

# A Case Series of Nicotine Nasal Spray in the Treatment of Tobacco Dependence Among Patients With Schizophrenia

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**A retrospective case series of 12 smokers with schizophrenia or schizoaffective disorder who had not successfully quit smoking with previous treatments for tobacco dependence were treated with nicotine nasal spray. All but one patient (92 percent) tolerated the nasal spray well, and nine (75 percent) used it at maximal doses for prolonged periods. After treatment five patients (42 percent) were abstinent from smoking for more than 90 days, and four patients (33 percent) substantially reduced the amount that they smoked. Ten patients (83 percent) used the spray in combination with other medications, and all received psychosocial support. Nicotine nasal spray was found to be well tolerated. (*Psychiatric Services* 55:1064–1066, 2004)**

Individuals with schizophrenia smoke at alarmingly high rates, are less likely to try to quit smoking, and are only half as successful at quitting as other smokers (1). Previous trials of nicotine replacement for smokers with schizophrenia have used only the

nicotine patch, even though the unique neurobiological abnormalities among individuals with schizophrenia suggest that treatments that provide rapid, pulsatile delivery of nicotine, which closely mimics the effects of smoking, may be more effective.

Abnormal electrophysiological (P50) measures among patients with schizophrenia, which are normalized with doses of nicotine, are linked to the alpha-7 nicotinic cholinergic receptor (nAChR). Constant nicotine dosing may result in the desensitization of nicotinic receptors. The alpha-7 nAChR, which is among the most rapidly desensitizing nicotinic receptor, requires high and intermittent doses of nicotine to be most effectively activated (2,3). Strategies of intermittent nicotine delivery remain unstudied among patients with schizophrenia, and the obvious hazards of tobacco smoke point to a need for a safer nicotine delivery device. This research supports an intermittent dose administration strategy, such as can be delivered by nicotine nasal spray, as possibly being more effective for modification of cigarette craving among patients with schizophrenia.

Nicotine nasal spray has unique features, such as a rapid onset of action, intermittent dosing, and more immediate relief from cravings. In clinical trials nasal spray has been found to be particularly effective among heavily dependent smokers (4), most likely because of its rapid nicotine delivery. Smokers with schizophrenia may be more willing to use nicotine nasal spray because of this property.

## Case series

We report on a retrospective case series of 12 smokers with schizophrenia or schizoaffective disorder who were treated from July 2001 to October 2003 with nicotine nasal spray in our clinical practice at the tobacco dependence program at the University of Medicine and Dentistry of New Jersey. The institutional review board at the University of Medicine and Dentistry of New Jersey approved the study. As shown in Table 1, the group consisted of six men and six women and had a mean±SD age of 45±7.5 years. The group had smoked for a mean of 25.9±11.1 years. The mean Fagerstrom score for nicotine dependence was 7.8±1.25, which is indicative of moderate to severe dependence. The smokers smoked a mean of 26.7±10.1 cigarettes per day and had a mean expired level of carbon monoxide (CO) of 22.3±8 parts per million when they began treatment with the nasal spray.

All 12 patients had attempted to quit during the past year by using methods that included medications and psychosocial treatment; all had trials of high-dose nicotine replacement, either with combination treatment or a 42 mg patch. Before beginning treatment with the nasal spray, patients were instructed to fill the nasal spray prescription so that they could receive their first dose during an individual counseling appointment. Patients were encouraged to set a quit date and use the spray at least once an hour, up to 40 doses daily (one dose equals one spray per nostril). Patients were given reassurance

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**Table 1**

Characteristics of 12 patients with schizophrenia in a case series of nicotine nasal spray in the treatment of tobacco dependence

Current number of cigarettes smoked per day	Number of days of continuous abstinence	Age	Sex	Baseline number of cigarettes per day	Fagerstrom score <sup>a</sup>	Years smoked	Expired levels of carbon monoxide (CO) before starting nicotine nasal spray (parts per million)	Expired levels of CO at last visit, while on nicotine nasal spray (parts per million)	Medication	Approximate number of sprays of nicotine nasal spray consumed per day	Length of time on nasal spray (days)
0	145	44	Female	40	9	25	29	1	Nicotine inhaler and patch and clozapine	40	171 <sup>b</sup>
0	376	39	Male	50	9	7	40	2	Bupropion SR, nicotine inhaler, and risperidone	40	548 <sup>b</sup>
0	101	44	Male	20	8	23	25	2	Nicotine inhaler and patch and clozapine	40	422 <sup>b</sup>
0	101	45	Female	20	8	26	13	2	Bupropion SR, nicotine inhaler, and fluphenazine	30	422 <sup>b</sup>
0	116	57	Male	25	9	39	16	6	Nicotine inhaler and risperidone	30	14
0–20	0	44	Female	35	8	30	18	2	Bupropion SR, nicotine inhaler, and risperidone	40	175 <sup>b</sup>
3	0	48	Male	20	7	40	20	2	Nicotine gum and inhaler, clozapine, and quetiapine	40	157 <sup>b</sup>
0–20	0	52	Female	20	5	37	22	6	Risperidone	30	99
20	0	51	Male	20	—	28	12	15	Nortriptyline and fluphenazine	40	811
0–20	0	33	Male	20	9	12	24	4	Nicotine patch and inhaler and olanzapine	20, intermittently	203 <sup>b</sup>
30	0	32	Female	30	7	11	19	23	Risperidone	15	2
20	0	50	Female	20	7	33	30	55	Nicotine inhaler and olanzapine	8	37

<sup>a</sup> As measured by the Fagerstrom Test for Nicotine Dependence; scores range from 0 to 10, with higher scores indicating greater severity of nicotine dependence.

