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Research article

Use of neuroleptics in a general hospital

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Abstract

Background: This study investigates the clinical use of neuroleptics within a general hospital in acutely ill medical or surgical patients and its relation with dementia three months after admission compared with control subjects.

Methods: Cases were defined as every adult patient to whom a neuroleptic medication was prescribed during their hospitalization in our Hospital from February 1st, to June 30th, 1998. A control matched by age and sex was randomly selected among patients who had been admitted in the same period, in the same department, and had not received neuroleptics drugs (205 cases and 200 controls). Demographic, clinical and complementary data were compared between cases and controls. Crude odds ratios estimating the risk of dementia in non previously demented subjects compared with the risk in non-demented control subjects were calculated.

Results: 205 of 2665 patients (7.7%) received a neuroleptic drug. The mean age was 80.0 ± 13.6 years and 52% were females. They were older and stayed longer than the rest of the population. Only 11% received a psychological evaluation before the prescription. Fifty two percent were agitated while 40% had no reason justifying the use of neuroleptic drug. Three months after neuroleptic use 27% of the surviving cases and 2.6% of the surviving controls who were judged non-demented at admission were identified as demented.

Conclusions: The most common reason for neuroleptic treatment was to manage agitation symptomatically in hospitalised patients. Organic mental syndromes were rarely investigated, and mental status exams were generally absent. Most of neuroleptic recipients had either recognised or unrecognised dementia.

Background

Neuroleptic drugs are commonly prescribed in acutely ill-hospitalised patients [1–3]. However, the use of such medication has not been extensively studied. Agitation and delirium are major clinical problems in hospitalised patients, especially in those who are elderly and demented

[4–6] The aetiology of delirium is complex, multifactorial, and it is significantly more frequent in patients with psychiatric comorbidity or dementia [7,8]. Delirium is also an predictor of adverse outcomes in older hospital patients, including longer mean length of hospital stay, poor functional status and need for institutional care, and mortality.[9]

Non-pharmacological and pharmacological interventions are effective in controlling the symptoms of delirium in acutely ill patients [10–15]. Treatments for agitation are imperfect, and clinicians should be prepared to work through several in order to find the most suitable for a given patient and clinical situation.[16] Ideally the use of pharmacological interventions should be reserved for situations where other measures have been unsuccessful, [12,16] however between 9.4 and 42.8% of non-psychiatric patients were prescribed psychoactive medications during hospitalisation, most of them because of agitation or delirium [1,3]. Efficacy, side effects, adverse experiences and strategies of drug selection based on the patient's diagnosis have not been frequently studied.

This study investigates the clinical use of neuroleptics within the medical and surgical departments of a General tertiary Hospital, to understand how these drugs are used in this setting and to determine whether the use of these drugs is an predictor of adverse outcomes or mortality during hospitalisation, at discharge or three months later. We collected in a retrospective study clinical features, outcomes and risk factors from two cohorts of hospitalised elderly patients who have been treated with and without neuroleptic drugs during admission.

Materials and Methods

This retrospective case-control study compares patients admitted to general medical or surgical units who received neuroleptics with age-sex matched controls who did not. Case is defined as every patient 18 years of age or older to whom a neuroleptic medication was prescribed during their hospitalisation in our Hospital from February 1st, to June 30th, 1998. Prescriptions for haloperidol (Haloperidol®), chlorpromazine (Largactil®), tiapride (Tiaprizal®), and thioridazine (Meleril®) were examined.

A control group matched by age (± 10 y) and sex was randomly selected among patients who had been admitted in the same period and had not received neuroleptic drugs. These patients were selected between patients admitted within two weeks of the index case was recruited and in the same department.

Five cases had no suitable controls.

The following information was obtained via chart review in cases and controls:

- **Demographic characteristics** (age, sex),

- **Length of hospitalization**

- **Previous diseases**: *chronic obstructive lung disease* (previously diagnosed based on clinical criteria), *hypertension* (previously diagnosed and treated or systolic pressure >160 mmHg and/or diastolic pressure >90 mmHg persistently observed during admission after the acute phase), *diabetes* (previously diagnosed and treated or fasting glucose 7 mmol/L (126 mg/dL) in two blood samples after the acute phase), *heart disease* (myocardial infarct, congestive heart failure or valvular disease previously diagnosed by a physician), *atrial fibrillation*, *dementia* or *cognitive impairment* (previously diagnosed by a physician) and the use of *bladder catheter*

- **Laboratory studies during admission**: plasma levels of creatinine, potassium, sodium, oxygen, CO_2 and bicarbonate.

