CURRENT RESEARCH TOPICS IN PHARMACY:

Therapeutic Drug Monitoring

March 29th, 2023 13.00 PM ISTANBUL

FOR REGISTRATION:

First Session- *Moderator: Esra TATAR 13.00-14.30 PM*

Welcome- Prof. Mesut Sancar
Marmara University, Istanbul, Türkiye

Analytical techniques used for therapeutic drug monitoring **– Dr.Mohd Younis Rather**
Government Medical College Srinagar, Srinagar, India

Combination of therapeutic drug monitoring and genotyping in pharmacotheraphy- Prof.Halit Sinan Süzen
Ankara University, Ankara Türkiye

Therapeutic drug monitoring of antipsychotics – Assist.Prof.Ana V. Pejcic
University of Kragujevac, Kragujevac, Serbia

Second Session – Moderator: Betül OKUYAN 15:00-16.30 PM

How to avoid perils and pitfalls when reading epidemiological studies– Dr.Pamela Xaverius
University of Health Science and Pharmacy in St.Louis, USA

Current themes in immunosuppressive therapies: TDM research and practice -Assist.Prof.Abdikarim Abdi
Yeditepe University, Istanbul, Türkiye

TDM of antimicrobials : Role of clinical pharmacist- Assist. Prof. Emre Kara
Hacettepe University, Ankara, Türkiye

Chair
Prof. Hatice Kübra ELÇİOĞLU

Vice Chairs
Prof. Levent KABASAKAL & Assoc. Prof. Esra TATAR

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THERAPEUTIC DRUG MONITORING OF ANTIPSYCHOTICS

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Antipsychotics are drugs that are primarily used in the management of schizophrenia and other disorders with psychotic features [1]. There are many antipsychotics available for clinical use [2]. They are traditionally divided into two groups based on the receptor-binding profile, incidence of extrapyramidal side effects and efficacy against negative symptoms: first-generation (also known as 'typical', 'classical' or 'conventional') antipsychotics such as haloperidol and chlorpromazine, and second-generation antipsychotics (also known as 'atypical' antipsychotics) such as clozapine, risperidone and aripiprazole [1, 2]. Therapeutic drug monitoring (TDM) refers to the quantification and interpretation of drug concentrations in blood to optimize pharmacotherapy [3, 4]. TDM has a long history in psychiatry, but routine TDM of antipsychotics has not yet been universally accepted as a standard clinical practice [3, 4]. In 2020, the American Society of Clinical Psychopharmacology and the Therapeutic Drug Monitoring Task Force of the German Association of Neuropsychopharmacology and Pharmacopsychiatry published a joint consensus statement with the aim to assist clinicians who regularly prescribe antipsychotics to effectively implement TDM of antipsychotics in their clinical practice [4]. The consensus statement provides four levels of recommendations regarding TDM for specific antipsychotics, their therapeutic reference range in blood and laboratory alert level (threshold level above which the risk for adverse drug reactions is expected to increase) [4]. Antipsychotics for which TDM is strongly recommended (level 1 recommendation) include clozapine, fluphenazine, haloperidol, olanzapine, perazine and perphenazine [4]. For these drugs, blood level within the therapeutic range is associated with favorable clinical outcomes in terms of efficacy, as well as safety and tolerability [4]. For aripiprazole, chlorpromazine, flupenthixol, paliperidone, quetiapine, risperidone, sertindole, and ziprasidone, there are fewer data linking therapeutic blood level ranges to benefit or harm, so TDM is recommended, but with a lower level of clinical confidence (level 2 recommendation) [4]. For brexpiprazole, cariprazine, chlorprothixene, iloperidone, loxapine, lurasidone, melperone, and pimozide, TDM is considered to be useful (level 3 recommendation), but the evidence is less supportive (the link between blood level and clinical effects has not been addressed yet or only retrospectively or in single case reports, so there is a need for more data) [4]. For asenapine, there is no available evidence associating clinical effects and blood level, so TDM is only considered potentially useful (level 4 recommendation) [4]. In addition, TDM is strongly recommended for a number of specific indications regardless of the level of recommendation for any particular antipsychotic [4]. These indications include, for

http://dx.doi.org/10.29228/jrp.548

example, uncertain adherence to antipsychotics, lack of clinical response within established therapeutic dose ranges, recurrence or relapse of symptoms during maintenance treatment, adverse drug reactions, concomitant use of medications which may interfere with the metabolism of antipsychotics, specific patient populations (e.g. patients with abnormally high or low body weight or body mass index, pregnant patients, lactating patients, children, adolescents, elderly, patients with intellectual disabilities, patients with hepatic or renal dysfunction, patients with severe cardiovascular disease…), switching between the original and generic forms of antipsychotics, switching between oral antipsychotics and long-acting injectable antipsychotics (LAIs), et cetera [4]. Blood sample should be taken at steady-state [4]. Appropriate sampling time during stable dosing of oral formulations is considered to be immediately before intake of the morning dose, i.e. 24 hours after the last dose if the antipsychotic is given once daily in the morning (for drugs taken in the evening the blood draw interval is 12 hours) or immediately before the next injection for LAIs [4]. It should be noted that the therapeutic reference ranges given in the consensus statement are an orienting, population-based tool that may not always be applicable to all patients, that they are derived mainly from studies on oral antipsychotics and that they apply to the primary/specific indication of antipsychotics (schizophrenia) [4]. The following information is needed for adequate interpretation of antipsychotic blood level: demographic and clinical characteristics of the patient, comedications, indication for the TDM request, formulation of the antipsychotic, time point of the blood draw, time since the last dose change, and clinical information regarding symptom severity and response or remission, as well as adverse drug reactions [4]. Despite the promise of TDM to improve the effectiveness and safety of antipsychotics in clinical practice, some limitations should be acknowledged: (A) Therapeutic blood level ranges are derived from groups of patients who agree to be studied and their data may not generalize to usual care patients who have more comorbidities and receive multiple medications; (B) Blood level ranges of antipsychotics are almost exclusively derived from patients with schizophrenia, so more data should be collected for many other approved and off-label indications of antipsychotics; (C) TDM results are only helpful if blood sample is obtained at an appropriate time and sufficient contextual information is available; (D) There is a need for more data regarding relationship between blood level ranges for many specific antipsychotics and clinical efficacy and tolerability, as well as for more evidence in specific populations of patients (e.g. elderly, children, adolescents); (E) Lack of laboratories for TDM and costs may be significant barriers for implementing TDM of antipsychotics in some clinical care settings [4]. Despite these limitations which could mostly be addressed by additional research, TDM has the potential to become a valuable tool for solving problems in antipsychotic treatment and improving efficacy and safety of antipsychotics in clinical practice [3, 4].

Keywords: Therapeutic drug monitoring; antipsychotics; recommendations.

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http://dx.doi.org/10.29228/jrp.548