

Utilisation of Lithium in Psychiatry in Lubumbashi. Case of the Jason Sendwe Provincial General Referral Hospital

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Abstract

Introduction: Lithium is regarded as the primary pharmacological intervention for managing bipolar disorder and various other psychiatric conditions. Nevertheless, owing to its limited therapeutic window, diligent monitoring is imperative to avert toxicity, even when administered at therapeutically effective doses. The present investigation was undertaken to explore the utilization of lithium in psychiatric practice within the context of Lubumbashi. **Method:** A hospital-based cross-sectional descriptive observational study was conducted on 22 patients undergoing lithium therapy at the Neuropsychiatry Department of HPGR Jason Sendwe between January and December 2023. The sample was inclusive, and data, anonymised, were sourced from patient consultation and follow-up records, subsequently input and analysed using Epi Info 7.2 and Microsoft Excel 2019 software. **Results:** The prescription rate of lithium was 4.17%. The primary indications included bipolar disorder and schizoaffective disorder (50.00%). No preemptive identification of high-risk patients was conducted. Lithium was predominantly prescribed in a sustained-release formulation (100%) at a daily dosage of 400 mg for the majority of patients (80.95%). Furthermore, a significant portion of cases exhibited psychotropic polypharmacy. Lithium was frequently co-prescribed with Haldol (50.00%), Chlorpromazine (40.91%), and Artane (22.73%). Treatment duration averaged 5.64 ± 4.45 days, with patients lacking any monitoring protocol. **Conclusion:** Our findings highlight the administration of lithium without adequate patient monitoring or follow-up. This deficiency in monitoring poses potential health risks to patients, including drug interactions and adverse effects. Substantial enhancements are essential to ensure the safe and efficacious utilisation of lithium in clinical settings.

Keywords: Bipolar Disorders, Lithium, Prescription, Side-effects, Survey, Treatment.

Introduction

Psychiatric disorders are prevalent in the Democratic Republic of Congo, ranking as the third most common reason for hospitalisation, despite the absence of national epidemiological data [1, 2]. An estimation derived from statistics at two psychiatric facilities, the Psychiatric Center for Mental Health Care (SOSAME) in the post-crisis region of Bukavu, and the Neuropsychopathological Center of Katwambi (CNPP) in the Kasai province,

reveals that 13 to 23% of patients exhibit mood disorders, encompassing manic episodes, depressive disorders, and bipolar disorder [2].

Lithium is recognised as the preferred pharmacological agent for managing bipolar disorder and various other psychiatric conditions. However, owing to its narrow therapeutic index, diligent monitoring is imperative to avert toxicity, even at therapeutic doses. Lithium toxicity typically manifests when blood levels surpass 1.5 mEq/L, with

potential for fatal consequences at concentrations exceeding 5 mEq/L [3-6].

Regular laboratory assessments every 3 to 6 months are advised to ensure proper monitoring. Monitoring protocols typically encompass initial and routine evaluations, electrocardiograms, plasma lithium concentration measurements, renal function tests, and assessments of thyroid and parathyroid function [6, 7]. Vigilant monitoring is critical to detect potential complications, such as T-wave flattening on electrocardiography, lithium-induced hypothyroidism, and nephrogenic diabetes insipidus. Additionally, lithium therapy may elevate creatinine levels, thyroid-stimulating hormone, neutrophil counts, and blood glucose levels [3].

It is crucial to highlight that close monitoring is essential for patients undergoing lithium treatment, as its use is contraindicated in settings lacking rigorous monitoring [3]. In the city of Lubumbashi, our research environment, challenges surrounding the appropriate utilisation of lithium in psychiatric care necessitate concerted efforts to ensure its judicious prescription. For many individuals with bipolar disorder, the administration of lithium salts is essential for mood stabilisation and the prevention of manic and depressive episodes.

Challenges within the local medical infrastructure in this region include inadequacies in facilities, equipment shortages, and limited laboratory capacities. Despite the pivotal role of laboratory tests in diagnostics and treatment planning, most medical laboratories in Lubumbashi lack the resources to conduct comprehensive medical examinations.

