NEUROLEPTIC DRUG UTILISATION FOR ACUTE SCHIZOPHRENIA

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ABSTRACT

The aim of this study was to find the dosage and pattern of neuroleptic drug utilisation for the treatment of acute schizophrenia in a general psychiatry ward. This is an uncontrolled study involving 112 schizophrenic inpatients. Patients' socio-demographic variables, the type and peak daily doses of neuroleptics prescribed to them were analysed. Chlorpromazine was the most commonly prescribed drug. The peak mean daily dose required by the patients was equivalent to 537 mg of chlorpromazine; and 400 to 600 mg/day of chlorpromazine or its equivalent was generally sufficient to treat acute psychosis. The majority of the patients received neuroleptics within this dose range. Low potency drugs were prescribed in lower doses than high potency drugs. Patients treated with depot preparation tended to receive higher doses of medication than those prescribed oral medication alone. The doses of neuroleptics were significantly correlated with duration of admission.

Keywords : neuroleptic drug, drug doses, schizophrenia, Malaysia

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INTRODUCTION

After decades of clinical use of neuroleptic drugs, the question of appropriate dosage has not been completely answered. Determination of lowest effective dose is regarded as a critical factor in clinical psychiatry especially when the facility to monitor plasma neuroleptic concentration is not available. Too low a dose not only increases side-effects but becomes less effective because of therapeutic window responses of certain drugs [1].

The tendency to give higher dose of neuroleptic than required is common in clinical practice. Survey of neuroleptic drug prescriptions for inpatients in various parts of the world showed that many patients were prescribed doses well above the recommended level, particularly if high potency drugs were used [2-4]. Controlled clinical trial had shown that moderate doses of neuroleptic (500-600 mg chlorpromazine per day or its equivalent) were adequate to treat most patients with acute psychotic episodes [5].

In a controlled study, Lind and Finder [6] found that Asian patients required lower dosage of neuroleptic than White patients. However, their findings were disputed by Sramek et al [7]. This paper reports a study of neuroleptic drug utilisation for inpatients in a general psychiatry ward. It is an uncontrolled study and therefore the dosage prescribed is expected to be higher than the recommended dose. The study will also explore the correlation between various socio-demographic variables and neuroleptic doses.

METHODOLOGY

The study was conducted at the University Hospital (USM), Kota Bharu, Kelantan on the east coast of Peninsular Malaysia. All patients admitted during the study period and prescribed neuroleptic drugs were included if they fulfilled the DSM-IIIR[8], criteria for schizophrenia. Those who were given electroconvulsive therapy (ECT), discharged against medical advice and prematurely transferred to other hospitals or wards, were excluded.

There is no standard guideline on the choice of neuroleptic practice in the hospital. Therefore, the type of neuroleptics and doses were selected by their attending psychiatrist, depending on the patient's mental status and the availability of the drugs. Benzhexol and/or other drugs were prescribed as needed. The psychiatrists were also allowed to prescribe depot preparations.

The patients' socio-demographic data and peak daily doses of neuroleptics were recorded in a standard form. The peak doses of neuroleptics were converted to equivalent dose of chlorpromazine. If more than one neuroleptic were administered at the time of peak dose, the sum of their doses were calculated. The conversion formula were 2.5 mg of oral haloperidol, 5 mg of trifluoperazine or 10 mg of perphenazine are equivalent to 100 mg of chlorpromazine. The equivalent dose of chlorpromazine and thioridazine and 40 mg of flupenthixol decanoate for every 2 to 3 weeks are equivalent to 300 mg/day and 400 mg/day of chlorpromazine respectively.

Students t-test was used to compare the peak daily doses of low and high potency drugs and the total daily doses received by patients who were prescribed oral drugs only, and those receiving depot preparations. The Pearson's correlation coefficient was employed to explore the relationship among dimensional variables.

RESULTS

1. Socio-demographic variables

A total of 124 schizophrenic patients were admitted during the study period. Of these, 112 (90.3%) were selected for the study. Those excluded were given ECT (2 patients); discharged against medical advice (6 patients); and prematurely transferred to other wards and hospitals (4 patients). About 90% of the patients were Malays; Chinese comprised 8% of the sample. Other ethnic groups (Indians and Thais) only formed less than 2% of the total number of subjects studied. The sex ratio between male and female patients was almost the same. Most of the patients were between 20 and 39 years of age, single, completed secondary school education and had been ill between 2 and 5 years. Patients' average body weight was 54 kg.

The majority of the patients had previous psychiatric admissions. About 90% of the patients did not have a steady job, although a small percentage of them helped their families in farming and daily housework. Thirty one percent of the patients

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had family history of schizophrenia among the first degree relatives. The average stay of patients was 26 days. Home leave was included in the duration of stay. Neuroleptic doses showed a significant correlation with duration of admission (Table I). The correlation with other socio-demographic variables was not significant.

