Available online at www.sciencedirect.com
SCIENCE DIRECT
Progress in Neuro-Psychopharmacology & Biological Psychiatry 28 (2004) 1195–1199
Progress In Neuro-Psychopharmacology & Biological Psychiatry
www.elsevier.com/locate/pnpbp

Case report

Nicotine treatment of obsessive–compulsive disorder

Stefan Lundberg[a], Arvid Carlsson[b], Per Norfeldt[a], Maria L. Carlsson[b,c,*]

[a]*Psychiatric Clinic, Kungälvs Sjukhus, Kungälv, Sweden*
[b]*Carlsson Research, Göteborg, Sweden*
[c]*Institute of Clinical Neuroscience, Section of Experimental Neuroscience, Neuropsychiatric Research Unit, Göteborg University, Göteborg, Sweden*

Accepted 29 June 2004
Available online 25 August 2004

Abstract

Following initial observations of marked effects of nicotine self-medication in a patient with obsessive–compulsive disorder (OCD), another four OCD patients were treated with nicotine for eight weeks in an open label fashion. Patients fulfilling DSM-IV criteria for OCD and with initial Yale-Brown Obsessive–Compulsive Scale (YBOCS) score>15 were included in the study. The patients were scored with YBOCS, Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), NIMH Global Obsessive–Compulsive Scale (NIMH) and Global Assessment of Functioning (GAF). Four of five patients receiving nicotine treatment displayed a favourable response with reductions in YBOCS scores. For these four patients, the nicotine chewing gum enabled a more adequate behaviour in stressful, OCD-eliciting, situations. We feel that these results are encouraging enough to warrant a larger, controlled study on nicotine treatment of OCD.

Keywords: Chewing gum; Nicotine; Obsessive–compulsive disorder; YBOCS

1. Introduction

Following initial observations of marked effects of nicotine self-medication in a patient with obsessive–compulsive disorder (OCD; Carlsson and Carlsson, 2000), the authors decided to test nicotine treatment during 8 weeks in another four OCD patients in an open label fashion. Below follows a description of the effects of nicotine in each of the five patients.

2. Materials and methods

All patients fulfilled DSM-IV criteria (Diagnostic and Statistical Manual of Mental Disorders, 1994) for OCD, with initial Yale-Brown Obsessive–Compulsive Scale (YBOCS) score>15. Exclusion criteria were: Tourette's syndrome, attention deficit hyperactivity disorder, severe depression, psychosis, severe somatic disease, pregnancy, smoking, snuff-taking or any other form of nicotine consumption. The patients were scored with YBOCS (Goodman et al., 1989), Beck Depression Inventory (BDI; Beck et al., 1961), Beck Anxiety Inventory (BAI; Beck et al., 1988), NIMH Global Obsessive-Compulsive Scale (NIMH; Insel et al., 1983) and Global Assessment of Functioning (GAF; Jones et al., 1995). BDI and BAI symptoms were rated by the patient, the other ratings were made by a psychologist (SL).

The present study was approved by the Göteborg Ethical Committee. Written consent was obtained by the participants following information about the study.

3. Results

3.1. Case 1 (pilot case)

The pilot case is a female patient, aged 40, with an OCD history of 17 years. She describes herself as being somewhat

Abbreviations: BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; CBT, Cognitive behavioural therapy; GAF, Global Assessment of Functioning; OCD, Obsessive–compulsive disorder; SSRI, Selective serotonin reuptake inhibitor; YBOCS, Yale-Brown Obsessive–Compulsive Scale.

* Corresponding author. Institute of Clinical Neuroscience, Section of Experimental Neuroscience, Neuropsychiatric Research Unit, Guldhedsgatan 19, SE-413 46, Göteborg, Sweden. Tel.: +46 31 73 693 96 22.
E-mail address: maria.carlsson@psychiat.gu.se (M.L. Carlsson).

0278-5846/$ - see front matter © 2004 Elsevier Inc. All rights reserved.
doi:10.1016/j.pnpbp.2004.06.014

anxious as a child but extroverted and with many friends. Academically she did well, both at school and at the subsequent university training. Her OCD symptoms began at the time she was pursuing her university studies and consisted initially of milder checking compulsions (stove, doors) which did not to any greater extent interfere with daily life. Over the years, however, these checking compulsions became increasingly time consuming and she also developed contamination fears and fear of driving a car (due to fear of running over someone). She also had considerable problems initiating and terminating activities, especially those involving household chores (cleaning, washing clothes and dishes). She also suffered from a rapid traffic of distressing thoughts and images, especially at night. Five years ago, she received selective serotonin reuptake inhibitor (SSRI) treatment and completed cognitive behavioural therapy (CBT) to which she responded well, though not completely. At the time she initiated self-medication with nicotine, she had been off SSRI treatment for more than a year. The decision to cease taking SSRI was her own, based on side effects she found disturbing, such as moderate dulling of focus, intellectual sharpness and motivation. For this pilot case, we only have scores from YBOCS.