Moreover, in the Democratic Republic of Congo, the high cost of healthcare relative to the population's income often renders medical services inaccessible to the economically disadvantaged [8]. The health system's financing primarily relies on direct user

payments, with over 93% of households requiring out-of-pocket payments for healthcare access. This financial burden significantly impedes access to medical facilities, laboratories, medicines, and healthcare services for the vast majority of the population living below the poverty threshold.

These challenging conditions compromise the feasibility of ensuring adequate monitoring for patients undergoing lithium therapy. The region's medical facilities lack the resources necessary to conduct plasma lithium concentration tests, hindering appropriate medication monitoring. Notably, local medical facilities cannot measure lithium levels, necessitating sample analysis in Belgium at a substantial cost of approximately 120 euros.

According to Andrade et al., infrastructure limitations and testing costs, where available, may influence the decision to prescribe lithium in regions with constrained universal healthcare access. The prohibitive costs associated with testing may explain the preference for alternative therapeutic options among mental health professionals in the private sector, where patients are required to cover the expenses of mandatory tests themselves [9].

Therapeutic alternatives that offer rapid efficacy without necessitating routine blood tests, such as certain antiepileptic agents (carbamazepine, lamotrigine, sodium valproate) and several antipsychotics, have gained prominence. These alternatives present viable solutions to circumvent the challenges associated with lithium prescription under local circumstances. Nonetheless, it is crucial to emphasise that despite the expenses related to lithium testing, its overall cost-effectiveness surpasses that of valproic acid and antipsychotics in both developed and developing nations [11].

Despite the risk of toxicity, lithium remains a highly specific medication supported by robust evidence for the acute and maintenance treatment of bipolar disorder and mood disorders in general [12-14]. Therefore,

enhancing the prescription practices of lithium in our setting is imperative.

This investigation was undertaken to assess the utilisation of lithium in psychiatric care in Lubumbashi, Democratic Republic of Congo, analysing its frequency, prescription modalities, and adherence to scientific guidelines. The study aims to identify the strengths and weaknesses of current practices, proposing avenues for improvement to ensure the optimal and safer use of this medication. This study represents the initial analysis of lithium usage and its intoxication risks in psychiatric care in Lubumbashi.

Methods

Our study, focusing on the utilisation of lithium in clinical practice, was conducted within the Neuropsychiatry Department of Jason Sendwe Provincial Referral General Hospital (Jason Sendwe HPGR). The selection of this healthcare facility as our study site was based on several key factors:

1. It boasts a cadre of skilled medical professionals, including specialists and professors affiliated with the University of Lubumbashi.
2. Healthcare services at this institution are priced affordably, ensuring accessibility for a significant portion of the population.
3. The hospital houses one of the largest Neuropsychiatry departments in Lubumbashi, catering to patients from diverse areas within the city and beyond.

Situated in the Lubumbashi health zone, Jason Sendwe Provincial Referral General Hospital is positioned in the eastern sector of Lubumbashi commune, bordered to the north by Sendwe Avenue, south by School Avenue, east by Wema High School, and west by Likasi Avenue. With a potential capacity of 1,200 beds, SENDWE Hospital ranks second only to the Kinshasa General Hospital. Our research was specifically carried out within the

Neuropsychiatry Department, which encompasses a dispensary, emergency services, two pavilions for inpatient care (Pavilions 7 and 11), as well as various offices and consultation rooms. The department's medical team comprises 3 neurologists, a neuropsychiatrist, 7 general practitioners, and 8 nurses, employed under civil servant, contractual, or volunteer roles.

This study presents a cross-sectional descriptive observational analysis of lithium utilisation. We included 22 patients who underwent lithium therapy and were hospitalised in the Neuropsychiatry Department of Jason Sendwe Provincial General Referral Hospital (HPGR Jason Sendwe) between January 1 and December 31, 2023. Patient medical records were scrutinised, encompassing demographic details such as age, gender, marital status, occupation, medical history, and psychiatric background. Additionally, information about lithium treatment, including prescribing frequency, indications, formulations, dosages, pre-treatment, ongoing, and post-treatment paraclinical assessments, as well as treatment duration, was compiled. Data collection occurred from January 25 to January 31, 2024. Collected data were input into survey sheets and subsequently analysed using Epi Info 7.2 and Microsoft Excel 2019 software. Patients with incomplete data were excluded from the analysis. Qualitative variables were delineated by proportions, while quantitative variables were represented by means and standard deviations (SD).

