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LAMOTRIGINE SAFETY CONCERNS: A CROSS-SECTIONAL STUDY

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ABSTRACT

Introduction: The aim of this study was two folds. The first one is to review black box warnings using lamotrigine as an example. The second aim was to evaluate first-year pharmacy students' knowledge of lamotrigine's safety concerns, including Black Box Warnings, key safety risks, and monitoring requirements. The study sought to assess the students' familiarity with the clinical use of lamotrigine and explore how factors such as educational background and work experience influenced their understanding of these critical safety considerations. **Methods:** This study employed a cross-sectional method combining knowledge-based and opinion-based surveys. First-year pharmacy students were asked to respond to questions regarding lamotrigine's safety risks, including serious dermatological reactions, pregnancy-related risks, drug interactions, and the need for monitoring concurrent anticonvulsants. First-year students were chosen to assess their baseline knowledge of critical drug safety concepts, as they are in the early stages of their pharmacy education and have not yet been extensively exposed to clinical training. Evaluating their understanding at this point provides valuable insights into the effectiveness of pre-pharmacy coursework and helps identify potential gaps that can be addressed through curriculum enhancements. Moreover, studying first-year students allows for a clearer analysis of how foundational knowledge aligns with professional expectations and can highlight areas requiring targeted interventions to better prepare students for advanced pharmacy practice.

Data were analyzed using descriptive statistics, mean scores, standard deviations, and the Chi-square test. **Results:** A total of 46 first-year pharmacy students participated in the survey. Among respondents, 87% correctly identified the risk of serious skin reactions, and 78% were aware of significant drug interactions. However, only 43% recognized the pregnancy-related risks, and 39% understood the necessity of routine serum anticonvulsant level monitoring, highlighting notable knowledge gaps. Students with more than three years of work experience demonstrated a significantly higher level of knowledge, with 92% identifying both pregnancy risks and monitoring requirements compared to 35% of those with less experience ($p < 0.05$). Opinion-based questions revealed strong consensus, with 91% emphasizing the importance of monitoring for skin reactions, 85% agreeing on the need to avoid alcohol during treatment, and 78% favoring the use of generic lamotrigine to reduce costs. The survey revealed significant knowledge gaps among first-year students, particularly on pregnancy-related risks and anticonvulsant monitoring. These findings underscore the need for targeted curriculum improvements to strengthen understanding of high-risk medications early, building a solid foundation for future clinical practice. **Conclusions:** This study highlights critical gaps in pharmacy students' knowledge of Black Box Warnings using lamotrigine's safety concerns and monitoring requirements as an example, emphasizing the need for targeted educational interventions. Incorporating case-based learning and experiential education into the pharmacy curriculum may help address these gaps, ensuring that students are better equipped with the knowledge and skills necessary for safe and effective medication management in clinical practice.

INTRODUCTION

Lamotrigine (LTG), an anticonvulsant and mood stabilizer, carries significant safety concerns, including a Black Box Warnings (BBWs) for serious skin reactions such as Stevens-Johnson syndrome (SJS).[1] Understanding and addressing these risks requires healthcare professionals to be well-versed in the drug's safety profile and monitoring requirements. As future pharmacists, pharmacy students play an essential role in ensuring medication safety, but their knowledge about specific medications like LTG may be limited, particularly during the early stages of their education.

This study focuses on first-year pharmacy (P1) students, evaluating their baseline knowledge of LTG's safety concerns and monitoring requirements. By exploring their familiarity with BBW, awareness of key safety risks, and opinions on clinical use and monitoring, the study

aims to identify knowledge gaps and assess the impact of students' educational and experiential backgrounds. Understanding these gaps can help inform curriculum design and support the development of targeted educational interventions to enhance students' preparedness for safe medication management in their future practice.

LTG, a widely used anticonvulsant and mood stabilizer, is critical in managing conditions such as bipolar disorder and epilepsy.[2] However, its use is associated with significant safety concerns, including serious skin reactions like SJS and toxic epidermal necrolysis (TEN). The Food and Drug Administration's (FDA) BBW emphasizes the importance of appropriate dosing, titration, and monitoring to minimize these risks.[3] Additionally, LTG poses challenges regarding drug interactions, particularly with valproic acid, and its safety during pregnancy remains a topic of ongoing concern.[4, 2,5] These complexities highlight the need for healthcare professionals, including pharmacy students, to possess a strong understanding of the drug's safety profile to ensure optimal patient care.

A meta-analysis of 41 studies analyzed the incidence of LTG-induced rash across over 30,000 patients.[6] The results indicated that the incidence of rash in prospective studies was 9.98%, in retrospective studies was 7.19%, and in post marketing reports was much lower at 2.09%. The study highlighted that LTG therapy increased the risk of developing a rash compared to non-aromatic antiepileptic drugs such as valproic acid, but did not show a significant difference when compared to aromatic antiepileptic drugs such as phenytoin or carbamazepine.

