Restlessness of Respiration as a Manifestation of Akathisia: Five Case Reports of Respiratory Akathisia

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Background: Akathista is a feeling of subjective or inner restlessness, which causes excessive, semipurposeful movements, commonly in the legs. However, restlessness in respiration, which presents as dyspnea but is best characterized as the sensation of being unable to breathe in a relaxed manner, has never been reported.

Case Reports: Five cases are reported in which dyspnea as a sign of akathisia followed the administration of antipsychotic medications. The clinical features of dyspnea were examined, and all patients manifested both subjective and objective tive restlessness. The dyspnea was characterized subjectively by the patients' inner feeling of restlessness in respiration, which was perceived as an inability to breathe in a leisurely, relaxed manner, and objectively as restless movements of respiration such as gasping or sighing. The dyspnea was momentarily suppressed when a patient took a quick, full breath to relieve the perceived restlessness and was exacerbated when the patient kept the respiration still. Response to medications commonly used in the treatment of akathisia was also examined in an open, uncontrolled therapeutic trial for each patient. The administration of such medications completely alleviated the respiratory restlessness.

Conclusion: Restlessness in respiration, which clinically presents as dyspnea, may be a manifestation of akathisia. This type of akathisia could be referred to as *respiratory akathisia*. (*J Clin Psychiatry 2000;61:737–741*)

kathisia, a neurologic side effect produced by antipsychotic drug therapy, is usually very distressing to the patient.¹⁻³ A common manifestation of akathisia reported by patients is a feeling of inner restlessness in the limbs, especially in the legs.⁴⁻⁷ The subjective report of restlessness in the legs is regarded as an important sign in the diagnosis of akathisia⁸ and is one of the signs present in akathisia rating scales.9-12 However, reports have indicated that akathisia occurs in other areas of the body such as the arms¹³ and abdomen.¹⁴ Interestingly, Raskin¹⁵ has stated that akathisia can occur in any area of the body. Therefore, it is possible that certain patients may report a feeling of restlessness in other areas of the body besides the legs. Clinical examples of 5 cases in which restlessness manifested in respiration as dyspnea following antipsychotic treatment are presented. In addition, the clinical features and therapeutic response of the patients to antiakathisia medications were examined in an unblinded, uncontrolled manner and are presented for each case

CASE REPORTS

Case 1

A 28-year-old woman with a 10-year history of bipolar disorder was admitted to the hospital because of the appearance of a manic episode (DSM-IV criteria) during maintenance therapy with 1500 mg/day of lithium. The patient was taken off lithium treatment and given 36 mg/day of haloperidol p.o. and 800 mg/day of carba-mazepine p.o. This treatment regimen led to a gradual abatement of her manic symptoms. However, 2 weeks after treatment, she suddenly complained of dyspnea and fell down. The intensity of the dyspnea fluctuated throughout the day, and she began to beat the wall and shout loudly that night. When asked why, she said, "I shouted because of irritation. I have difficulty breathing comfortably. Help me."

After carefully questioning the patient about her dyspnea and irritation, it was discovered that she felt an inner restlessness in breathing. For example, she felt that she could not respire leisurely nor stop breathing at any time because of this restlessness in respiration. Sighing or taking in a full breath relieved her restlessness in respiration

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momentarily. In addition to her subjective restlessness in respiration and restless movements in respiration such as sighing, she displayed other signs of restless movements such as frequently changing her position in her bed and walking about in the ward, although she denied restlessness in the legs. She also exhibited a slight finger tremor. The patient was administered 5 mg i.m. of biperiden.¹⁶ Her restlessness in respiration and dyspnea, as well as her other restless movements, simultaneously disappeared approximately 30 minutes later. Subsequently, the dose of haloperidol was reduced to 9 mg/day, and 9 mg/day of oral biperiden was added to the treatment regimen. No signs or symptoms of akathisia have appeared in this patient following the institution of this treatment regimen.

Case 2

A 25-year-old man was admitted to the hospital for the first time with delusional and violent behaviors 2 years after a similar episode. He was diagnosed as having schizophrenia (DSM-IV criteria) on the basis of his symptoms and previous history. The patient was given 6 mg/day of risperidone p.o., and 1 week later, the dose was increased to 12 mg/day. During the second week of treatment, he complained of chest discomfort and nausea and began to bang his head on a table. He said, "I want to die. I want to go home. I can't breathe easily. I feel uneasy."