Results

Throughout the study duration, a total of 528 patients were admitted to the Neuropsychiatry department of HPGR Jason Sendwe. Among these patients, lithium was prescribed to 22 individuals, constituting a proportion of 4.17%.

Table 1. Demographic Data of Patients Treated with Lithium

Variables	No. (22)	%
Sex		
Male	11	59.09
Female	9	41.11
Age		
14 - <23	3	13.64
23 - <32	7	31.82
32 - <41	8	36.36
41 - <50	1	4.55
50 - <59	2	9.09
68 - ≤	1	4.55
Marital status		
Bachelor	6	27.27
Divorce	6	27.27
Married	10	45.45
Occupation		
Butcher	1	4.55
Driver	1	4.55
Electrician	2	9.09
Teacher	1	4.55
Student	5	22.70
Engineer	1	4.55
Mason	1	4.55
Housewife	8	36.36
Welder	1	4.55
Saleswoman	1	4.55
Residency (Municipality)		
Annexe	7	31.82
Other*	1	4.55
Kamalondo	1	4.55
Kampemba	2	9.09
Katuba	3	13.64
Lubumbashi	8	36.36

*Outside Lubumbashi (Kasumbalesa)

Table 1 illustrates that the majority of patients were male (59.09%), resulting in a sex ratio of 1.44. Their ages ranged from 14 to 68 years, with an average age of 36.55 ± 13.15 years. A considerable portion of the patients were married (45.45%), engaged in household occupations (36.36%), and resided in the

Lubumbashi and Annexe municipalities (68.18%).

Among the 22 patients treated with lithium, a majority had a history of psychiatric crises (59.09%). Notably, 22.73% reported alcohol consumption, 13.64% tobacco use, and 4.55% had a history of head trauma (Table 2).

Table 2. Medical and Psychiatric History of Patients Treated with Lithium

Medical and psychiatric History	No. (22)	%
Alcohol	5	22.73
Tobacco	3	13.64
Head trauma	1	4.55
Psychiatric crisis	13	59.09

Lithium prescriptions were exclusively made by general practitioners, targeting various indications: bipolar disorder (27.27%), schizoaffective disorder (22.73%), schizophreniform disorder (13.64%), agitated depression (13.64%), recurrent mania, and

delusional disorder (9.09%). The sustained-release formulation of lithium was predominantly prescribed (100%), with a mean dosage of 400 mg administered once daily in most patients (80.95%). The average treatment duration was 5.65 ± 4.45 days (Table 3).

Table 3. Lithium Prescription Terms

Variables	No. (22)	%
Quality of the prescriber		
General practitioner	22	100.00
Indications		
Agitated depression	3	13.64
Recurrent mania	3	13.64
Bipolar disorder	6	27.27
Delusional disorder	2	9.09
Schizoaffective disorder	5	22.73
Schizophreniform disorder	3	13.64
Route of administration		
Oral	22	100.00
Formulation		
Immediate-release	0	0.00
sustained-release	22	100.0
Dose (mg)		
200	5	14.29
400	17	80.95

Table 4. Medications Associated with Lithium

Related medications	No. (22)	%
Anafranil (Clomipramine)	2	9.09
Artane (Trihexyphenidyl Hydrochloride)	5	22.73
Haloperidol (Haldol)	11	50.00
Chlorpromazine	9	40.91
Promethazine	3	13.64
Tegretol (Carbamazepine)	1	4.55
Vitamin B1	1	4.55
Diazepam	1	4.55

Table 4 highlights a notable frequency of psychotropic polypharmacy, with lithium commonly co-prescribed alongside other medications such as Haldol (50.00%), Chlorpromazine (40.91%), and Artane (22.73%).