- **Clinical data during admission**: fever (temperature over 38°C), surgical procedures, use of bladder catheter, neuropsychological assessment, death and its cause.

- **Diagnostic criteria for dementia**: A physician (RB) who searches for specific diagnostic criteria for dementia determine the presence or absence of dementia based on information from neurologic and functional examinations at admission and 3 months after discharge. Diagnosis of dementia was based on the clinical judgement of the examining physician, but no standard criteria were applied for the diagnosis.

- **Follow up**: Three months after discharge medical records were reviewed by a physician (RB) who searches for specific diagnostic criteria for dementia. To be accepted as demented there had to be documented evidence of decline of intellectual and/or cognitive and social function that was irreversible with medical or psychiatric treatment. Death was also recorded. Whenever possible, the cause of death was ascertained from the hospital records.

Statistical analysis

Demographic, clinical and complementary data were compared between cases and controls. The two-tailed Student's t test for quantitative variables and the χ^2 test for dichotomous variables were used. The Odds-Ratios and 95% confidence intervals were estimated from the logistic regression coefficients.

To determine the incidence of dementia three months after admission, we defined an incidence cohort composed by non demented cases and controls at baseline who were followed over three months. Newly demented subjects were enumerated in the neuroleptic and control cohorts. Crude odds ratios (OR) estimating the risk of dementia in the neuroleptic group compared with the risk in control subjects were calculated.

In order to identify predictors of dementia three months after admission, we performed a logistic regression analyses in which dementia was considered the dependent variable, for both cases and control subjects combined (total 175). Clinically relevant variables and those with statistical significance ($p < 0.1$) in the univariate analyses were introduced as independent variables. A logistic regression analysis, with backward stepwise procedure and $p > 0.10$ as the criterion for exclusion, was used to find the best predictive model of dementia after neuroleptic use during admission.

All these analyses were performed with SPSS for Windows version 9.0 (SPSS Inc)

Results

During the study period 2665 patients over 18 years were admitted at the medical and surgical departments of our Hospital, and in 205 (7.7%) a neuroleptic drug was prescribed during the stay. One hundred and eighty (88%) of the study patients received haloperidol as the only neuroleptic drug. Twenty-five (12%) had either an alternative drug or a combination of drugs. Indication for prescribing neuroleptic drugs were as follows: agitation 107 (52.2%), impossibility to sleep 8 (3.9%), other 8 (3.8%), none 82 (40%). Sixty-one cases (29.8%) were discharged from the hospital on a neuroleptic drug. In the cohort, only 22 cases (11%) underwent neuropsychological assessment. These cases did not differ in age or sex from those who were not examined, but 20 of them were in a medical service and only two in a surgical department (14% versus 4%; OR 3.7 CI95% 0.9–16.7; p = 0.07). Cases to whom mental status examinations were performed were more likely to be receiving the drug at discharge (20% versus 9%; OR 2.5 CI95% 1.1–6.3; p = 0.036).

The mean age was 80.0 ± 13.6 years (range 42–102 y) from cases and 78.3 ± 7.1 (range 51–96 y) from controls; 107 cases and 98 controls were female (52% versus 49 %; p = 0.551).

Fifty six cases (27.3%) and 16 controls (8%) were demented (OR 1.3 IC 95% 1.1–1.4; p < 0.0001) and 51 cases (24.8%) and 24 controls (12%) were classified as having cognitive impairment before hospitalisation. Twenty-two cases (11%) and 4 controls (2%) did not complete a clinical neurological examination and were not tested.

Mean hospitalisation time was11.2 ± 11.5 days which was longer than the hospital's average length of stay (5.2 ± 13, p < 0.0001) and longer than the control group (6.8 ± 6.4, p < 0.0001).

