European Psychiatry 54 (2018) 117–123

Contents lists available at ScienceDirect

European Psychiatry

journal homepage: http://www.europsy-journal.com

Original article

Severe hair loss associated with psychotropic drugs in psychiatric inpatients—Data from an observational pharmacovigilance program in German-speaking countries

Katrin Druschky[a,*], Stefan Bleich[b], Renate Grohmann[c], Katharina Burda[b], Helge Frieling[b], Thomas Hillemacher[b,d], Alexandra Neyazi[b], Susanne Stübner[e], Sermin Toto[b]

[a] Department of Neurology, University of Erlangen-Nuernberg, Erlangen, Germany
[b] Department of Psychiatry, Social Psychiatry and Psychotherapy, Hannover Medical School, Hannover, Germany
[c] Department of Psychiatry and Psychotherapy, Ludwig Maximilian University of Munich, Munich, Germany
[d] Department of Psychiatry and Psychotherapy, Paracelsus Medical University Nuernberg, Nuernberg, Germany
[e] Department of Psychiatry, Kbo-IAK, Academic Teaching Hospital of the Ludwig-Maximilian University, Haar, Munich, Germany

ARTICLE INFO

Article history:
Received 28 May 2018
Received in revised form 20 August 2018
Accepted 20 August 2018
Available online xxx

Keywords:
AMSP programme
Severe hair loss
Antipsychotic drugs
Antidepressant drugs
Psychotropic drugs

ABSTRACT

Background: The study aimed to investigate severe hair loss related to psychotropic drugs (PDs) by using data from the drug safety programme Arzneimittelsicherheit in der Psychiatrie (AMSP).
Methods: Data on PD utilization and reports of severe PD-related hair loss were collected in 83 psychiatric hospitals in Austria, Germany and Switzerland during the period 1993–2013.
Results: Out of 432,215 patients under surveillance, 404,009 patients were treated with PDs for the main indications of depression, schizophrenic disorder, neurosis, mania, and organic psychosis. Severe hair loss related to PD treatment was reported in 43 cases (0.01%). The rates of hair loss under antipsychotic drugs were slightly lower than the mean rates of all PDs and antidepressant drugs. Valproic acid was related to the highest risk. In 6 of the 43 cases, hair loss was imputed to multiple drugs, with 4 cases imputed to double drug combinations and 2 cases to triple combinations. Rates of severe hair loss under valproic acid (VPA) and lithium salts were distinctly lower as compared with the overall rates reported in literature. Severe hair loss under PD treatment was reported significantly more often in female patients than in male patients ($p < 0.01$).
Conclusion: The rate of severe PD-related hair loss was very low in the present survey. The large number of patients included in this multicentre study allows for assessment and comparison of hair loss rates related to different PDs and groups of PDs and provides new and supplementary information on PD-related hair loss.

1. Introduction

While the occurrence of psychotropic drug (PD)-associated hair loss is considered a rare or infrequent event [1], when it occurs its psychological and psychosocial effects are significant. There are still no reliable treatments available for hair loss and only few successful management options reported in the literature, including for example, topical and oral corticosteroids and the sensitizing agents diphenylcyclopropenone and dinitrochlorobenzene as potentially effective treatments for alopecia areata [2].

The currently available information on PD-associated hair loss from the medical literature is rather weak and often limited to case reports [3]. Confirmation of drug-induced hair loss is difficult indeed since evidence in the strict sense requires both resolution after discontinuation and reoccurrence after reexposure, the latter not easily being tolerated by affected individuals. Daily loss of up to 150 hairs is regarded as normal, yet, 25–50% of the head hair must be lost before hair thinning becomes clinically apparent [4,5]. Hair loss can occur for many reasons, ranging from genetic to environmental factors. Androgenetic hair loss, by far the most common cause of hair loss [6], develops in hereditarily predisposed men and women and may be considered part of the natural ageing process. Non-androgenetic hair

* Corresponding author at: Department of Neurology, University of Erlangen-Nuernberg, Schwabachanlage 6, 90451 Erlangen, Germany.
E-mail address: katrin@druschky.de (K. Druschky).

http://dx.doi.org/10.1016/j.eurpsy.2018.08.003
0924-9338/

loss can appear under treatment with various drugs or because of toxins, infections, trauma, stress, autoimmune diseases, malnutrition, and endocrine dysfunctions [7,8]. Hair growth essentially comprises two main cyclical phases: the anagen and telogen phases. In the anagen phase, which lasts from several months to a decade, new hair shafts are produced. Approximately 80–90% of the scalp's hair follicles are in this active stage [9]. Telogen, the resting phase, lasts from 2 to 4 months and results in the shedding of the hair shaft. Drug-induced hair loss can either affect the anagen or the telogen phase. Anagen hair loss is typically seen with chemotherapeutic medications and occurs at the time of toxic exposure in a dose-related manner [3,4]. By contrast, telogen effluvium is based on the premature interruption of growth with an early entry of anagen follicles into the resting phase [10]. The established causative factors of telogen effluvium include: iron deficiency, anemia, hyper- or hypothyroidism, delivery, inadequate diet, oral contraception or its discontinuation, accidental exposure to toxic substances, chronic renal insufficiency, and secondary syphilis [11,12]. Causative medications comprise beta-blockers, angiotensin-converting-enzyme inhibitors, anticoagulants, oral contraceptives, antithyroid medications, nonsteroidal anti-inflammatory and uricosuric agents, histamine-2-antagonists, lipid-lowering agents, chemotherapy, anticonvulsants, and psychotropic drugs such as several mood stabilizers, certain antidepressants, and some antipsychotics [7,11–13]. Hair loss related to these medications usually appears a few months after starting the medication and is a reversible phenomenon [1].