Moreover, it is noteworthy that only 6 patients (27.27%) underwent paraclinical

examinations before commencing treatment. These tests primarily served diagnostic purposes and included urea tests (100.00%), creatinine tests (100.00%), complete blood counts (83.33%), and electroencephalography (83.33%) (Table 5).

Table 5. Paraclinical Assessment of Patients Treated with Lithium

Paraclinical assessment	No.	%
Non	16	72.73
Yes	6	27.27
Total	22	100.00
Paraclinical Tests Conducted	No. (22)	%
Creatinine	6	100.00
Urea	6	100.00
EEG	5	83.33
FBC	5	83.33

Discussion

Frequency and Indications

Lithium has served as a cornerstone in the treatment of psychiatric conditions for over five decades [4]. Despite its narrow therapeutic window, lithium remains the predominant pharmacological choice for managing bipolar disorder due to its well-established efficacy [15]. However, globally, its utilisation is waning for various reasons. Primarily, concerns regarding side effects and the potential for toxicity have deterred many patients. Moreover, factors such as the absence of robust pharmaceutical marketing, patient reluctance, the delayed onset of action, and inadequate resources for vigilant monitoring have collectively contributed to this declining trend [10]. Additionally, the diminishing use of lithium, particularly in manic episodes, can be attributed to the emergence of more aggressively promoted and rapidly effective therapeutic alternatives that do not necessitate regular blood tests. These alternatives encompass medications initially developed for other conditions, including specific

antiepileptic agents (carbamazepine, lamotrigine, sodium valproate) and many antipsychotics [10].

Conversely, Spain exhibits a higher lithium utilisation rate, potentially influenced by a local inclination favouring its administration. Several factors underpin this inclination: Firstly, the transfer of expertise from seasoned therapists to less-experienced practitioners may perpetuate this practice. Furthermore, institutional backing facilitating the establishment of appropriate monitoring infrastructures for patients on lithium, such as specialised clinics and national registries, might bolster its utilisation. Ultimately, the active advocacy for lithium use by local scientific societies appears to be a pivotal determinant in sustaining this practice in Spain, contrary to observations in other nations [16].

In Lubumbashi (DRC), lithium prescription rates are comparatively lower than in other countries. In our study, only 4.17% of patients received lithium, in contrast to rates of 70% in the Netherlands, 55% in Sweden, 41.7% in Denmark, 26.2% in Germany, 22% in Scotland,

and 17% in the United States [10]. Several factors could account for this disparity, including the availability of alternative treatments, the absence of extensive lithium marketing in Lubumbashi, and its high cost. Notably, our study did not encompass prescriptions for outpatients. Thus, we posit that this frequency is underestimated, emphasising the necessity for more comprehensive studies to ascertain the true prevalence and elucidate the rationales behind the subdued prescription of lithium in Lubumbashi.

Lithium finds primary indications in the treatment and prophylaxis of bipolar disorders (manic-depressive illnesses). It is also employed to alleviate affective symptoms linked with schizophrenia and other psychiatric conditions such as post-traumatic stress disorder, schizoaffective disorder, acute manic episodes, and neuropathies [4, 15, 17]. Our findings are consonant with existing literature, with bipolar disorders and schizoaffective disorders representing the most prevalent indications in our study (50%).

Factors Associated with Lithium Toxicity

Lithium is a medication associated with serious effects and risks of interaction, and poisoning. For this reason, patients undergoing lithium treatment must be closely monitored to prevent and quickly diagnose side effects, poisoning and treatment failures [4].

To this end, a detailed baseline assessment of the patient's medical history, thyroid, heart and kidney function can provide doctors with valuable information. These elements make it possible to identify risk factors for lithium poisoning, such as advanced age, comorbidities and concomitant drug treatments, which reduce lithium tolerance [18].