After careful inquiry, he acknowledged dyspnea and inner restlessness in respiration with vague anxiety. Specifically, he reported feeling unable to breathe leisurely or stop breathing even for an instant because of this restless feeling when breathing. He also acknowledged an inability to be still. He tossed and turned in his bed frequently, gasping or sighing. However, he denied restlessness in the legs or other body areas except for the chest. He showed no signs or symptoms of parkinsonism. He was given 5 mg of biperiden i.m., and his anxiety and restless symptoms ceased after 30 minutes. The patient was placed on 6 mg/day of risperidone p.o. and 9 mg/day of biperiden p.o., and he has shown no dyspnea while following this regimen.

Case 3

A 40-year-old schizophrenic man (DSM-IV criteria) complained of vague discomfort, an oppressive and uneasy feeling in his chest, as well as the urge to walk about when out of bed 1 week after beginning treatment with 9 mg/day of haloperidol p.o. He said, "I have difficulty in my chest. I can't breathe calmly." After the patient was questioned, he stated that he felt uneasy or restless when breathing and that when he took a full breath or sighed, the dyspnea abated momentarily. He also acknowledged restlessness in the legs, although the intensity was mild, and he showed slight finger tremor. The patient received 5 mg of biperiden i.m., and 40 minutes later, both his walking about and dyspnea disappeared.

Subsequently, the dose of haloperidol was reduced to 5 mg/day, and 9 mg/day of oral biperiden was added to the regimen. However, the next day, dyspnea reappeared. The patient was again given 5 mg of biperiden i.m., and the dyspnea ceased. The dyspnea and other signs of restlessness have not appeared since that time.

Case 4

A 28-year-old female schizophrenic patient (DSM-IV criteria) began to complain of severe anxiety after receiving 6 mg/day of haloperidol p.o. for 3 weeks. She mentioned the inability to feel comfortable in any position or be still. Upon careful questioning, she acknowledged that she felt dyspnea and restlessness in respiration and that she could not breathe in a relaxed manner and frequently sighed and shifted her position. Her dyspnea abated momentarily when she took a sigh or a fast, deep breath. She did not manifest any signs or symptoms of parkinsonism. Five mg/day of biperiden was injected i.m., and her restless in respiration ceased 30 minutes later, as did her behavior of shifting positions. The dose of haloperidol was reduced to 3 mg/day, and 9 mg of oral biperiden was added to her daily regimen. The next day, anxiety and dyspnea appeared again, although the intensity was not as significant as in her first episode. Dyspnea continued for a week with a fluctuation in intensity. Therefore, 1 week after the onset of dyspnea, haloperidol and biperiden were discontinued owing to the disappearance of the patient's positive symptoms. One week after the discontinuation of haloperidol and biperiden, dyspnea and the feeling of restless anxiety had completely disappeared.

Case 5

A 39-year-old male schizophrenic patient (DSM-IV criteria) complained of chest discomfort 2 weeks after receiving 12 mg/day of risperidone p.o. He acknowledged dyspnea with vague anxiety and a subjective restlessness in respiration that manifested as a feeling of inability to breathe calmly and leisurely. In addition, he repeatedly lay down and sat up in his bed. On questioning, he denied restlessness in his limbs or other parts of his body. The patient stated that the dyspnea was alleviated briefly when he took a quick, full breath or exercised.

The patient received 5 mg of biperiden i.m., and his dyspnea and restless movements abated 30 minutes later. However, dyspnea appeared 5 hours after the first treatment with biperiden, and the patient was given an additional 5 mg i.m. of biperiden, which considerably reduced the intensity of the dyspnea. Subsequently, the dose of risperidone was reduced to 6 mg/day, and 9 mg/day biperiden p.o. was added to the patient's regimen. However, dyspnea reappeared for the next 2 days despite the fact that the patient was given 30 mg/day of diazepam p.o. Biperiden, 5 mg i.m., was given each time dyspnea was present during these 2 days. The patient received

80 mg/day of propranolol, in addition to oral diazepam and biperiden, on the fourth day after the first appearance of dyspnea. However, dyspnea, as well as restless movements, reappeared. The dyspnea with vague anxiety and other restless movements completely ceased 3 days after the patient was switched from 6 mg/day of oral risperidone daily to 150 mg/day of oral chlorpromazine (on the seventh day after the first appearance of dyspnea). The patient continued receiving oral biperiden, propranolol, and diazepam on a daily basis.

