Letter to the editor

Use of psychotropic drugs in physically disabled patients: One-shot prevalence and medical practice assessment in a physical and rehabilitation medicine ward

The use of psychotropic drugs in France has increased over the last 2 decades and is considered the highest in Europe [1–3]. The main drugs are anxiolytics, antidepressants, hypnotosedatives and neuroleptic agents. All are responsible for severe adverse drug reactions and addiction associated with chronic or excessive consumption over several months. Besides inter-individual variability related to genetic or pathophysiological factors, the types and occurrence of adverse events vary across the psychotropic drug classes. Drug-related adverse events commonly observed are movement disorders and spasticity (with neuroleptic agents); cardiovascular and anticholinergic effects (antidepressant drugs); and confusion and changes in cognitive status (sedative and anxiolytics agents). However, unlikely adverse events could also occur. To prevent drug abuse or misuse, psychotropic drug prescriptions are now closely controlled and monitored in terms of dosage, therapeutic indication and duration with national public policies [1,3]. However, the use of psychotropic agents (sometimes in the long-term) can be necessary in rehabilitation units to treat neurological, psychological or behavioural disorders such as epilepsy, depression, anxiety, agitation or sleep disorders.

In brain injury rehabilitation units (BIRU), particular attention must be paid to psychotropic drugs for their negative effect on central nervous system recovery and cognition after stroke or brain injury [4]. Moreover, the effects of psychotropic drugs are usually studied in the general population but not specifically in patients with brain injury. Thus, little is known about the adverse and cumulative effects of psychotropic drugs in such patients.

This present study aimed to examine the prevalence of psychotropic drug use in an inpatient BIRU rehabilitation population. We conducted a one-day quick-audit of psychotropic drug prescription in the BIRU of our hospital on July 3, 2014 to assess the prescription prevalence and type of prescriptions and to evaluate professional practice. Hospitalized patients receiving antiepileptics, antidepressants, benzodiazepines (BZDs), neuroleptics and histamine-H1 antagonists were included and their treatments studied. Data on patients and treatments were collected from patient medical files and computerized medical prescriptions (computerized physician order software Pheidra®,)

In total, 55 patients (mean age 51.9 ± 18.3 years; 38 males) were hospitalized on the day of the audit. Most (n = 33; 60%) were admitted for vascular aetiology (stroke or cerebral haemorrhage), 10 (18%) severe traumatic brain injury (TBI) and 8 (15%) other types of brain injury (autoimmune or infectious encephalitis). A total of 46 (84%) were receiving at least one psychotropic drug and 31 (56%) had received a prescription before hospitalization. The prevalence of this type of prescription was 1.8-fold higher than in the French general population [3].

The characteristics of drug prescriptions are in the Table 1. For the 38% of psychotropic drugs that were introduced during hospitalization, the prescription was explicitly justified in the patient’s medical record in only two thirds of cases (62%). Therefore, the implementation of clinical guidelines could be helpful for physicians in choosing and justifying the most appropriate drugs, especially after stroke, as was recently published for TBI [5]. Levetiracetam and pregabalin were the 2 second-generation antiepileptic drugs most often prescribed. Norepinephrin and/or serotonin re-uptake inhibitors (NSRI) and/or SSRI) were the most common antidepressants used: paroxetine and fluoxetine (SSRIs) and venlafaxine (NSRI).

Neurobehavioural sequelae are commonly described in rehabilitation medicine after stroke or TBI [6,7]. The incidence of seizure has been extensively studied and ranges from 4% to 50%, depending on the population studied [8–10]. Although data are controversial, the risk of seizure would be 20- to 40-fold higher after stroke than in the general population [8]. In our study, when anti-convulsant medication was required, the use of a second-generation antiepileptic drug such as levetiracetam was predominant. Pregabalin was exclusively used for neurological pain. Indeed, these second-generation drugs have been recommended over older-generation drugs (e.g., phenytoin or phenobarbital) for both safety and efficacy [10,11]. Moreover, most of these new-generation drugs do not have clinically important enzyme-inducing or -inhibiting effects involved in the management of drug–drug interactions frequently observed in polymedicated patients. Similarly, mood disorders such as depression and anxiety are also frequent after stroke or TBI, with an estimated prevalence of 30% [12]. The frequency of antidepressant drug prescriptions we found (28%) supports these epidemiological data.

