

Effect of Antiviral Amantadine Treatment on Elderly Chronic Schizophrenia Patients

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ABSTRACT: **Background:** In compliance with public health measures initiated by the Israel Ministry of Health following an outbreak of influenza, amantadine was administered to all patients in the psychogeriatric department of Lev Hasharon Mental Health Center to reduce transmission and illness severity in this susceptible population.

Objectives: To evaluate the potential beneficial effects of amantadine on elderly hospitalized patients with persistent schizophrenia.

Methods: We conducted a retrospective case review of the treatment effects of amantadine on the mental, cognitive and clinical states of elderly chronic schizophrenic patients who received concomitant amantadine treatment and were routinely evaluated with the Positive and Negative Syndrome Scale, the Mini Mental State Examination, and Sandoz Clinical Assessment Geriatric Scale.

Results: No significant differences before and after amantadine treatment were noted.

Conclusion: Amantadine did not influence the mental, cognitive and clinical states of elderly schizophrenia patients and thus can be considered as an anti-influenza preventive measure for this population, when indicated.

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KEY WORDS: amantadine, antiviral, psychogeriatric, schizophrenia, cognition

Seasonal (or common) flu is a respiratory illness that can be transmitted from person to person. The rates of serious illness, hospitalization and deaths depend on the virulence of the virus and differ by an order of magnitude between more and less severe scenarios. Risk groups for severe and fatal infection cannot be predicted with certainty but are likely to include the elderly. A flu vaccine is the first and best defense against the flu, but "influenza antiviral drugs" can be an important second line of defense to treat the flu or prevent flu infection [1].

Among emergent and re-emergent viral infections, influenza constitutes one of the major threats to humans [2].

Although influenza vaccine can prevent influenza virus infection, the only therapeutic options to treat influenza virus are antiviral agents [3]. Antiviral drugs are used to help control flu outbreaks in places where a large number of people at high risk of serious flu complications live in close contact with each other, such as long-term care facilities [1]. There are four influenza antiviral drugs approved for use in the United States (oseltamivir, zanamivir, amantadine and rimantadine). When used to prevent the flu, antiviral drugs have been reported to be about 70% to 90% effective [1].

In compliance with public health measures initiated by the Israel Ministry of Health following an outbreak of influenza, the antiviral agent amantadine was administered to all patients in the psychogeriatric department of Lev Hasharon Mental Health Center to reduce transmission and illness severity in this susceptible population. Amantadine is also used to alleviate symptoms of Parkinson's [4] and drug-induced extrapyramidal signs and symptoms [5], for attenuation of olanzapine-induced weight gain [6,7], and to enhance cognition and clinical symptomatology in schizophrenic patients [8-10]. This psychoactive influence may be related to its effect on augmentation of dopaminergic neurotransmission in the central nervous system.

Several reports have suggested that amantadine has beneficial effects on global status and cognition in patients with mild to moderate Alzheimer's disease [11,12]; however, exacerbation of schizophrenia associated with amantadine treatment has also been reported [13,14]. The effects of amantadine on cognition were investigated in schizophrenic patients [8] but not in the elderly schizophrenic patient population.

Amantadine is an antiviral drug primarily used for the treatment and chemoprophylaxis of flu. The mechanism by which amantadine inhibits influenza virus replication has not been fully elucidated. However, there is considerable evidence that amantadine inhibits an early event in the virus replication cycle, either by preventing virus penetration or virus uncoating or by blocking primary transcription [15].

The potential benefit of amantadine treatment for influenza in the psychogeriatric population outweighed the risk of exacerbation of the mental state sometimes associated with amantadine treatment. Thus, as per the guidelines of the

Israel Ministry of Health, amantadine was administered to all elderly schizophrenic patients hospitalized in the psychogeriatric department following an outbreak of seasonal influenza. Due to the risk of exacerbation of psychiatric morbidity, the mental and cognitive states of the patients were evaluated regularly.