DISCUSSION

In these case reports, dyspnea, or breathing discomfort, was apparently related to a subjective feeling of restlessness in respiration. The feeling was described as an inability to breathe calmly and comfortably, as well as an inability to stop breathing. This description is similar to that of patients with restlessness in the legs who state that they feel unable to quiet or still leg movements and feel the constant urge to move their legs. The patients indicated that their restlessness of respiration, manifested as dyspnea, was briefly alleviated when they took a full, quick breath. This also is similar to the experience of patients with leg restlessness, who report abatement in the restlessness when they move their legs or walk.⁷

The patients in this report were diagnosed as having antipsychotic-induced acute akathisia on the basis of their subjective restlessness in respiration and restless move ments of the respiratory apparatus. For example, in all cases, dyspnea appeared several weeks after treatment with antipsychotic drugs was instituted, and these agents are known to elicit akathisia within this time period. Furthermore, in all cases, the restlessness in respiration disappeared after the administration of agents known to be effective in ameliorating akathisia. A significant reduction also occurred in the intensity of the akathisia in some cases following a reduction in dose and/or switching to a lower potency antipsychotic drug. Thus, the above information suggests that dyspnea in these cases may be considered a manifestation of akathisia, although the symptoms of motor restlessness exhibited by the patients, particularly the characteristic patterns of restless movement associated with akathisia, are limited. It may be possible that if one of the main manifestations of akathisia is restlessness of respiratory movement, then there may be a relative lack of other characteristic restless movements in the limbs, such as pacing or rocking from foot to foot when standing.

It may be argued that dyspnea in these cases might be due to other medical problems known to produce dyspnea, such as panic attacks and various cardiac or pulmonary diseases. Respiratory symptoms in these patients were similar to those experienced in panic attacks in that the patients had chest discomfort or sensations of shortness of breath or nausea. However, other symptoms of panic attack, such as light-headedness, derealization, fear of losing control or going crazy, fear of dying, paresthesias, and chills or hot flashes, were absent. For example, in case 2, the patient had a panic-like anxiety; however, he did not have anxiety about dying but a desire to die in order to escape his distressing anxiety. This suggests that the patient's anxiety may have been experienced as ego-alien, which is characteristic of akathisia.¹⁷ In addition, the intensity of the symptoms in the current cases was exacerbated when respiration was kept still and abated with a forceful breath or hyperventilation, which typically does not occur in panic attacks. Furthermore, the amelioration of the respiratory restlessness with anticholinergic agents indicates that the patients were unlikely experiencing panic attacks, since these agents are not effective in patients with panic disorders. Finally, no patient had history of panic disorder before or after treatment. Thus, on the basis of the above information, panic disorder, as well as various cardiac or pulmonary disorders, could be ruled out as a cause of the respiratory restlessness.

Respiratory dyskinesia^{18,19} is considered a type of tardive dyskinesia involving respiratory muscles, which manifests as dyskinetic movements of the respiratory muscles such as the diaphragm. Respiratory dyskinesia presents as dyspnea, gasping, sighing, and forceful breathing,¹⁹ all of which occurred to some extent in the patients described in this report. However, such symptoms in respiratory dyskinesia are not due to a restless feeling in respiration, but to involuntary movements of respiratory muscles that are manifested as an irregularity of rate or rhythm of respiration. Dyspnea in akathisia presents as irregular movements of breathing such as sighing and full breathing, but these are voluntary movements on the part of the patients to relieve their inner restlessness. Furthermore, respiratory dyskinesia generally develops after long-term exposure to antipsychotic drugs, as does tardive dyskinesia, and is commonly accompanied by dyskinetic movements in some other muscles, e.g., orofacial.²⁰ However, respiratory symptoms in the current cases appeared within several weeks following the administration of antipsychotic medication and were not accompanied by dyskinetic movements in other muscles. Finally, dyspnea in respiratory dyskinesia is not improved on treatment with biperiden,²¹ and it is not alleviated briefly following exercise.²² Therefore, dyspnea in the patients in this report can be distinguished from respiratory dyskinesia.