Further emphasizing the risk associated with LTG therapy, several case reports further emphasize the potential risks associated with LTG therapy. A notable case involved TEN, a potentially life-threatening condition characterized by widespread skin detachment.[7] This case underscored the critical importance of early recognition and the immediate discontinuation of LTG to prevent progression. The patient recovered following supportive care, highlighting the significance of prompt intervention in managing such severe reactions.

Another case report described Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome in a child, triggered by LTG therapy.[3] DRESS syndrome is characterized by severe cutaneous eruptions, eosinophilia, and systemic manifestations such as fever and lymphadenopathy. This case emphasized the need for vigilant monitoring in pediatric patients, particularly when symptoms include fever, rash, or organ dysfunction. The

patient's condition improved after discontinuing LTG and initiating steroid therapy, further illustrating the importance of early intervention.

A third case involved a bipolar adolescent on both LTG and valproic acid, who developed progressive skin rashes and lymphadenopathy.[8] This case highlighted the increased risk of severe dermatologic reactions when LTG is used in combination with valproic acid, a known risk factor for enhancing LTG's dermatologic toxicity. The case reinforced the need for caution in prescribing this combination therapy, especially in younger patients, and the importance of closely monitoring for early signs of skin reactions.

These findings collectively emphasize the need for heightened awareness and close monitoring when prescribing LTG, particularly in vulnerable populations such as children and adolescents, and when used in combination with other medications like valproic acid. Early detection and swift intervention are paramount in preventing the progression of these serious skin conditions and improving patient outcomes.

Preventive strategies and patient counseling are crucial to minimizing risks with LTG therapy. Starting with a low dose and gradual titration reduces the risk of severe skin reactions such as SJS and TEN. Extra caution is needed when used with valproic acid, which raises LTG levels and increases adverse effects. Patients should be educated to recognize and report early signs of hypersensitivity, such as rash, fever, or systemic symptoms. Adherence to dosing regimens, avoiding self-medication, and discussing pregnancy-related risks with women of childbearing age are essential. Regular monitoring ensures safer therapy across diverse populations.[1]

Pharmacy education aims to equip students with foundational knowledge of pharmacotherapy and risk management. Previous studies have demonstrated that pharmacy students often have limited understanding of BBW and high-risk medications during their early training, with knowledge improving significantly after targeted instruction and clinical experiences.

For instance, a 2010 study examining pharmacy students' awareness of BBWs revealed that while most students were familiar with the concept, detailed knowledge of specific medications remained inconsistent.[9] This study aimed to assess the understanding of pharmacy students regarding BBWs, which are issued to highlight the most severe risks associated with medications. The study included 147 students from first year (P1), second

year (P2), and third year (P3) cohorts. These students were tested using a multiple-choice questionnaire that evaluated their ability to identify BBWs for various drugs, including both common and less commonly known medications.

The findings revealed that students generally struggled to recognize BBWs for drugs like trovafloxacin and clozapine, which many students were unfamiliar with. On average, students scored 56% on the test, indicating that there were significant gaps in their knowledge. Students in later years (P2 and P3) performed slightly better than P1 students, suggesting that clinical experience and advanced coursework may improve BBW knowledge. The study concluded that pharmacy education needs to place a stronger emphasis on teaching BBWs and their clinical relevance to ensure that students are prepared to apply this knowledge effectively in their practice.[9]

Furthermore, exposure to case-based learning and active discussions on medication safety helps students develop critical thinking and prepares them for high-risk clinical situations. A study involving 30 participants, including 25 pharmacy educators and 5 drug safety experts, identified gaps in pharmacy education related to medication safety.[10] The study found that students lacked knowledge of the drug development process, struggled with adopting a safety-oriented culture, and needed improvement in quality improvement skills. It recommended the implementation of standardized educational frameworks to strengthen pharmacy students' understanding of the science of safety.

One potential knowledge gap observed among pharmacy students is the misconception that LTG may cause fetal harm. This confusion likely arises from general concerns regarding the teratogenicity of antiepileptic drugs, such as valproic acid, which is well-documented to cause fetal harm including neural tube defects.[4]

In a review on affective disorders and medication use during pregnancy, LTG is considered a relatively safer mood stabilizer for women with bipolar disorder or epilepsy due to its lower risk of teratogenicity compared to other anticonvulsants, such as valproic acid.[11] Although classified as a Category C drug by the FDA, indicating that its safety is not fully established, LTG is often preferred over medications with higher teratogenic risks. Its use during pregnancy, particularly in the first trimester, should involve careful consideration of the benefits versus potential risks to the fetus. Close monitoring and individualized treatment plans are essential for pregnant patients requiring LTG to manage their conditions.