We report the effects of amantadine administered to elderly schizophrenic patients in compliance with public health measures. This "aggressive action" was in response to the flu outbreak and aimed to reduce the spread and severity of illness. The effect of adjunct amantadine therapy on clinical symptoms, cognition, overall functioning, and mental status of hospitalized psychogeriatric patients was evaluated.

PATIENTS AND METHODS

All inpatients (n=60) in the two departments of the psychogeriatric nursing facility at Lev Hasharon Mental Health Center were potential candidates for this retrospective case review study. Though all 60 patients in the psychogeriatric nursing facility had received flu vaccines, 12 developed influenza and were transferred to a general hospital. An additional 10 patients had been receiving memantine as ongoing treatment and therefore did not receive amantadine.

Amantadine treatment (100 mg/day administered in the morning) was given to the remaining 38 patients (mean age 78, range 65–99) in compliance with Ministry of Health treatment guidelines for the elderly inpatient population. All patients met DSM-IV Axis I criteria for schizophrenia disorders, according to case information. All participants had chronic schizophrenia, were chronically hospitalized for many years, had no current or previous DSM-IV diagnosis of drug or alcohol dependence, and none were suffering from a first episode. They were all treated with atypical antipsychotic agents and received the same medication for at least 3 months with no change in dosage for at least 4 weeks prior to administration of amantadine.

Routine clinical assessments included the Positive and Negative Syndrome Scale [16], the Mini Mental State Examination [17] to assess mental status and cognitive functioning, and the Sandoz Clinical Assessment Geriatric Scale [18] to examine any post hoc correlations to amantadine treatment. The retrospective case review was approved by the Institutional Review Board. All questionnaires and data were archival and derived from the patients' medical records.

STATISTICAL ANALYSIS

Standard *t*-tests were used to compare treatment effects before and after treatment with amantadine. Spearman's bivariate correlation analysis was used to examine the association between variables, and a partial correlation analysis was performed to determine the effects of potential con-

founding sociodemographic variables. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS).

RESULTS

Amantadine did not influence the mental or cognitive states of the patients. There were no significant differences in the treatment effects of amantadine with respect to: Positive and Negative Syndrome Scale ($P = 0.74$), Sandoz Clinical Assessment Geriatric Scale ($P = 1.00$), and the MMSE ($P = 0.21$). In addition, there was no further exacerbation of psychotic symptoms. No significant correlations were noted between test variables and sociodemographic variables.

DISCUSSION

Amantadine is a necessary antiviral treatment in the event of an outbreak of influenza [19]. Though it has been associated with an exacerbation of the mental state of some psychiatric patients [13,14], there are also reports of improved cognition following amantadine treatment, hence our report on this issue. Several studies recently reported that the administration of amantadine to elderly Alzheimer's patients revealed beneficial effects on global status and cognition [11,12]. In contrast, our study did not show improved global status. While Silver and colleagues [8] reported that amantadine was associated with improved visuomotor coordination in schizophrenia patients, in agreement with our findings, they found no significant changes in cognitive functions, particularly with regard to the MMSE, which was used to measure general cognitive function. The lack of effects on clinical symptomatology after receiving amantadine treatment in our study was in agreement with the report of Silver and Geraisy [9,10]. The apparent lack of treatment side effects may be due to the small sample size and the lack of a control group. In contrast, there are reports of exacerbation of schizophrenia associated with amantadine treatment [13,14]. Our case report review did not reveal amantadine-induced exacerbations, supporting the option of concomitant amantadine therapy for elderly schizophrenic patients. Thus amantadine can be considered as an anti-influenza preventive measure for this population, when indicated.

This information is relevant to the elderly population, especially those in institutional settings, whether retirement homes or treatment facilities for persons with mental illness. This study does have limitations, namely, it was a retrospective case review study with no control group and the study population was small.

Considering the inconsistent findings in the literature regarding the therapeutic effects on patients and the apparent

MMSE = Mini Mental State Examination

lack of studies examining these effects in elderly patient populations, further study is warranted. Since amantadine is widely used in the prophylaxis and treatment of flu [19], collection and evaluation of the data for amantadine-treated patients may contribute to a more comprehensive assessment of the overall treatment effects of adjunctive amantadine therapy.

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