It should be pointed out that some cases of respiratory dyskinesia are accompanied by tardive akathisia.²³ No published reports have described respiratory dyskinesia that manifests as an inner restlessness in respiration. It is possible that there may be cases in which respiratory dyskinesia occurs with akathisia that is manifested by an inner restlessness in respiration. However, it is likely that restlessness in respiration may be due to akathisia but not

dyskinesia. If one contrasts respiratory dyskinesia with akathisia due to respiratory restlessness, the latter could be referred to as respiratory akathisia.

The possibility of acute dystonia as the cause for the respiratory symptoms in these cases could be ruled out by the absence of tonic contractions of respiratory muscles. The abnormal respiratory movements such as gasping or sighing in the current cases were mostly voluntary ones to ameliorate restlessness rather than involuntary muscular spasms. In addition, voluntary forceful exercise of respiratory muscles was able to assuage the distress, which may not be true of dystonia.

Respiratory akathisia may not be clinically uncommon; of 63 patients with antipsychotic-induced akathisia whom the author treated during the past 2 years, 19 reported a restlessness in respiration. However, respiratory akathisia was not identified in patients in our hospital until the author paid close attention to respiratory symptoms and asked the patients about dyspnea. Indeed, one of the causes for the wide difference in reported incidence of akathisia is considered to be principally related to the clinicians' attitude toward akathisia,²⁴ e.g., whether emphasis is laid on the subjective feelings or the objective movements of akathisia. All authors stressing the objective phenomena report lower rates, whereas authors emphasizing the subjective features report higher rates of akathisia,^{5,24-26} even though they all must have been alerted to akathisia.

Therefore, it is possible that dyspnea in akathisia may be overlooked or misdiagnosed as a symptom of anxietydisorders or an agitation of psychosis. This may result from the fact that dyspnea, or restlessness in respiration, is a patient's subjective experience that does not always or spontaneously manifest itself as the verbal expression of "dyspnea" or "restlessness in respiration" to clinicians. These subjective symptoms may be altered on the patient's articulation of his or her feelings. In fact, initially, almost all patients were unable to spontaneously articulate that they were experiencing dyspnea or restlessness in breathing. They might have been regarded as having "vague anxiety or agitation" or "restlessness in mind or trunk" or "somatic complaints such as chest discomfort or nausea," which have been reported in akathisia^{5,6,17,27} and as adverse effects of antipsychotics²⁸⁻³² not related to akathisia. However, once the terminology dyspnea and restlessness in breathing was suggested to the patients, they definitely acknowledged it and were able to articulate it by themselves afterward. This is similar to reports of patients with subtle akathisia who did not initially appear to have prominent signs or symptoms of akathisia.^{17,22}

Thus, it is important to consider the possibility of akathisia in patients that complain of vague anxiety, chest discomfort, or dyspnea following antipsychotic medication, and one may need to ask specific questions about restlessness in breathing to recognize this type of akathisia. Incidentally, subjective restlessness and objective restless movements in respiration are not listed in published akathisia rating scales¹⁰⁻¹² or in the research criteria for acute antipsychotic-induced akathisia in DSM-IV.8 Therefore, clinicians should use caution and be thorough in their assessment for respiratory restlessness. One of the reasons that akathisia may be underdiagnosed^{3,17} is that it might be manifested as restlessness in other body areas that are not recognized as being related to akathisia. Therefore, this case series suggests that adding dyspnea and restlessness in respiration to the list of symptoms of akathisia may increase the number of patients that are diagnosed with akathisia. In addition, these results suggest that further research is warranted regarding the origin of anxiety following the administration of antipsychotic drugs, which is usually reported as one of the non-extrapyramidal side effects of treatment,^{28,29,31,32} i.e., the anxiety is not related to extrapyramidal symptoms such as akathisia.

In this study, the medication used to treat antipsychoticinduced akathisia was given to the patients in an uncontrolled, unblinded manner with no use of formal rating scales. Consequently, it would be of interest to conduct controlled clinical trials with an appropriate rating scale to objectively determine the response of patients reporting dyspnea to medications used to treat akathisia.

Drug names: biperiden (Akineton), carbamazepine (Tegretol and others), chlorpromazine (Thorazine and others), diazepam (Valium and others), haloperidol (Haldol and others), propranolol (Inderol and others), risperidone (Risperdal).

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