The BZD prescription analysis showed that alprazolam was most represented in this study, which agrees with the French BZD consumption survey [1]. However, the duration of BZD dose was therefore higher (mean of 62 days/prescription) than usually recommended by French guidelines (as short as possible) [1]. Overall, 10% of our patients received co-prescription with other BZDs or BZD-like agents (zopiclone or zolpidem), especially for sleep disorders and agitation. Many patients receive a prescription for anxiolytic or hypnotosedative drugs during hospitalization: up to 33% to 60% of hospitalized patients [13]. The use of these drugs is also not an exception in the BIRU. However, this type of prescription should be performed cautiously and gradually because of a risk of dependence after long-term treatment and attention deficiency and deleterious effects on neuronal plasticity. Therefore, anxiolytics and hypnotosedative drugs should not be co-prescribed and should be stopped as soon as possible when their prescription is no longer needed, as for other psychotropic drugs. Indeed, GABA agonists such as BZD could be responsible for a great

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number and multiple adverse effects because of the wide distribution of receptors found in a number of areas, including the spinal cord, cerebellum, limbic areas and cerebral cortex [14]. Moreover, despite increasing evidence that psychotropic agents may affect structural and/or functional plasticity, the benefit or deleterious effects of these drugs on neuroplasticity is currently debated. Cellular and molecular imaging studies have revealed that antiepileptics and antidepressants (SSRIs and tricyclic antidepressants) could enhance the plasticity of neuronal connections by amplifying intracellular signaling cascades [15]. Within the group of neuroleptic agents, neuroplasticity would depend on the molecule: first-generation molecules (e.g., haloperidol) would be associated with neurotoxic effects (decline in brain-derived neurotrophic factors), whereas second-generation agents such as olanzapine and clozapine could promote neuroplasticity [15].

Our findings suggest a lack of evidence for the deleterious effects of some psychotropic drugs in the recovery of brain-damaged patients, especially after stroke, whereas current recommendations restricting psychotropic prescription are based on general population data. Specific studies including patients with brain injury as well as specific recommendations are needed for good clinical practice.

Finally, we found that behavioural disorders were rarely managed with neuroleptics as compared with BZDs, which are still the most commonly prescribed psychotropic agents despite a benefit-to-risk ratio that has yet to be demonstrated. This observation could be explained by the prescribing habits of physicians, which are mostly oriented to symptoms rather than evidence-based medicine. Moreover, these compounds are known to be deleterious for rehabilitation and could increase the risk of stroke [16]. For these previous reasons, the use of BZDs and/or neuroleptics should be reserved for very short-term second-line therapy to treat behavioural disorders after TBI [5].

Despite the limitations of this one-day quick-audit (observational data, short time to collect data, limited number of patients), this study allowed us to take a snap-shot of the prescription characteristics in these cases and especially confirms that psychotropic drugs are widely used for the management of rehabilitation in these cases. However, their use should be subject to a benefit/risk evaluation and must be amply justified to avoid a deleterious effect on rehabilitation and functional recovery [17].

As described by Pettrissans et al. in a 6-month psychotropic drug prescription retrospective study [18], our findings demonstrate that psychotropic treatments could be optimized in clinical practice. According to the French Physical and Rehabilitation Medicine Society (SOFMER) guidelines for evaluation, treatment and follow-up concerning behavioural disorders, some specific points could be improved, such as the use of beta-blockers (propranolol) for aggressiveness instead of BZDs in TBI patients [5]. Moreover, the use of neuroleptics should be limited to loxapine only for crisis emergency. Efforts will also be made to avoid BZD co-prescription and to improve traceability and pharmacological justifications in the patient’s medical file. In addition, systematic and constant relevance assessment of pharmacological and/or non-pharmacological treatment is essential to improve care.

Disclosure of interest

The authors declare that they have no competing interest.

References


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Table 1

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number of drugs prescribed/patient, mean ± SD</th>
<th>Number of psychotropic drugs prescribed/patient, mean ± SD</th>
<th>Number of patients receiving ≥ 2 psychotropic drugs</th>
<th>Duration of psychotropic drug treatment (days), median (min–max)</th>
<th>Number of psychotropic drugs introduced during hospitalization</th>
<th>Class of psychotropic drugs prescribed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of drugs prescribed/patient, mean ± SD</td>
<td>10.1 ± 4.2</td>
<td>2.3 ± 1.0</td>
<td>34 (74)</td>
<td>48.5 (1–332)</td>
<td>17 (38)</td>
<td>Antiepileptic drugs</td>
</tr>
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<td>Benzodiazepines or benzodiazepine-like agents</td>
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<td>17 (38)</td>
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<td>10.1 ± 4.2</td>
<td>13 (28)</td>
<td>Histamine-H1 antagonists</td>
</tr>
<tr>
<td>Number of psychotropic drugs introduced during hospitalization</td>
<td>17 (38)</td>
<td>13 (28)</td>
<td>11 (24)</td>
<td>4 (9)</td>
<td>2 (4)</td>
<td>Neuroleptic drugs</td>
</tr>
<tr>
<td>Class of psychotropic drugs prescribed</td>
<td>Antiepileptic drugs</td>
<td>Antidepressant drugs</td>
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Data are no. (%) unless indicated.