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Length of mechanical restraint following haloperidol injections versus oral atypical antipsychotics for the initial treatment of acute schizophrenia: A propensity-matched analysis from the Japanese diagnosis procedure combination database

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ABSTRACT

Differences in effectiveness between haloperidol injection and oral atypical antipsychotics in the acute-phase treatment of schizophrenia are not well examined. We retrospectively investigated whether these treatment options affected the length of mechanical restraint. We used the Japanese Diagnosis Procedure Combination Database to identify schizophrenia patients who were involuntarily hospitalized and receiving mechanical restraint between July and December, 2006–2009. Data included patient demographics, use of antipsychotics, and number of days on which patients underwent mechanical restraint. Propensity score matching was performed to compare the number of days of mechanical restraint between the haloperidol injection group and the oral atypical antipsychotics group. We used survival analysis to examine whether the initial difference in treatment affected the number of days of mechanical restraint. Cox regression was performed to compare the concurrent effects of various factors. Among 1731 eligible patients, 574 were treated with haloperidol injections and 420 with atypical antipsychotics. Matching produced 274 patients in each group. Cox regression analysis showed that the initial therapeutic agents did not significantly affect the number of days of mechanical restraint. The results indicate that atypical antipsychotics were as effective as haloperidol injections in the acute-phase treatment of schizophrenia.

1. Introduction

The use of atypical antipsychotic drugs has become widespread for the first-line treatment of schizophrenia. In Japan, the atypical antipsychotic risperidone became available in 1996; olanzapine, quetiapine, perospirone, aripiprazole, and blonanserin between 2001 and 2008; and clozapine in 2009. Since the introduction of haloperidol, clinical experience has suggested that haloperidol is indeed an effective antipsychotic, particularly beneficial for those who are experiencing acute hallucinations and delusions (Joy et al., 2006). Although numerous studies have compared the efficacy of atypical antipsychotics versus that of haloperidol, there have been only a few studies that compared effectiveness between oral atypical antipsychotics and conventional intravenous or intramuscular haloperidol injection in psychiatric emergencies and the acute-phase treatment of psychosis (Hatta et al., 2009). McCue et al. showed that haloperidol, olanzapine, and risperidone were significantly more effective than aripiprazole, quetiapine, and ziprasidone based on

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improvements of mental status to the point where patients did not need acute inpatient care (McCue et al., 2006). The research of Hsu et al. in Taiwan showed that both intramuscular olanzapine and olanzapine tablets are more effective than intramuscular haloperidol within 90 min, but no significant difference was found after 90 min (Hsu et al., 2010). When only the symptom of agitation was examined, risperidone, olanzapine, and quetiapine were as effective as haloperidol (Villari et al., 2008). However, to our knowledge, there has been no study comparing the length of mechanical restraint between conventional haloperidol injections and oral atypical antipsychotics.

The duration of mechanical restraint could be one feasible indicator of the effectiveness of medication for acute-phase schizophrenia. Mechanical restraint is basically efficacious in preventing injury and reducing agitation, but it is accompanied by substantial anguish to patients (Fisher, 1994). Several studies reported that patient aggressiveness, excessive activity, hallucinations and delusions were associated with the use of mechanical restraint and seclusion (Husum et al., 2010; Gaskin et al., 2007). Therefore, release from mechanical restraint is considered to reflect a lessening of psychopathological symptoms.

We hypothesized that the length of mechanical restraint would be shorter in the haloperidol injection group than in the oral atypical antipsychotics group. To test this hypothesis, we collected data on inpatients with schizophrenia derived from a national administrative claims database in Japan, and we compared the length of mechanical restraint between patients receiving the two different treatment options.

2. Methods

2.1. Data source

The Japanese Diagnosis Procedure Combination (DPC) database is a national database of general hospital patients in Japan; it contains administrative claims data and discharge information of acute care inpatients (Yasunaga et al., 2010; Nakamura et al., 2012). The database started with 82 teaching hospitals in 2002, and the number of participating hospitals gradually increased each year to include 818 in 2009. Data are collected over 6 months (from July 1 to December 31) of each year. In 2009, data from approximately 2.6 million inpatients (in all disciplines, including non-psychiatric and psychiatric) were collected, representing approximately 40% of all acute care inpatient hospitalizations in Japan.

The database includes the following information: unique hospital identifier; type of hospital (teaching or non-teaching); patients' age and sex; diagnoses and comorbidities coded according to the International Classification of Disease and Related Health Problems, Tenth Revision (ICD-10); procedures; drugs and devices used; type of psychiatric admission (voluntary or involuntary, details shown below); and disposition of patient (discharged to home, discharged/transferred to a nursing facility, discharged/transferred to other hospital, or died during hospitalization).

This study was based on a secondary analysis of the administrative claims data. Because of the anonymous nature of the data, the requirement for informed consent was waived. Approval for the study was obtained from the Institutional Review Board at the University of Tokyo.

