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Absent response to niacin skin patch is specific to schizophrenia and independent of smoking

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Abstract

This study investigated the differences in niacin skin flush responses between patients with schizophrenia, bipolar mania, and normal controls. We applied niacin patches of three concentrations (0.001 M, 0.01 M, and 0.1 M) to the skin of 61 patients with schizophrenia, 18 patients with bipolar mania, and 40 normal controls for 5 min. Flush responses were rated at 5, 10 and 15 min after application. Flush responses were significantly different among three groups at the concentrations of 0.1 M and 0.01 M at all of the three rating time points. The use of nicotine did not have significant influences on the flush responses. Absent response was significantly more prevalent in the schizophrenia group than in the other two groups, but was not significantly different between the bipolar and the control group. The greatest degree of differentiation in flush responses among groups occurred at the 0.01 M concentration, and the rating time point of 10 min with 49.2% of schizophrenic patients but only 7.5% of controls and 11.1% of bipolar patients not showing a flush response. The niacin skin test for schizophrenia had 49.2% sensitivity and 92.5% specificity compared with controls. This study found that absent response to niacin skin patch was specific to schizophrenia and independent of smoking status.

Keywords: Schizophrenia; Bipolar affective disorder; Niacin skin patch; Nicotine use

1. Introduction

Flushing of the face and trunk has been reported in 92% to 100% of patients receiving oral nicotinic acid treatment for hyperlipidemia (Mosher, 1970). The vasodilatory response was caused by stimulating the release of prostaglandin (PG), in particular, PGD2 from the skin (Morrow et al., 1989, 1992). Absent or diminished flush

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responses in schizophrenic patients after niacin intake was first reported by Hoffer (1962) and was proposed as a possible simple biochemical test for schizophrenia by Horrobin (1980). Although two subsequent studies failed to replicate these findings (Fiedler et al., 1986; Wilson and Douglass, 1986), this has been attributed to using too low a dose of NA (Hudson et al., 1997). However, using a higher 200 mg dose of NA, Rybakowski and Weterle (1991) and Hudson et al. (1997, 1999) reported that approximately 25–40% of schizophrenic patients showed no vasodilatory response.

Ward et al. (1998) observed a diminished flush response to topically applied methyl nicotinate in about 83% of schizophrenic patients using visual inspection for assessment of flush responses. Several follow-up studies using the same method also demonstrated impairment to topically applied methyl nicotinate in schizophrenic patients, though the proportion of impairment was not so high (Shah et al., 2000; Puri et al., 2001, 2002; Maclean et al., 2003). One study failed to show a significantly higher prevalence for absent flush responses to topical niacin in schizophrenic patients (Tavares et al., 2003). The studies using other methods for assessment of flush responses also revealed significantly diminished flush responses in schizophrenic patients, including those using laser Doppler flowmetry (Messamore et al., 2003; Ross et al., 2004a) and those using optical reflection spectroscopy (Smesny et al., 2001, 2003, 2005).

Whether the abnormal skin flush response to niacin is present only in schizophrenic patients, and not in bipolar patients, remains unclear. Bipolar patients were reported to have either an accentuated flush response to oral NA (Hudson et al., 1997) or an attenuated response to topical methyl nicotinate (Maclean et al., 2003). In addition, a significantly higher prevalence of cigarette smoking was present in schizophrenia than in the normal population (Hughes et al., 1986; Fowler et al., 1998). A possible effect of nicotine on niacin response was first considered by Vaddadi (1981) due to the similarity of niacin and nicotine. Therefore, its possible confounding effect upon the abnormal niacin skin flush in schizophrenia should be considered.

The samples of the above studies come mainly from Caucasian subjects. It is unclear if the phenomenon of diminished responses to niacin skin patch in schizophrenic patients is also present in the samples of different ethnic background.

This study investigated the differences in niacin skin flush responses between patients with schizophrenia, bipolar affective disorder, and normal controls, and it also examined the confounding effect of smoking on niacin skin flush responses in a sample of ethnic background other than Caucasian.

2. Methods

2.1. Subjects

Three groups of subjects, schizophrenic patients, bipolar manic patients, and healthy controls, were recruited. All subjects were required to meet the inclusion criteria of no past history of drug and food allergy, no major systemic illness (especially heart disease, autoimmune disease, and severe allergic disease such as asthma and severe skin allergic disease), and no use of steroid and non-steroid anti-inflammatory drugs within a week before niacin skin test. Sixty-one patients who met the DSM-IV criteria for schizophrenia were recruited from either the acute psychiatric ward or the day care unit of the National Taiwan University Hospital. Eighteen patients who met the DSM-IV criteria for bipolar I disorder, most recent episode manic, were recruited from the acute psychiatric ward. Patients with schizophrenia were assessed using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) and those with bipolar mania were assessed on the Young Mania Rating Scale (YMRS) (Young et al., 1978). Forty healthy controls were recruited from the hospital staff through a brief interview to rule out a history of major psychiatric disorders. After informed written consent was given, data collection began and skin tests were performed. Data on clinical variables and smoking history were collected from the interview with the patients and controls and from medical charts.

Table 1 shows the demographic characteristics, psychopathological ratings, medication status and cigarette smoking in the three study groups. There are no significant differences in age and sex, but the prevalence of current smoking and the quantity of smoking in pack-year in the schizophrenic group are significantly higher than those of the other two groups. The durations of illness of schizophrenic and manic patients are relatively long. Five schizophrenic patients and four manic patients are in their first episode, and most of them are in multi-episode courses. The PANSS scores of schizophrenic patients reveal that they have a mild to moderate severity of illness. The YMRS scores of manic patients reveal that they are in the manic state. All of the schizophrenic patients received neuroleptic medication and two-thirds of them received atypical antipsychotics, including risperidone, olanzapine, zotepine, quetiapine, ziprasidone, and clozapine. The manic patients received mood stabilizers, neuroleptics or two combined.