial agonism at the NMDA receptor at low concentrations and antagonism at high concentrations.

- This "bi-phasic" effect may "normalize" glutamatergic transmission in the brain areas responsible for alcohol craving[7].

In this study, 4 patients meeting criteria for ICD according to validated, self-administered scales were treated with acamprosate in an open-label manner.

- 3 of 4 patients reported subjective reduction in their abnormal behaviors while treated with acamprosate for one month.
- Objective data from rating scales can quantify the degree of change in ICD.
- Improvement in ICD was achieved without changing dopaminergic therapy in these patients.
- 1 patient experienced side effects while taking acamprosate, but this did not limit treatment with this medication.

This study is limited by the open-label design and short duration of follow-up, but these preliminary results support the suspected pathophysiology of ICD in patients with PD.

- The possibility of other factors contributing to changes in behavior cannot be excluded.
- Longer follow-up with these and other patients will be needed to determine if acamprosate is a viable treatment option for ICD.

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