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Changes in compulsion and anxiety symptoms with nicotine transdermal patches in non-smoking obsessive-compulsive disorder patients

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ABSTRACT

Objective. Some of the obsessive-compulsive disorder (OCD) symptoms can be elicited in rats by the administration of quinpirole (D2/D3 dopaminergic agonist). Nicotine administration blocked some aspect of checking behavior in that model. The main goal of this study was to determine if the clinical manifestations of OCD non smoking patients change with the administration of transdermal nicotine patches. ***Material and methods.*** Eleven patients were studied (6 female and 5 males), average age 29.7 ± 5.5 years. All of them were OCD according to DSM-IV criteria. Clinical scorings were done with Yale-Brown Obsessive Compulsive Scale (Y-BOCS), Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI). Nicotine (17.5 mg/day) or placebo transdermal patches were randomly administered for five continuous days. ***Results.*** Nicotine administration reduced the total Y-BOCS and the compulsive score of that scale, but did not reduce obsessions. Also anxiety was reduced as was shown by the BAI scores, when patients were on nicotine patches, no changes were observed in BDI. ***Conclusions.*** The present results replicated the animal findings about reduction in compulsive behavior after nicotine administration. Also suggest that nicotine depending on the dysfunction of the different neurotransmitter systems may produce different behavior or cognitive effects, also that even nicotine showed some beneficial effect in OCD patients, the low rate of nicotine smoking in this type of patients, may show other mechanisms than may protect to smoke in some psychiatric patients.

La administración de parches de nicotina transdérmicos en pacientes con trastorno obsesivo-compulsivo produce cambios en las compulsiones y síntomas de ansiedad

RESUMEN

Objetivos. *Se ha observado que algunos de los síntomas del trastorno obsesivo-compulsivo (TOC) pueden ser provocados en la rata con la administración de quinpirol (agonista de los receptores dopaminérgicos D2/D3). La administración de nicotina en ese modelo animal reduce la conducta de revisar. El principal objeto del presente trabajo fue el determinar si las manifestaciones clínicas de pacientes con TOC no fumadores se modificaban cuando se administró nicotina transdérmica por cinco días.* ***Material y métodos.*** *Se estudiaron a 11 enfermos (seis mujeres y cinco hombres) de 29.7 ± 5.5 años. Todos ellos fueron diagnosticados como pacientes con TOC de acuerdo con una entrevista estructurada basada en el DSM-IV. Además se efectuó la aplicación de la escala de Yale-Brown, para TOC, la cual detecta la severidad del trastorno. Se aplicaron también el Inventario de Beck para Depresión (IBD) y el Inventario de Beck para Ansiedad (IBA). Estos instrumentos clinimétricos se aplicaron en las condiciones previas a la aplicación de los parches y el último día de la administración de cada una de las maniobras con los parches. Se utilizaron parches de nicotina de 17.5 mg (Nicotinell CIBA-Geigy) o placebo de manera aleatorizada, en un diseño de cuadrados latinos por cinco días continuos, con una semana de intervalo entre una maniobra y otra.* ***Resultados.*** *La administración de nicotina redujo la calificación total de la escala de Yale-Brown para TOC, y la subescala de compulsiones, pero no la de obsesiones. También se observó una reducción en el componente ansioso, como se evidenció por una reducción en la IBA, sin cambios en las calificaciones para depresión.* ***Conclusiones.*** *Los resultados del presente estudio reproducen los datos reportados en el modelo animal de TOC. Además sugieren que la nicotina*

puede modificar la conducta dependiendo del estado de alteraciones preexistentes en el sistema nervioso al ser administrada. Es importante observar, que si bien existe un mecanismo de alivio de la sintomatología del TOC con nicotina, la frecuencia de utilización de nicotina en pacientes con TOC está por debajo de lo esperado, lo cual puede indicar otros mecanismos de protección contra el consumo de nicotina en esta población de enfermos psiquiátricos.

Key words. Nicotine. Obsessive-compulsive disorder. Dopamine.