Age and Gender

It is now well-established that elderly patients exhibit a lower tolerance to lithium

compared to their younger counterparts. They are prone to developing serious adverse effects more rapidly, even at lower doses or serum levels [18]. The heightened vulnerability of the elderly can be attributed to two primary factors: the natural ageing process affecting the functionality of the brain, heart, and kidneys, leading to a decline in their efficiency; and the increased prevalence of comorbidities in this demographic, elevating the associated risks.

Moreover, individuals over the age of 50 may experience a decrease in physical resilience due to ageing and/or heightened polypharmacy, both of which predispose them to lithium intoxication. This susceptibility may also be exacerbated by advanced cerebral arteriosclerosis, suggesting that cerebral structural damage contributes to lithium-related neurotoxicity [5].

Furthermore, lithium toxicity is more likely to manifest in women than in men, and in patients with mood disorders as opposed to those with schizophrenia [19]. In our study cohort, the age range of patients undergoing lithium treatment spanned from 14 to 68 years, with an average age of 36.55 ± 13.15 years and a male predominance indicated by a sex ratio of 1.44 (59.09%). The majority of patients did not exhibit a significant risk of poisoning based on their age. However, 13.64% of patients receiving lithium were aged over 50 years, placing them at higher risk for developing lithium toxicity.

Clinical Features

Patients with specific comorbidities, including cardiovascular conditions (such as hypertension, heart failure, and atherosclerosis), neurological disorders (such as Parkinson's disease, epilepsy, dementia, schizophrenia, and stroke), and kidney diseases, are at an elevated risk of lithium poisoning. These underlying health conditions can impede renal function and diminish the clearance of lithium, which is the sole elimination mechanism for this medication.

Additionally, some of these comorbidities lower the threshold for lithium-induced cardiotoxicity and neurotoxicity [18]. Research has indicated that pre-existing neurological disorders may heighten the susceptibility to developing toxicity [19].

Interestingly, in the patient cohort under study, there was no systematic screening for these comorbidities before treatment initiation, nor was there a history of lithium intoxication documented. However, a comprehensive initial evaluation would enable the identification of these risk factors and allow for treatment adjustments accordingly. The only documented medical history included psychiatric crises (59.09%), alcohol and tobacco consumption (22.73% and 13.64%, respectively), and head trauma (4.55%).

Formulation, Dosage and Associated Medications

Lithium is available in immediate or sustained-release preparations, with dosages typically commencing at a low level [15, 20]. In older patients, lithium doses should be reduced by approximately 20% compared to younger patients, as determined by the treating clinician [21]. It is crucial to adhere to the prescribed lithium dosage regimen, without doubling missed doses. Single daily dosing can be convenient and is sometimes preferred over divided doses. Altering the brand or type of lithium salt used may necessitate dosage adjustments under medical supervision. Gradual discontinuation of lithium is recommended to prevent relapse into mania or depression, unless urgent medical reasons mandate rapid cessation under close medical observation. Reduction of lithium dosage can be safely achieved by decreasing the daily dose by 20–25% every 2 weeks [16].

In our study, sustained-release lithium was the predominant formulation prescribed to patients (100%), typically at an average dose of 400 mg once daily in the majority of cases (80.95%). The average treatment duration was

5.65 ± 4.45 days. Notably, all patients received a uniform dosage without considering age and other risk factors. Furthermore, treatment cessation was often abrupt and unsupervised in the majority of patients treated with lithium.

Lithium, an alkali metal, is not metabolised and is directly absorbed from the gastrointestinal tract. It does not bind to serum proteins, existing either freely in extracellular fluid or within cells. The transition from the extracellular to intracellular compartments occurs over several hours, rendering the prediction of tissue toxicity challenging based solely on serum levels. The elimination half-life of lithium varies from 12 to 48 hours, with chronically treated individuals and the elderly exhibiting longer half-lives. Renal elimination primarily drives lithium excretion, and medications that impede renal function, such as ACE inhibitors, NSAIDs, and diuretics, can significantly affect lithium elimination, potentially leading to toxicity [15].