The intensity of the symptoms in this patient was highest during the morning hours and late at night. The score (comprising items 1–5, obsessions, and items 6–10, compulsions) on YBOCS before nicotine treatment, was 11 on both the obsessions and the compulsions scales, i.e., a total score of 22. Initially, this patient took a 2-mg nicotine chewing gum twice a day, one at about 9.30 am and the other at about 3.30 pm. A few weeks later in the course of treatment, she sometimes added a third 2 mg gum at about 7 pm. During the months to follow, she increased the dose gradually to 8–10 nicotine chewing gums per day since she noticed this permitted a higher work and stress load and increased performance and efficiency in all domains. YBOCS score after 8 weeks of nicotine treatment was reduced to 6 on both the obsessions and the compulsions scales, i.e., a total score of 12. After 18 months of nicotine treatment, the score was 5 on both the obsessions and the compulsions scales, i.e., a total score of 10. The patient reports a great satisfaction with her higher degree of functionality as well as with the greatly reduced traffic of disagreeable thoughts and images, as a result of the nicotine treatment. When she compares SSRI treatment to nicotine, she has a clear preference for the latter. One reason for this is that while she experienced a dulling effect of SSRI on intellectual capacity, she experiences the opposite with nicotine, which increases mental acuity, thereby enabling a more rational behaviour.

Cases 2–5 received nicotine treatment for 8 weeks. To minimise the risk for side effects, nicotine was administered transdermally the first 3 weeks, 5 mg/16 h the 1st week and 10 mg/16 h the 2nd and 3rd weeks. Weeks 4–8, the patients were treated with nicotine chewing gum, in average, 2 chewing gums of 2 mg per day. The patients were evaluated with YBOCS, BDI, BAI, NIMH and GAF 1 week before the nicotine treatment started, and thereafter at 1, 3, 8, 10 and 15 weeks. They had all previously completed a cognitive behavioural therapy (CBT) program. A condition for entering the study was that the patient agreed to cease the nicotine treatment after 8 weeks and refrain from taking nicotine for at least 8 weeks. This would give the patients time to reflect over the effects of the nicotine treatment and avoid dependence in a situation where no benefits of nicotine were experienced.

3.2. Case 2

Case 2 is a 30-year-old woman with a 5-year OCD history, but with milder OCD symptoms dating back to adolescence. She describes herself as being an active but anxious child. In school, she did well both academically and socially. The impression she gives is of a warm, intelligent and responsible person with a high power of endurance. Her OCD was markedly aggravated following a miscarriage 5 years ago and was focused on fear of chemicals, which she handled at work in an oil refinery. Thereafter, the symptoms abated somewhat during a period but were again accentuated in connection with another pregnancy. Marital problems ensued, eventually resulting in divorce.

The obsessions of this patient also include fear of contamination with micro-organisms, fear of harming others and of not taking necessary preventive measures. Her compulsions include various checking rituals (groceries, doors, windows, stove). At the time she was enrolled in the present nicotine study, she had just started a training program to become a swimming instructor as part of her rehabilitation. She has not received SSRI or clomipramine treatment, since she has declined them.

Table 1 shows that YBOCS and especially BAI decreased during the 8-week nicotine treatment period for this patient, whereas GAF increased; the improvement remained after nicotine had been withdrawn. The average daily nicotine chewing gum consumption was 1.7 gums/day. The patient feels she benefited from the nicotine chewing gums and wishes to continue the treatment. She feels that without the nicotine gum, it had hardly been possible for her to get off to and participate in the swimming instructor lessons.

3.3. Case 3

Case 3 is a 26-year-old man with an OCD history of 8 years. He had a happy childhood with a stable family situation and many friends, and he did well in school. He has the typical personality features associated with OCD: A low degree of aggression, a strong dislike for violence, and high moral standards. He enjoys sports like running and badminton, but not more aggressive sports.

