



ORIGINAL ARTICLE

# Evaluation of Defined Daily Dose, percentage of British National Formulary maximum and chlorpromazine equivalents in antipsychotic drug utilization



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## KEYWORDS

Antipsychotics;  
Chlorpromazine equivalents;  
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Schizophrenia

**Abstract Objective:** The present study was carried out to investigate and compare the three methods for calculating total antipsychotic dose among outpatients with schizophrenia attending primary psychiatric health care centers. The three methods were: Defined Daily Doses (DDD), chlorpromazine equivalents (CPZeq) and percentages of the British National Formulary (BNF) maximum.

**Methodology:** Antipsychotic drug dosing data for 250 patients with schizophrenia were investigated by calculating Spearman's rank correlation coefficients. Factors associated with antipsychotic dose, expressed as DDDs, CPZeq and percentages of the BNF maximum recommended daily dose, were investigated by means of linear regression analysis.

**Results:** Spearman's correlation showed that there is a significant relationship between all pairs of the three dosing methods. In all three methods, coherence was strongest when dealing with first generation antipsychotics (FGA). Linear regression analyses showed a high degree of coherence

**Abbreviations:** %BNFmax, percentage of British National Formulary maximum; CPZeq, chlorpromazine equivalents; DDD, Defined Daily Dose (DDD); FGA, first generation antipsychotics; SGA, second generation antipsychotics.

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between antipsychotic doses expressed as DDDs, CPZeq and percentages of the BNF maximum recommended daily dose.

*Conclusion:* All three tested methods are reliable and coherent for calculating antipsychotic dosing.

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## 1. Introduction

Drug utilization studies are important in detecting drug related-problems and in assessing conformance of clinical practice to international recommendations. Such studies are not meant to find blame, but to implement regulations, and cost-effective treatment protocols. Schizophrenia is a devastating mental illness that affects around 0.3–0.7% of people at some point in their life, or 24 million people worldwide as in the World Health Organization (WHO) report 2011 (WHO, 2011). The introduction of chlorpromazine to clinical use in early 1950s and subsequent antipsychotic agents have revolutionized the treatment of schizophrenia and has led to an increase in prescribing of this category of drugs for various mental disorders. The interest in antipsychotic agents stimulated researchers in several countries to publish data regarding antipsychotic drug utilization (Alonso et al., 2004; Piparva et al., 2011). Such studies focus not only on the pattern of antipsychotic prescribing but also on the appropriateness of antipsychotic dose which is mentioned in international guidelines (Buchanan et al., 2009; NICE, 2011). Calculation of the dose of antipsychotic agents has been a subject for debate. The three methods suggested to calculate the antipsychotic dose are: Chlorpromazine equivalents (CPZeq), percentage of British National Formulary (BNF) maximum, and Defined Daily Dose (DDD) (Nose et al., 2008). Few studies have been carried out to investigate the coherence between these methods. A study by Nose et al. showed a high degree of coherence between antipsychotic doses expressed as DDDs, CPZeq and percentage of BNF maximum recommended daily dose and that the DDD system is a reliable tool for standardizing antipsychotic doses in drug utilization research (Nose et al., 2008). However Rijcken et al. found a great discrepancy between CPZeq and DDD methods of comparing antipsychotic drug doses and recommended further research in this regard (Rijcken et al., 2003).

Studies comparing the various methods for calculation of antipsychotic dosing are few. Therefore, this study was carried out to further investigate and compare the three methods for calculating total antipsychotic dose among outpatients with schizophrenia attending primary psychiatric health care centers.

## 2. Methods

The data for the present study were based on a cross sectional study conducted between August 2011 and February 2012 to investigate the prescribing pattern of antipsychotics in primary healthcare centers in northern West-Bank, Palestine. The Palestinian territories, where the study took place, comprise the West Bank, Gaza Strip and East Jerusalem. This study was carried out at four governmental primary psychiatric health-care centers located in Nablus, Tulkaram, Jenin and Qalqilia in northern West-Bank, Palestine. Patients who fulfilled the

following criteria were considered for the study: (1) their age was above 16 years, (2) they were diagnosed with schizophrenia as defined by Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), (3) they had not been suffering from an acute attack of psychiatric illness during the past year, and (4) their drug regimen had not been changed in the past 6 months as evident from their medical files. Patients who had the following characteristics were excluded from the study: (1) newly diagnosed patients and (2) patients who were not on any antipsychotic medication. The final sample collected during the study period was 250 patients. We developed data collection forms that covered the following areas: socio-demographic variables, psychiatric history, antipsychotic medication currently being used, and history of psychiatric hospitalization. Focus group discussions were continuously held between the research team to maintain rationale of the data collection process. Regular evaluations took place throughout the abstraction period to identify any problems in the data collection, the interpretation of definitions, and the application of study criteria. Before commencing data analysis, an extensive series of checks were performed for data consistency, proper sequences of data, and an evaluation of missing or incomplete data. The data collection form was modified by the principle researchers and the modified version was reviewed by experts to ensure content and construct validity. Data from the pre-test evaluation were not included in the final analysis. Approval to perform the study was obtained from the Palestinian Ministry of Health, the College of Graduate Studies at An-Najah National University and the Institutional Review Boards (IRB) committee at An-Najah National University.

### 2.1. Tested variables

#### 2.1.1. Chlorpromazine dose equivalents (CPZeq)

The CPZeq is a measure of the relative antipsychotic potencies of neuroleptics. They are generally expressed as a ratio, relative to the arbitrary value of 1, which corresponds to the antipsychotic effects of chlorpromazine. The daily dose of antipsychotic medication prescribed to each patient was converted into milligram equivalents of chlorpromazine according to conversion factors derived from the literature (Davis, 1976; Rey et al., 1989; Woods, 2003; Xiang et al., 2008; Joseph et al., 2011). Total CPZeq was constructed by calculating a total daily dose of each antipsychotic listed in the medical file. Then each converted antipsychotic-specific CPZeq amount is added to arrive at a total dose. This CPZeq equivalency is most often based on the antidopaminergic action and in general does not take into account the influence of antipsychotics on serotonergic, histaminergic, cholinergic, and adrenergic receptors. Generally, CPZeq-equivalent values per drug are ambiguous in the literature (Rey et al., 1989). The origin of the used equivalency value per study is in general quite opaque. Most likely, researchers base their equivalencies on pharmacologic drug registration studies and other available literature. As a result of this nontransparency,

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