Cases did not differ significantly from controls in terms of atrial fibrillation, diabetes mellitus, chronic heart or lung disease prevalence (Table 1). Hypertension was significantly more frequent in controls than in cases (53% versus 40%; OR 1.7 IC95% 1.3–2.5; p = 0.013). During admission fever (41% versus 27.6%; OR 1.3 IC 95% 1.1–1.6; p = 0.007) and the use of bladder catheter (68.6 versus 30.6; OR 2.2 IC 95% 1.6–3.0; P < 0.0001) were more frequent in cases than in controls, while surgical procedures (25.3% versus 25.5%; OR 0.7–1.2) did not differ in both groups (TABLE 1). There were no significantly differences between groups in the haematological and biochemical complementary studies (data not shown).

Thirty cases and 14 controls died during the admittance (16% versus 7%; OR 1.4 IC 95% 1.2–1.8; p = 0.007), and 42 cases and 18 controls died during the 3 months following discharge (30% versus 12%; OR 3.1 IC 95% 1.7–5.7; P < 0.0001)

Table 1: Comparison between cases and controls: demographic data, previous diseases and clinical data during admission

	Cases (n = 205)	Controls (n = 200)	Odds Ratio* (95% CI)
Mean age, y (SD)	80.0 ± 13.6	78.6 ± 7.1	1.01 (0.9–1.1)
% < 60 y	2 (1%)	2 (1%)	1.03 (0.1–10.2)
%>90 y	16 (4.3%)	9 (4.5%)	1.8 (0.7–4.5)
Females (%)	52%	49%	1.13 (0.6–2.1)
High blood pressure	71 (40%)	109 (53%)	0.7 (0.6–0.9)
Diabetes	35 (19.7%)	51 (24.6%)	0.8 (0.6–1.1)
Heart disease	78 (44%)	96 (46.6%)	0.9 (0.7–1.1)
Atrial fibrillation	42 (23.6%)	46 (22.5%)	1 (0.8–1.3)
Lung disease	63 (35%)	80 (38.8%)	0.9 (0.7–1.1)
Incontinent	80 (46%)	27 (13%)	2.2 (1.7–2.6)
Previous dementia	59 (33%)	15 (7.3%)	2.1 (1.7–2.4)
Fever	76 (41%)	55 (26%)	1.4 (1.1–1.7)
Surgery	49 (25.3%)	52 (24.6%)	1 (0.8–1.3)
Urinary catheter	81 (68.6%)	39 (30%)	2.3 (1.7–3.1)
Death during admission	30 (16%)	15 (7.1%)	1.4 (1.1–1.8)

* chi-square test

Incident dementia

In order to identify the incidence of dementia three months after neuroleptic use we compared the surviving

non-demented at admission cases and controls. Among the study population 127 cases and 180 controls were non-demented at admission and of these, 59 subjects were compared with 116 controls. The difference in the study population was accounted by 30 who died before 3 months (22 during admission) and 38 with incomplete information about their neurological status. In the control group the difference was accounted by 10 who died before 3 months (7 during admission), and 47 who were not testable (TABLE 2). The 38 lost cases and the 47 lost controls were older than the testable patients (cases: 75.7 ± 17 versus 82.6 ± 11; p = 0.021; controls 79.7 ± 6.5 versus 76.5 ± 6.5; p = 0.004) but did no differ in gender or previous diseases (data not shown).

Table 2: Sample attrition at different steps of the study in non-demented patients.

	Cases n = 205	Controls n = 200
Non-demented at admission	127 (62%)	180 (90%)
Death during admission	22	7
Death during the next three months after discharge	8	10
Lost follow up	38	47
Analysed*	59	116

* Surviving non-demented cases with completed examination.

Sixteen (27%) of the surviving cases and 4 (2.6%) of the surviving controls who were judged non-demented at admission were demented three months after admission. The unadjusted odds of having dementia after admission in the neuroleptic prescribed group compared with the odds in the control sample was OR 10.4 95% IC 3.3–32.9; p < 0.0001. We used a multiple logistic regression model to estimate de Odds Ratio of dementia adjusting for age, sex and cardiovascular risk factors (hypertension, diabetes, heart disease). The adjusted Odds ratio was 12.0 95% IC 3.6–39.