A few days after graduating from senior high school, he experienced his first OCD attacks, where fear of hurting

Table 1
Clinical ratings for cases 2–5

	Before	1 week	3 weeks	8 weeks	10 weeks	15 weeks
	I	II	III	IV	V	VI
Case 2						
YBOCS	17	17	16	14.5	13.5	14
Obsessions	9.5	9.5	9	8	7	8
Compulsions	7.5	7.5	7	6.5	6.5	6
BDI	16	16	7	15	14	11
BAI	21	13	10	13	10	6
NIMH	5	5	4	4	4	4
GAF	60	60	65	70	70	70
Case 3						
YBOCS	17	17	15.5	13	13	10.5
Obsessions	10	10	9.5	7.5	7.5	6.5
Compulsions	7	7	6	5.5	5.5	4
BDI	8	4	7	5	2	3
BAI	16	10	12	15	12	13
NIMH	7	7	7	6	6	5
GAF	65	65	65	70	70	75
Case 4						
YBOCS	16.5	21.5	21.5	16	16	23
Obsessions	8.5	10.5	10.5	8.5	8.5	10.5
Compulsions	8	11	11	7.5	7.5	12.5
BDI	12	14	13	11	10	18
BAI	10	9	8	8	8	7
NIMH	6	8	8	6–7	6–7	9
GAF	75	65	65	70	70	60
Case 5						
YBOCS	27	–	27	18.5	22	23.5
Obsessions	13.5	–	13.5	10	12	13
Compulsions	13.5	–	13.5	8.5	10	10.5
BDI	12	–	10	9	16	24
BAI	6	–	20	5	9	13
NIMH	9	–	9	7	8	9
GAF	55	–	55	60	58	55

other people, especially children, was the predominant symptom. For instance, while out taking walks, he was afraid of accidentally pushing a child into the roadway, and when driving a car, he was afraid he might run over someone without noticing. His obsessions compelled him to scan the papers and phone all hospitals in the city by the end of the day to make sure he had not hurt anyone. In parallel, he also developed contamination fears and he engaged in extensive moral ruminations.

At the time of his first admission to a psychologist (SL) 2 years ago, this young man was severely disabled by his OCD to the extent that he could hardly leave his home. He had by then finished his university training as a journalist but was unable to continue working at the newspaper where he was employed, since it became increasingly difficult to leave home for fear he might hurt someone out in the streets.

Subsequently, following SSRI treatment and CBT, the patient was gradually able to resume work, on a freelance basis, as well as driving.

When entering the present study, this patient was receiving medication with sertraline, 125 mg/day.

Table 1 shows improvement on YBOCS during the 8-week nicotine treatment for this patient; the improvement remained also after nicotine had been discontinued. He reported that the nicotine chewing gum helped him in stressful situations. His average consumption was 1.1 gums/day (some days no gum, other days up to three gums).

3.4. Case 4

Case 4 is a 25-year-old man with a 10-year history of OCD. He has had contacts with child psychiatrists since the age of 8. As a young child his predominant problem was that he could not stand to be separated from his parents, who had to accompany him wherever he went. His OCD symptoms became prominent when he was 15 and at that time he also started to suffer from depressive episodes. In spite of this, he did extremely well academically, graduating from senior high school with top scores. At the university, he has pursued a technical training with very good results, in addition to holding a job at the side to support himself.

Socially, on the other hand, he has been very isolated from an early age, not being able to interact with peers due to his severe OCD. Initially, his symptoms consisted of checking compulsions and hand washing, but today obsessions and mental rituals predominate. He has received medications since the age of 15, initially clomipramine, which was later replaced by paroxetine. He has never had a girlfriend.

The impression he gives is of a very likeable, responsible and intelligent young man, burdened however by very high demands on himself and an array of guilt-driven intricate moral rules and restrictions which result in abstaining from anything that can be regarded as enjoyable, such as going to the movies or eating an ice-cream. He also suffers from a high degree of anxiety-driven indecisiveness, ranging from not being able to decide which groceries to buy to spending half an hour in the morning not being able to decide whether to put down the right or the left foot when getting out of bed. Three years back, he received treatment with CBT which considerably decreased his OCD symptoms and increased the quality of life, enabling various social activities, but his disease still has a waxing and waning course with a high degree of disability during bad periods, which usually coincide with increased external stress load, e.g., examinations.

When entering the present study, this patient was receiving medication with paroxetine, 40 mg/day.

As can be seen in Table 1, this patient did not show improvement on any of the rating scales. He does not want to continue the nicotine treatment. His average nicotine consumption was 2.8 gums/day.