In the present report, we will describe hair loss as a severe adverse drug reaction related to psychotropic drugs in the routine treatment of psychiatric inpatients using data from the Arzneimittelsicherheit in der Psychiatrie drug safety programme in psychiatry (AMSP). The rates of severe hair loss associated with antidepressants, antipsychotics, mood stabilizers, and other psychotropic drugs were assessed, along with the underlying psychiatric diseases, dosages administered, patient age and sex, and other known risk factors causing hair loss in the respective cases. The large sample size of over 430,000 patients included in this multicentre study will for the first time enable direct comparisons between different PDs and groups of drugs with respect to their related risks of hair loss.

2. Methods

The AMSP project was started at the Psychiatric University Hospital of Munich in October 1993 as a continuous multicentre drug surveillance programme serving to assess severe adverse drug reactions (ADRs) in the routine clinical treatment of psychiatric inpatients. ADRs of basically all different organ systems (e.g., psychic, neurologic, gastrointestinal, dermatologic, cardiovascular, haematologic) are acquired. For AMSP purposes, psychotropic drugs also include neurologic drugs such as anticonvulsants and antiparkinsonian drugs.

2.1. Severe adverse drug reactions

An ADR is generally rated as severe for three reasons: if it is potentially life-threatening or seriously endangers the patient's health; if it considerably impairs everyday functioning; or if it requires the patient's transfer to another department providing more intensive care [14]. In addition to these overarching criteria, the AMSP study protocol provides additional, more specific guidelines to better coordinate with individual organ classes [15].

2.2. Severe drug-related hair loss and risk factors

Severe hair loss in the present study was determined if the patient and the treating physician ascertained a marked or extreme degree of loss in terms of bundles or bunches when combing, washing, or running the fingers through the hair. Other hallmarks included significant thinning of the head hair with the scalp becoming clearly visible and significant loss of body hair including the eyelashes, eyebrows and pubic hair.

Risk factors of hair loss were ascertained by comprehensive medical history, clinical assessment, and laboratory diagnostics through the attending physicians and documented in the case report files. The influence of the documented risk factors on the assessed APD related hair loss rates was addressed by the detailed analysis of each single case (see 2.4 Probability Ratings).

2.3. Pharmacovigilance methods

Psychotropic drug utilization data and reports of PD-related rates of severe hair loss were collected in 83 university, municipal, and state psychiatric hospitals in Austria, Germany and Switzerland during the period 1993–2013. The AMSP's pharmacovigilance methods have been described in detail elsewhere [14,15]. In short, pharmaco-epidemiological data are gathered at two established, fixed dates per year and include detailed information on drug prescriptions, daily dosages, and individual patient parameters (age, sex and primary psychiatric diagnosis), along with the total number of patients treated per year and per hospital. Specific information on severe adverse drug reactions under psychotropic drug treatment is collected in a second dataset. Trained psychiatrists, known as 'drug monitors', question the ward psychiatrists on a regular basis (i.e., at least every 2 weeks) about the occurrence of severe ADRs, in an open manner assisted by an item list. ADR cases are documented using standardized questionnaires. The generated reports contain a detailed description of the ADR, history, diagnosis, medication, alternative hypotheses on the causes of the ADR, relevant risk factors, countermeasures taken, course of the ADR thereafter, and previous exposures to the drug. The reported cases are discussed at regional and central case conferences that are attended by the drug monitors, representatives from the national drug regulatory authorities, and drug safety experts from the pharmaceutical industry. Assigned ADR probability ratings and the completed case reports are submitted to the relevant authorities and pharmaceutical companies and are stored in the central surveillance database for further analysis. Psychiatric diagnoses are encoded according to the WHO International Classification of Disease (ICD-10). Patient-related data are kept in anonymous form.

2.4. Probability ratings

Probability ratings for drug-related severe hair loss were based on the proposals by Hurwitz and Wade [16] and by Seidl et al. [17] and on the AMSP study guidelines [14]. Accordingly, an ADR is rated as "possible" if the ADR is not known for the drug in question, if the time course or dosage of the drug is unusual, or if alternative explanations are more probable. An ADR is rated as "probable" if the ADR is known for the given drug, the time course and dosage are in accordance with previous experience, and if alternative explanations are less likely. ADRs are rated as "definite" if the criteria of "probable" are fulfilled and if re-exposure to the drug elicits reappearance of the ADR.

A preliminary probability rating of AMSP cases is done by the drug monitor. The cases are first sighted by a senior physician of the hospital and then reviewed in detail by senior members of the AMSP management. Finally, cases are discussed at regional and central case conferences. At the regular central AMSP case conferences, attended by clinicians as well as drug safety experts from the medicines regulatory authorities and from the pharmaceutical industry, probability levels (i.e. "definitely", "probably",