Table I – The correlation of socio-demographic variables with neuroleptic doses.

Variables (n=112)	Pearson's r
Age	– 0.16
Sex (1= male, 2= female)	– 0.12
Positive family history	0.15
Years of education	– 0.10
Duration of index admission	0.25[a]
Duration of illness	0.18
Number of hospitalisations	0.17

[a] $p < 0.01$

2. Dosage and types of neuroleptics

Chlorpromazine was the most commonly prescribed drug (44%). This was closely followed by haloperidol (41%) and trifluoperazine (9%). The other drugs used were phenphenazine (5%) and thioridazine (1%). The majority (61.6%) of the patients received peak daily dose of 400 to 600 mg of chlorpromazine or its equivalent (Table II). The peak mean daily dose was equivalent to 537 mg of chlorpromazine (range 250 to 1,800 mg). Six patients (5.4%) received more than 1,000 mg/day of chlorpromazine or its equivalent.

Combination of neuroleptic was rare. However, about 14% of the patients received a combination of chlorpromazine with haloperidol and chlorpromazine with trifluoperazine. In both circumstances, chlorpromazine was given at night because of its sedative effect. Benzhexol was almost concurrently prescribed together with haloperidol but not with other neuroleptics.

Fifty-four (48.2%) patients received high potency drugs or a combination of high and low potency drugs, had an average peak daily dose equivalent to 601 mg of chlorpromazine. Fifty-eight (51.8%) patients were prescribed low potency drugs and their average peak daily dose was equivalent to 477 mg of chlorpromazine. Although the difference was not significant, patients who were prescribed high potency drugs tended to receive higher dose of medication than those who were only prescribed low potency drugs.

Twenty-one (13.8%) patients received additional depot preparation. Their mean peak daily dose (including the oral medication) was equivalent to 643 mg of chlorpromazine, whilst patients prescribed oral medication alone received an average peak daily dose equivalent to 512 mg of chlorpromazine. However, the difference was small and failed to reach statistical significance.

Table II – Doses of neuroleptic drugs required by patients

Peak daily doses (in mg of chlorpromazine)	Total patients (%) n=112
< 400	14 (12.5)
400 – < 600	69 (61.6)
600 – < 800	14 (12.5)
800 – < 1000	9 (8)
1000 – < 1200	3 (2.7)
> 1200	3 (2.7)

DISCUSSION

Although methodologically it was an uncontrolled study, there was no discrepancy between the recommended doses of neuroleptic (500 to 600 mg of chlorpromazine or its equivalent) and the doses actually prescribed (peak daily dose) to the patients. As a comparison with other uncontrolled studies, our peak mean daily dose of 537 mg chlorpromazine or its equivalent was much lower than the average daily dose prescribed for inpatients in Australia, 1126 mg [2]; United States, 2653 mg [3] and Spain, 1290 mg [4].

Patients who respond poorly to neuroleptic treatment usually end up consuming high doses of such medication [5]. In such patients, the neuroleptic doses are often inappropriately raised, thereby giving the impression that it was the increased in medication that reduced the symptoms, when in actual fact, it was the passage of time on medication. This was in line with our finding that the length of stay was significantly correlated with doses of neuroleptics. The patients who stayed longer tended to receive high doses of medication in view of their poor response to the treatment. We also observed the trend that high potency drugs were given at higher doses than low potency drugs as noted in earlier studies [2,3].

There are three explanations why the prescribed dose was much lower than what was found in other uncontrolled studies. Firstly, the patients might have required less amount of drugs due to lower body weight as compared with Caucasians. The existence of ethnic variation in drug requirement was also supported by other observations and clinical impressions [9,10]. Secondly, the majority of the patients were neither aggressive nor chronic. As a teaching hospital, we manage to control the admission rate of such patients. Aggressive or chronic patients were sent to a nearby psychiatric unit of a general hospital. For less disturbed and chronic patients, the drug requirement was lower. Peralta et al [4] found that high doses of neuroleptics were employed to control disruptive behaviour rather than treating the psychotic episode. Lastly, we are not under any pressure to discharge patients by including rapid remission with high doses of neuroleptics or putting patients on ECT unnecessarily.

CONCLUSION

This uncontrolled study, though not conclusive, provides compelling evidences that Asian patients may need lower doses of neuroleptics. The final conclusion on whether Asian patients really require lower doses of neuroleptics or not, could be answered by a well-designed, fixed-dose comparative study which can be conducted within Asia and other countries, in order to avoid cultural bias.

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