The deterioration seen in this patient at weeks 1, 3 and 15 is in all likelihood related to enhanced stress load, as the worsening of symptoms coincided with periods of examinations (this patient was doing his last semester of a technical training at the university).

3.5. Case 5

Case 5 is a 37-year-old man with an OCD history dating back to adolescence. He suffers from both obsessions and compulsions but the compulsions consist mainly of mental neutralising rituals. He engages extensively in moral ruminations, brooding about right and wrong and rehashing mistakes made previously in life.

This patient was unemployed during 8 months, 2002–2003. In February 2003, he started working for an OCD patient organisation as part of his rehabilitation.

He has previously received medication with the tricyclic antidepressant clomipramine, the SSRIs sertraline and paroxetine, the monoamine oxidase inhibitor moclobemide and the neuroleptics flupentixol and pimozide.

He is not on any medication at present apart from hypnotics as needed. He does not present with symptoms of depression and states, when questioned about it, that he has no desire to put an end to his life. He adds, on the other hand, that he would take his life if it was easy to do so.

This patient does not experience any therapeutic effect of the transdermal nicotine treatment, but at the consultation at week 8, following 5 weeks with the nicotine chewing gum, he reports that the nicotine has helped him. When struck by anxiety, he feels calmer after taking a chewing gum. This is also evident from the YBOCS score, which has decreased from 27 to 18.5 (Table 1). Also, his ability to concentrate is increased by the nicotine treatment. At this time point, he works half-time for the OCD patient organisation and he enjoys this. For this patient, there was no evaluation at 1 week.

His average nicotine consumption was 1.65 gums/day.

At the consultation at week 10, i.e., 2 weeks after ceasing taking nicotine, he reports that he is negatively affected by the discontinuation. It worries him that he cannot use nicotine when he wants to, and because of this, he avoids stressful situations. His mental condition has deteriorated to some extent since the last visit (Table 1). At the last visit at week 15, he reports that the past weeks have been difficult, he has felt more tense and says that he looks forward to being able to resume the nicotine treatment because of the calming effect it has on him.

4. Discussion

Transmitters that have been discussed in relation to the pathophysiology of OCD include serotonin and glutamate (Carlsson, 2001). There is also some evidence, mostly circumstantial, that central cholinergic systems might be involved: Firstly, the orbitofrontal cortex, repeatedly shown to be hyperactive in PET/SPECT studies, receives a substantial cholinergic innervation. Secondly, the amygdala, which is central for conditioned fear and aversion processes (Davis et al., 1994, Zald et al., 1998), and has reciprocal glutamatergic connections with the orbitofrontal cortex, is one of the most densely cholinergically innervated structures in the brain (Mesulam et al., 1986). Thirdly, the growth hormone response in OCD subjects following challenge with the acetylcholinesterase inhibitor pyridostigmine has been found to be markedly increased compared to healthy controls (Lucey et al., 1993). Fourthly, clomipramine, which is generally regarded superior to SSRI in the treatment of OCD, has anticholinergic properties.

The present report describes five patients who have received nicotine treatment for 8 weeks or more. Cases 1–3 and 5 displayed clear-cut reductions in YBOCS scores, and for these four patients, the nicotine chewing gum enabled a more adequate behaviour in stressful, OCD-eliciting, situations. Since these patients had previously received CBT, it is conceivable that the cognition enhancing properties of nicotine contributed to the beneficial behavioural effects by facilitating the application of what had previously been learned in CBT. Also, the mood elevating effects of nicotine might have contributed to the beneficial effects. Interestingly, the three patients (cases 1,

2 and 5) who were most positive to the nicotine treatment were not on concomitant treatment with SSRI or other serotonin reinforcing agents; thus, there is possibly an interaction between nicotine and SSRI that is not beneficial. In this context, it should be recalled that nicotine influences the turnover of a number of transmitters, including serotonin (Gäddnäs et al., 2002); it remains to be elucidated to what extent a possible therapeutic effect of nicotine in OCD can be ascribed secondary effects on, e.g., monoamine turnover.

For Case 1, where we have the longest follow-up period (24 months), there is a pronounced and stable improvement. Of the four patients who completed the 8-week trial, the two patients who were not on concomitant SSRI treatment (cases 2 and 5) expressed most satisfaction with Nicorette and wished to continue the nicotine treatment. The third patient found nicotine helpful in certain stressful situations, whereas the fourth patient felt he did not benefit from the nicotine treatment.