<sup>b</sup> Denotes clients who are still using the nicotine nasal spray

and education about the product's side effects and were told that they would likely remit with continued use.

All 12 patients received monthly individual psychosocial treatment for to-

bacco dependence, and eight (67 percent) attended group treatment for smokers with mental illness, although attendance was highly variable. Combination pharmacotherapy was common in this group. The nasal spray was

viewed as the primary form of nicotine replacement.

Five patients (42 percent) were abstinent for more than 90 days (mean of 168±118 days). Self-report of abstinence was verified by measuring ex-

pired CO levels at every monthly visit. Four of the seven patients who did not quit (57 percent) had substantial reductions in the number of cigarettes that they smoked and in expired CO levels (mean CO level of  $21 \pm 2.6$  parts per million before beginning treatment with nicotine spray and mean CO level of  $3.5 \pm 1.9$  parts per million at the last visit). Three patients (25 percent) continued at the same rate of smoking.

Nine patients (75 percent) used at least 30 doses of nicotine nasal spray per day; three of the five patients who were continuously abstinent (60 percent) still used it at 40 sprays per day, with one 10 mL bottle consumed every three days. Increased use of the spray seemed to be correlated with better outcomes. Three patients (25 percent) preferred to use more nasal spray and reported spraying two to three sprays per nostril, especially in times of stress, without any adverse effect. Spray usage was restricted by prescribing four to five 10 mL bottles every two weeks. Smith and colleagues (5) employed a regimen in a laboratory setting that used multiple sprays per nostril for smokers with schizophrenia to mimic the effects of cigarettes; no adverse reactions were found in that study.

The mean length of time that all 12 patients were treated with nasal spray was  $257 \pm 245.2$  days (range, 14 to 811 days), and three of the five who were abstinent (60 percent) used the spray for months before achieving abstinence. Nine (75 percent) asked to use the spray for long periods, even when they continued to smoke, although all but one had intermittent periods of abstinence. Three (25 percent) were sensitive to brief discontinuations of spray and quickly relapsed back to smoking when the spray was not available. Brief substitution of another form of nicotine medication was not helpful in these cases. It was only when treatment with the spray was reinitiated that these patients were able to return to abstinence.

Only one patient (1 percent) reported discontinuing the nasal spray because of side effects (facial rash), and no patients developed nicotine toxicity, even when the spray was used while smoking or with another nicotine replacement. Although nearly all patients experienced some initial irritat-

ing side effects, such as sneezing, cough, and rhinorrhea, none discontinued the spray for these reasons. These patients developed tolerance to these side effects in the first week with repeated use.

All patients were covered by Medicare or Medicaid, which covers nicotine nasal spray in New Jersey. One patient had his nasal spray treatment terminated by a managed Medicaid plan, rather than by clinical need, and two other patients experienced lapses in treatment because of inadequate pharmacy supply, which was related to their high use of the product.

### Discussion

It is our clinical experience that smokers with schizophrenia responded well to nicotine nasal spray, with good tolerability, few side effects, and high satisfaction. Patients immediately liked the product and wanted to continue using it, with one remarking that it "felt good in his brain." Many expressed a preference for the spray, having already tried other nicotine medications. The low discontinuation rates that we observed are in contrast to those in the general population (6), and our patients commonly used the spray at the maximum dose and for extended periods. Although it appears that dependence on the nasal spray may develop among smokers with schizophrenia, ongoing use of the spray seems preferable to continued smoking. Nicotine nasal spray has a tendency for longer use and more potential for dependence than other forms of nicotine replacement (7). Increased use of the spray—that is, more doses per day—seemed to be correlated with better outcomes (8). However, the nasal spray was not effective for everyone in this case series: two patients used it for extended periods without achieving clinical gains.

### Conclusions

Although all patients were receiving adjunctive psychosocial treatment and nearly all patients were receiving additional pharmacotherapy for tobacco, we observed significant clinical gains when nasal spray was added to the regimen. The role of bupropion SR or clozapine could not be determined in our study, although other studies have found a positive effect (9,10). Adjunc-

tive nicotine replacement usually was with an inhaler and was added when the nasal spray was being used at the maximum dose, which suggests that the total dose of nicotine replacement may be a key factor in the success of these patients. Combination pharmacotherapy that involves the nicotine nasal spray and psychosocial support may be a promising treatment for tobacco dependence among persons with schizophrenia. ♦

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