Palabras clave. *Nicotina. Trastorno obsesivo-compulsivo. Dopamina.*

INTRODUCTION

Obsessive-compulsive disorder (OCD), is one of the leading causes of mental disorders,[1-3] OCD is characterized by recurrent and persistent thoughts experienced as intrusive and inappropriate and that cause marked anxiety or distress and/or repetitive behavior or mental acts that drive person to perform in response to an obsession, but which are recognized as excessive or unreasonable.[3] Several lines of evidence from preclinical and clinical investigation implicate dopamine (DA) in the mediation of certain types of repetitive behavior like Tourette's syndrome (TS), one of the syndromes of the OCD spectrum.[4] Some OCD patients improve with a DA antagonist[5,6] also, neuropathological and neuroimaging studies have demonstrated differences in DA innervations in the basal ganglia between patients and matched controls, as well in orbitofrontal-subcortical circuits.[7,8]

Rats treated with quinpirole (QNP) (D2/D3 receptor agonist), developed locomotor sensitization[9,10] and exhibited compulsive checking of specific areas, a profile that may represent an animal model of OCD.[11] Because nicotine blocks various behaviors induced by ontogenic administration of QNP administration, Tizabi, et al,[12] proposed that nicotine could attenuate QNB-induced compulsive checking. They administered saline or QNP for 14 to 16 injection, and on the last two injections rats were treated randomly with nicotine or saline, and the effect on checking behavior was examined. Nicotine administration attenuated compulsive checking behavior.

The main goal of the present study was to determine if the clinical manifestations of OCD in non smoking patients changes after transdermal nicotine administration as in the animal model of OCD.

METHODS

Eleven patients from the psychiatry outpatient clinic were studied. All of them were drug free for more than a month. After the protocol was fully explained a signed consent form was obtained. Complete medical and neurological examination, general laboratory screening and Structured Interview for DSM-IV (SCID)[13] were performed. Demographics and axis I and III diagnoses are showed in table 1. No medical conditions that could worsen with nicotine administration were allowed. All patients were non-smokers, according to the following definition: no nicotine consumption one year before entering the study, and no more than three cigarettes per year in the lifetime.

Table 1. Demographyc variables y OCD patients.

Patient	Age (years)	Diagnosis of OCD (age)	Gender	Axis I	Axis III
MC	24	16	M	OCD	None
IA	28	21	M	OCD	None
GH	39	35	F	OCD - Panic attacks	Diabetes mellitus type 2
ME	30	20	F	OCD - Simple phobia	None
SC	28	18	M	OCD	Atopic dermatitis
AER	29	26	F	OCD	None
NV	37	27	F	OCD	None
VR	37	30	M	OCD	None
GA	27	12	F	OCD	None
RD	22	14	M	OCD	None
MCA	26	13	F	OCD	None

Clinical examination and scorings with clinical scales were done one day before patches administration, on day five (the last day of patch administration). One week later the procedure was repeated, either with placebo or nicotine patches. Scoring was done with Yale-Brown Obsessive Compulsive Scale (Y-BOCS), Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI). A side effect scale was also obtained.

Nicotine 17.5 mg (Nicotinell - CIBA Geigy) or placebo patches, were randomly administered for five continuous days. Patients attended the clinic daily for removal of the patch and placement of new one on the other arm. On the fifth day a clinical evaluation was performed. The statistical analysis was done with one way ANOVA for repeated measures and Student "t" test for repeated measures as a "post-hoc" test.

RESULTS

Eleven OCD patients were studied (6 female and 5 males), average age 29.7 ± 5.5 years. Average age when they started with OCD manifestation was 21.09 ± 7.5 years old. None of the eleven patients smoked more than three cigarettes/year or had a history of nicotine ingestion/consumption or other type of nicotine administration in their life times; all were drug free for at least one month or more before entering to study.

Nicotine administration reduced the total Y-BOCS score (Figure 1) (ANOVA: $F = 6.86$, $p < 0.005$), due to a decrease in the compulsion score (ANOVA: $F = 6.0$, $p < 0.03$) but not in the obsessive one (ANOVA: $F = 2.8$, $p = 0.084$) (Figure 1).

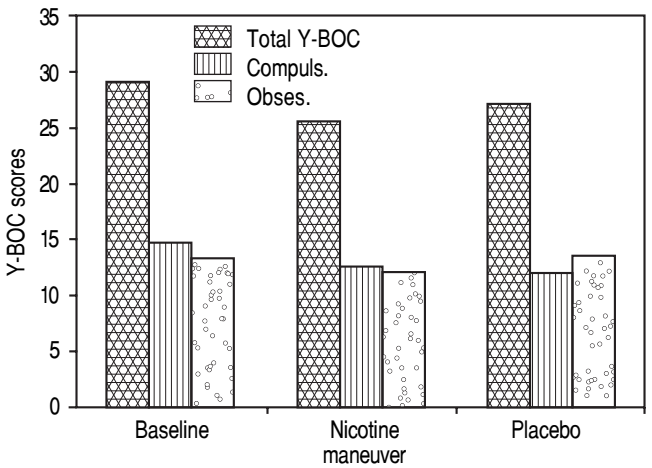

Figure 1. *A reduction of total Y-BOCS and compulsion were observed when patients received nicotine patches.*