It is crucial to be mindful of drug combinations, a common cause of lithium poisoning, especially when used concomitantly with diuretics or ACE inhibitors [5, 20]. Furthermore, individuals treated with antipsychotic medications such as haloperidol, risperidone, or quetiapine alongside lithium are at higher risk of neurotoxicity. Therefore, psychotropic polypharmacy should be avoided, particularly in patients with pre-existing neurodevelopmental disorders [19]. In our investigation, a notable frequency of psychotropic polypharmacy was observed, with lithium frequently prescribed alongside other medications like Haldol (50.00%), Chlorpromazine (40.91%), and Artane (22.73%).

Identifying at-risk patients and prescribing appropriate lithium dosages are crucial in preventing poisoning. Nonetheless, healthcare providers need to recognise that lithium toxicity can occur even in the absence of apparent risk factors. Consequently, regular monitoring of all

patients treated with lithium is imperative to promptly detect any signs of toxicity [18].

Pre-therapeutic Assessments and Monitoring

Lithium continues to be a crucial component in the management and prevention of bipolar disorder. Rigorous monitoring and consistent medical oversight are essential to prevent side effects, drug interactions, and severe poisoning. Patients should undergo thorough monitoring at the initiation of treatment, during dosage adjustments, and throughout maintenance therapy [4]. Regular laboratory tests, recommended every 3 to 6 months, are vital for evaluating serum lithium levels [3].

Precise measurement of blood lithium levels is paramount. Initially, this should occur around 1 week after the first dose, followed by weekly assessments for the first month, at least monthly for the subsequent 3 to 6 months, and then every 3 to 6 months thereafter. Blood samples should be reliably collected at consistent intervals (preferably approximately 12 hours post the last daily dose) and about a week after any dosage alteration. Treatment dosages are guided by physician-monitored blood lithium concentrations, typically aiming for levels between 0.50-0.80 mEq/L. Additionally, creatinine (to assess kidney function), sodium, potassium, calcium, thyroid, and parathyroid hormone levels should be measured before treatment commencement and at least once or twice annually thereafter [16].

In addition to monitoring blood lithium levels, clinicians should also oversee patients' cardiac, renal, thyroid, and overall health. Factors such as advanced age, comorbidities, and concurrent medications should be taken into consideration [18].

In our study, only 27.27% of patients underwent paraclinical examinations before treatment initiation. Most of these tests were conducted for diagnostic purposes, including urea (27.27%), creatinine (27.27%), complete blood count (22.73%), and

electroencephalography (22.73%). Not only were at-risk patients not identified, but adequate monitoring was lacking at the outset and during treatment, despite being contraindicated without close supervision.

This situation raises concerns about the continued prescription of lithium in our setting, given the numerous obstacles encountered. Alongside infrastructural limitations and equipment shortages (including unavailable lithium dosages), the absence of patient risk identification before treatment initiation, monitoring, and patient education is regrettable. This perpetuates the risk of poisoning in patients, particularly those with additional risk factors such as comorbidities, advanced age, or polypharmacy. Failure to recognise toxicity promptly may lead to irreversible neurological symptoms, known as irreversible lithium neurotoxicity syndrome, impacting quality of life or potentially resulting in fatality [3].

Despite the risk of intoxication, lithium remains a highly specific medication supported by robust evidence for the acute and maintenance treatment of bipolar disorder. Hence, it is imperative to enhance the prescription conditions for lithium in our environment.

In this context, investigations are warranted. Firstly, it is essential to determine the frequency of lithium poisoning in our environment, where not all conditions for prescribing lithium are met. Secondly, evaluating the knowledge, attitudes, and practices of healthcare professionals regarding lithium usage is crucial.

Conclusion

Our findings highlight the utilisation of lithium in psychiatric practice without adequate patient monitoring. This deficient monitoring approach poses health risks for patients, especially concerning side effects and drug interactions. Enhancements are imperative to guarantee the safe and efficacious utilisation of lithium in clinical settings. This underscores the significance of enhancing local capacities to

conduct these tests in a cost-effective and accessible manner, alongside the training and awareness of healthcare providers regarding the risks linked with specific treatments.

Conflict of Interest

The authors declare no conflict of interest.

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Ethical Approval

Not applicable.

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