The observation that the apparently beneficial effect in cases 2 and 3 remained after the withdrawal of nicotine has a parallel in observations on patients with Tourette's disorder: Dursun et al. (1994) found that administration of two 10-mg transdermal nicotine patches during 2 consecutive days reduced tics up to 4 weeks. The mental condition of case 5, however, deteriorated rapidly following discontinuation of the nicotine treatment.

Side effects were noted by cases 1, 2 and 5, i.e., by the patients who were most in favour of the nicotine treatment. The side effects were mild and transient and consisted mainly of nausea and shortness of breath. With respect to the potential risk of more serious adverse effects following nicotine treatment, this issue has been addressed in a meta-analysis study of 5501 patients receiving transdermal nicotine. The incidence of adverse cardiovascular outcomes was not elevated in the groups receiving transdermal nicotine compared to the controls, consisting of 3752 placebo recipients (Greenland et al., 1998).

5. Conclusion

We feel that these results are encouraging enough to warrant a larger, controlled study, which should perhaps preferably be conducted in patients that are not receiving concomitant SSRI treatment.

Acknowledgements

The present study was supported by grants from the Swedish Medical Research Council (9067) and Stiftelsen Psykiatriska Forskningsfonden, Göteborg, Sweden.

References

Beck, A.T., Ward, C.H., Mendelson, M., Mock, J., Erbaugh, J., 1961. An inventory for measuring depression. Arch. Gen. Psychiatry 4, 561–571.

Beck, A.T., Epstein, N., Brown, G., Steer, R.A., 1988. An inventory for measuring clinical anxiety: psychometric properties. J. Consult. Clin. Psychol. 56, 893–897.

Carlsson, M.L., 2001. On the role of prefrontal cortex glutamate for the antithetical phenomenology of obsessive compulsive disorder and attention deficit hyperactivity disorder. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 25, 5–26.

Carlsson, M.L., Carlsson A., 2000. Use of a nicotine receptor agonist in the treatment of obsessive compulsive disorder. Europe (EPC), Patent No. 1 126 846; New Zealand, Patent No. 511 226.

Davis, M., Rainnie, D., Cassell, M., 1994. Neurotransmission in the rat amygdala related to fear and anxiety. TINS 17, 208–214.

Diagnostic and Statistical Manual of Mental Disorders. Ed. 4. Rev, 1994. Washington, DC: American Psychiatric Association, Washington.

Dursun, S.M., Reveley, M.A., Bird, R., Stirton, F., 1994. Longlasting improvement of Tourette's syndrome with transdermal nicotine. Lancet 344, 1577.

Gäddnäs, H., Pietilä, K., Alila-Johansson, A., Ahtee, L., 2002. Pineal melatonin and brain transmitter monoamines in CBA mice during chronic oral nicotine administration. Brain Res. 957, 76–83.

Goodman, W.K., Price, L.H., Rasmussen, S.A., Mazure, C., Fleischmann, R.L., Hill, C.L., Heninger, G.R., Charney, D.S., 1989. The Yale-Brown Obsessive Compulsive Scale. I. Development, use, and reliability. Arch. Gen. Psychiatry 46, 1006–1011.

Greenland, S., Satterfield, M.H., Lanes, S.F., 1998. A meta-analysis to assess the incidence of adverse effects associated with the transdermal nicotine patch. Drug Safety 18, 297–308.

Insel, T.R., Murphy, D.L., Cohen, R.M., Alterman, I., Kilts, C., Linnoila, M., 1983. Obsessive-compulsive disorder. A double-blind trial of clomipramine and clorgyline. Arch. Gen. Psychiatry 40, 605–612.

Jones, S.H., Thornicroft, G., Coffey, M., Dunn, G., 1995. A brief mental health outcome scale. Reliability and validity of Global Assessment of Functioning (GAF). Br. J. Psychiatry 166, 654–659.

Lucey, J.V., Butcher, G., Clare, A.W., Dinan, T.G., 1993. Elevated growth hormone responses to pyridostigmine in obsessive-compulsive disorder: evidence of cholinergic supersensitivity. Am. J. Psychiatry 150, 961–962.

Mesulam, M.-M., Volicer, L., Marquis, J.K., Mufson, E.J., Green, R.C., 1986. Systematic regional differences in the cholinergic innervation of the primate cerebral cortex: distribution of enzyme activities and some behavioral implications. Ann. Neurol. 19, 144–151.

Zald, D.H., Lee, J.T., Fluege, L.K.W., Pardo, J.V., 1998. Aversive gustatory stimulation activates limbic circuits in humans. Brain 121, 1143–1154.