2.2. Overview of involuntary admissions and psychiatric emergency system in Japan

Involuntary admissions for acute-phase psychiatric patients were permitted under the Mental Health and Welfare Law. Under this law, all patients admitted were examined by a psychiatrist licensed by the Ministry of Health, Labour and Welfare (Hattori and Higashi, 2004).

There are two main types of involuntary admission: Involuntary Hospitalization Ordered by Prefectural Governor (IHOPG) and Hospitalization for Medical Care and Protection (HMCP). IHOPG is determined by a licensed psychiatrist for patients who are mentally disordered and are likely to hurt themselves or others. Patients were admitted for HMCP when their guardians consented to hospitalization for medical care and protection, provided that a licensed psychiatrist required it. The psychiatric emergency system in Japan is operated by local governments. Some of the involuntary admission patients receiving psychiatric emergency services are charged by the police because of behavioral problems (Sawayama et al., 2009). In some urban prefectures, hospitals providing acute psychiatric care are separated from those providing sub-acute and long-term care. For example, the Tokyo Metropolitan Government's psychiatric emergency service is available at night and during holidays (Niizato et al., 2003). This system is run as follows: four Metropolitan hospitals provide the initial 1–2 days of care, and subsequent care is taken over by other hospitals since the four Metropolitan hospitals have to prepare four beds every night for the next psychiatric emergency patients. In rural prefectures, psychiatric hospitals and general hospitals that have a psychiatric department provide psychiatric acute emergency care and subsequent care by turn.

The DPC database includes information from general hospitals but not from psychiatric hospitals. As of 2008, the number of psychiatric beds was 8221 in DPC hospitals and 15,669 in all general hospitals in Japan; the coverage rate of the DPC was 56% of general hospitals.

2.3. Inclusion/exclusion criteria

Data for this survey were extracted from the DPC database from 2006 to 2009. We first identified the records of all patients who entered the psychiatric department. We only included involuntarily admitted patients because they were considered to be in a worse condition than voluntarily admitted patients. We then selected patients diagnosed with schizophrenia or psychosis (ICD-10 codes, F20–29). Only patients who received mechanical restraint at admission were included. We then identified the following two groups: (i) patients who were given intravenous or intramuscular haloperidol injection on the first day of admission (the haloperidol group) and (ii) patients who were given atypical antipsychotics but did not use haloperidol (the atypical antipsychotics group). Patients who were initially treated with oral typical antipsychotics or intramuscular levomepromazine injection were excluded.

2.4. Patient background and outcome

Patient background factors examined were age and sex, psychiatric diagnoses and comorbidities, and Global Assessment of Functioning Scale (GAF) score at admission. Hospital factors included type of hospital (teaching or non-teaching hospitals) and hospital volume. Hospital volume was defined as the annual number of involuntarily admitted schizophrenia patients receiving mechanical restraint in each hospital. Hospital volume was categorized into tertiles so that the numbers of patients in each category were almost equal. The primary outcome was the length of mechanical restraint, as defined by the number of consecutive days on which patients underwent mechanical restraint; that is, days from the day of admission to the last day when the restraint was applied. In Japan, patients are not necessarily kept under restraint for a whole day, but are released from restraint for several hours each day (Noda et al., 2009). The actual duration of restraint in each day is not recorded in the database.

We performed univariate comparisons of patient characteristics using chi-square tests between the two groups assigned to different types of initial medication (haloperidol injection or atypical antipsychotics).

2.5. Statistical analyses

We conducted one-to-one matching between the two groups with different initial medication (haloperidol injection or atypical antipsychotics) based on the estimated propensity score of each patient (Rosenbaum and Rubin, 1985; Ayanian et al., 2002). The propensity score approach assesses the issue of selection bias in retrospective observational studies, where outcomes can reflect a lack of comparability rather than the effects of treatment. This approach tries to approximate a randomized experiment-like situation where both groups are comparable in terms of observed prognostic factors. To estimate the propensity score, we fitted a logistic regression model for the receipt of haloperidol as a function of patient demographic and hospital factors, including age, sex, GAF score, diagnosis, type of hospital, and hospital volumes. The C-statistic for evaluating the goodness of fit was calculated. Each patient who received haloperidol injection was matched with a patient who received atypical antipsychotics with the closest estimated propensity on the logit scale within a specified range (≤ 0.25 of the pooled standard deviation of estimated logits). Chi-square tests were used to compare background characteristics between patients who received haloperidol injection and those who received atypical antipsychotics, among all cases and in the propensity-score-matched groups.

Because the DPC data do not include post-discharge information, patients who were transferred to other hospital under mechanical restraint could not be followed up after discharge. To circumvent such incomplete follow-up data, we adapted survival analysis (Quesenberry et al., 1989). In survival analysis, when the observation is censored, the variable is considered to be equal or larger than the value at the time of censoring. In our study, a patient's length of mechanical restraint was censored from the analysis if it was equal to length of stay, because the patient was transferred to another hospital under restraint and was lost to follow-up. We compared the proportions of patients who were released from mechanical restraint between the two groups assigned to different initial medications (haloperidol or atypical antipsychotics) using the Kaplan–Meier method and a log-rank test among the propensity-matched patients. Cox proportional