Risk of dementia estimated by logistic model

We use a logistic model to determine predictors of dementia three months after admission. Dementia was considered as the dependent variable for both non previous demented case and control subjects combined. Atrial fibrillation, diabetes mellitus, hypertension, heart disease, previous incontinence and use of neuroleptics were used as independent variables. The overall adjusted OR was 12.5 (IC 95% 3.4–45.2) in neuroleptic group. A subject (case or control) with previous incontinence has a risk of dementia 10.6 times (IC 95% 2.0–57.1) the risk of a subject without incontinence. There are not significantly differences between patients with or without diabetes, hypertension, heart disease or atrial fibrillation.

Discussion

Neuroleptic drugs are commonly prescribed to treat agitation or delirious states in acutely ill hospitalised patients [1,3]. In our cohort, patients who received neuroleptic drugs were often elderly, seriously ill, stayed in the hospital longer and had a higher mortality rate during hospitalisation and three months later than patients who did not.

There have been few controlled trials about the most commonly used drugs to guide therapy in delirium and agitated patients [1–3,11,14,16–18]. To successfully treat these conditions, an adequate description of behavioural target symptoms to be corrected and a thorough investigation to identify precipitating causes are essential. [8,16,19]. Behavioural problems in hospitalised patients may result from physical illnesses, adverse drug effects, environmental changes, psychiatric syndromes or dementing illnesses [5,8,12,13,20–23]. However only 11% of our cases had a neuropsychological evaluation prior to neuroleptic prescription. Some authors have suggested that physicians may be reluctant to seek psychiatric consultation in older patients [24] however a neuropsychological evaluation could give essential information to ascertain the aetiology of agitation.

This study shows that neuroleptic drugs were prescribed to 7% of a general hospital inpatients, although diagnostic indications were discovered only in a few of them. The lack of documentation supporting a diagnosis justifying the use of a neuroleptic drug noted in this study has been observed elsewhere [1,3]. The descriptions of agitation may seem to be an adequate reason for treatment, however both dementia and delirium are not an easy diagnosis, and both are often underdiagnosed in the acute care. [6,15,25–27]. As neuroleptics are not innocuous drugs,[28] physicians must recognize that these drugs can promote important side effects, and prior investigators have demonstrated than physicians often lack sufficient knowledge about the therapeutic use and pharmacokinetis of these medications. [2,29,30] This study suggests that more education regarding the use of neuroleptic drugs is indicated.

Compared with patients to whom neuroleptics are not prescribed during admission, the risk of being diagnosed as demented three months later is at least ten times higher even after adjusting by age and sex. Probably these patients have a mild cognitive impairment that has not been previously identified. Some studies have shown that most of the elderly patients admitted in a general hospital who have presented delirium could be identified as demented

during hospital stay using explicit criteria [4]. We think that the early identification of patients with mild cognitive decline could be important as it would allow for some interventions to improve better quality care.[31]

The study has some design-based limitations. The diagnosis of dementia was based on clinical information, and we did not use any of the standard criteria or neuropsychological tests that can be uniformly applied. It is probable that dementia was underdiagnosed, since it is known that the use of neuropsychological test might uncover a larger number of clinically unobvious cases. If only the most overt cases were labelled as demented, one interpretation is that our estimation describes a minimum frequency. Supporting the validity of our findings, other studies have documented acceptable agreement between a clinician's diagnostic impression and findings from formal mental function tests, [32] with a sensitivity and specificity of diagnosis about 79% and 80%, respectively.[33]

This study, performed in a community hospital may not be generalizable to other settings, however more studies are recommended in order to confirm this data and to determine if overuse of neuroleptics is a isolated problem of several hospitals or a extended medical problem.

This study confirms the high rate of neuroleptics use among hospitalised patients and its association with adverse outcomes such as prolonged hospital stays. The high death rate in neuroleptic recipients suggests the fragility of this group, while the diagnosis of dementia three months after admission is probably related with a high rate of previous unrecognised dementia. In spite of the use of these drugs to treat agitation symptoms, they rarely concur with a formal diagnosis of cognitive decline or the request of a neuropsychological consultation. Future research should explore the effectiveness of both diagnostic and management approaches to the confused agitated elder and the prognostic effect of delirium on the outcome of older hospital medical inpatients.

Competing interests

None declared

Authors' contributions

(RB) and (JBG) designed the study, (RB) performed dementia diagnosis (HMA) and (IGA) performed the charts review (RB) and (CGH) performed the statistical analysis, (VCC) participated in it's design and co-ordination.

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