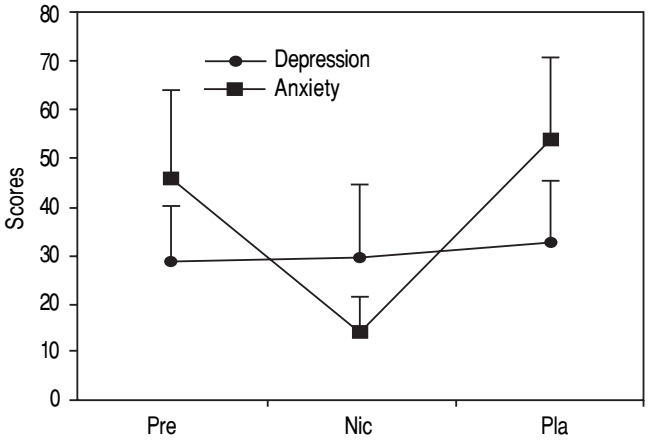

Figure 2. *Beck's Anxiety and Depression scores, showed that a major change was observed in anxiety when the patients were on nicotine patches but not in the depression scores.*

Nine (81.8%) of 11 patients showed a reduction in compulsion scores, but in only two the reduction was 30% or greater from baseline. BAI scores decreased significantly (ANOVA: $F = 12.35$, $p < 0.001$) during the nicotine administration, but no changes were observed in BDI (Figure 2). Anxiety reduction was observed in all patients, and seven (63.6%) had a reduction of 50% or more in their BAI baseline scores. Subjective reports included: two patients reported mild side effects (trembling, nausea and headache), and no benefit; six patients reported mainly a decrease in their anxiety and also of their different compulsions, without side effects, three patients reported neither a change in symptoms nor any side effects.

DISCUSSION

The main findings of this study were a reduction in both the compulsive component and anxiety and almost no side effects in non-smoking patients treated with transdermal nicotine patches.

Nicotine use has been related to some neuropsychiatric disorders. There is a strong association between smoking and both schizophrenia and depression[14-16] and even in Tourette's syndrome;[17] however, the incidence of smoking in OCD patients has been reported to be lower, than in the general population (14% *vs.* 25% respectively).[18]

Glassman, et al[19] were able to analyze the Epidemiologic Catchment Area (ECA) data from St. Louis and found no significant increase in the prevalence of smoking among OCD patients. The findings in the

present study counter positive-effect theory of smoking, which proposes smoking as a self medication.

Nicotine presynaptic receptors may be involved in the release of different neurotransmitter systems when nicotine is administered,[20] such as serotonin, dopamine, acetylcholine and norepinephrine.[21] All are involved in OCD biochemistry, thus difficult the identification of the mechanisms by which nicotine improves some aspects of OCD. Our findings are in agreement with previous observations that nicotine attenuates compulsive checking in rats after QNP administration.[12] The possibility that some nicotine agonist may be useful, alone or in combination with Selective Serotonin Reuptake Inhibitors (SSRI) or other types of double reuptake inhibitor (i.e., venlafaxine or duloxetine) remains as an unanswered question.

The reduction in anxiety with nicotine administration, as measured by BAI, may contribute in some way to the reduction in compulsion. Hughes, et al,[22] surveyed 277 outpatients of which 46% had anxiety disorders, 47 major depression and 45% personality disorder and smoked. Are these figures evidencing an indirect anxyolitic effect of nicotine? The placebo or nicotine patch maneuver showed no significant changes in BDI. Albeit none of the patients had an axis I diagnosis of major depression. Salin-Pascual, et al,[23] and Salin-Pascual and Drucker-Colin,[14] showed that nicotine reduced in major depressed patients the depression scorings. On the other hand normal volunteers in a previous study[24] did not show significant changes in mood, thus suggest the possibility that nicotine, depending on the dysfunction or imbalance of different neurotransmitter systems, may produce different behavioral and cognitive effects. One of the main problems of the present study was the reduced number of subjects, it needs to be replicated with higher number of patients. The answer to this incognito would greatly further promote the development of preventive smoking and nicotine addiction prevention programs.

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