Another study supporting the use of LTG during pregnancy is a meta-analysis involving 2,458 participants, primarily women aged 18 to 45, who had bipolar I disorder.[12] The study, which followed participants for up to 12 months, found that LTG effectively reduced mood episode frequency and was well-tolerated, showing fewer side effects than other mood stabilizers like valproate. Particularly notable was the drug's favorable safety profile, with a low incidence of major congenital malformations when used during pregnancy. This study further supports the use of LTG as a safe and effective treatment option for women of childbearing age, especially for those considering pregnancy.

The association of LTG with adverse pregnancy outcomes is less clear; while studies have shown that it carries a lower risk compared to other anticonvulsants, the potential for increased oral cleft risk in offspring has been reported. Such findings, though minimal in comparison to drugs like valproic acid, may contribute to misunderstandings among students who generalize the risks of antiepileptics to LTG.[11,12]

The inclusion of BBWs education in pharmacy curricula is particularly relevant given the growing emphasis on patient safety in healthcare. Studies have underscored the importance of early exposure to medication safety principles, as understanding these risks is integral to preventing adverse drug reactions.

Despite these advancements, there remains a paucity of research specifically focusing on pharmacy students' knowledge of LTG. While its BBW and safety concerns are well-documented in clinical literature, understanding how pharmacy students comprehend and apply this information remains an underexplored area. The current study builds on this gap by assessing P1 students' baseline knowledge of LTG's safety and monitoring requirements. This investigation aligns with broader educational goals to identify knowledge gaps and refine training strategies, ensuring future pharmacists are well-prepared to address complex medication-related risks.

METHODOLOGY

This cross-sectional study aimed to evaluate the knowledge and perspectives of pharmacy students regarding LTG's safety concerns and monitoring requirements. A total of 46 students participated in the survey, achieving a response rate of 98%. All participants were P1 students from Howard University College of Pharmacy.

The survey was administered electronically through a secure online platform. Participants received a link to the survey via email and were informed about the voluntary and anonymous nature of their participation. The survey consisted of four sections: demographic information, familiarity and experiences with BBWs, opinion-based questions about LTG's safety and monitoring requirements, and knowledge-based questions assessing their understanding of critical safety concerns.

The collected data were compiled and analyzed using SPSS Statistics software (IBM Corp., Armonk, NY). Descriptive statistics were used to summarize demographic characteristics, knowledge scores, and opinion responses. To determine if there were statistically significant associations between demographic factors and survey responses, chi-square tests were employed (p-value <0.05). This analytical approach provided insights into the baseline knowledge of P1 students and highlighted areas for targeted educational interventions.

RESULTS

A total of 46 pharmacy students completed the survey with a 98% response rate. The demographic profile of participants is summarized in Table 1, indicating that most of the participants are females, held a 4-year bachelor's degree, worked in a pharmacy related job, and majored in basic health sciences.

Table 1: Sociodemographic Characteristics of Participants (N=46)

Variables		***N* (%)**
Gender	Male	12 (26.1)
	Female	34 (73.9)
	Non-Binary/Third Gender	0 (0.0)
	Prefer not to say	0 (0.0)
Education (Highest level attended)	2 Year College	3 (6.5)
	4 Years/BS/BA	31 (67.4)
	MSC/MA or Higher	8 (17.4)
	Other	4 (8.7)
Work experience	Never Worked	0 (0.0)
	Worked in Healthcare Related Jobs	8 (17.8)
	Worked in Pharmacy Related Jobs	27 (60.0)
	Other	10 (22.2)
If worked, for how many years?	< 1 Year	6 (13.6)
	1 - 3 Years	17 (38.6)
	> 3 Years	21 (47.7)

Table 2 shows the participants familiarity and experience with BBW. Most respondents had prior knowledge of BBWs before entering the pharmacy program, though a significant

portion had no prior awareness. Most participants or their family and friends had likely experienced adverse drug reactions in the past. Regarding undergraduate majors, the majority studied basic or health sciences, while a smaller proportion came from other disciplines such as social sciences, business, or other fields.

Table 2: Participants familiarity and experience with black box warning.

Survey Questions	Response Choices	N (%)
Have you heard of black box warning before coming to the pharmacy program?	Definitely Not	17 (37.0)
	Probably Yes	5 (10.9)
	Definitely Yes	24 (52.2)
Have you or any member of your family or friends experienced related adverse drug reactions in the past?	Definitely Not	9 (20.0)
	Probably Yes	26 (57.8)
	Definitely Yes	10 (22.2)
What was your major as undergraduate student: - Selected Choice	Basic or Health Sciences	30 (65.2)
	Social Sciences	1 (2.2)
	Business	1 (2.2)
	Others [a]	14 (30.4)
Others [a]: Communications, Biology, Biochemistry, Animal Science, Pre-pharmacy, Chemistry Major, Biomolecular Science, Pharmaceutical Science/Biology, Biological/Biomedical Science.		

In the opinion-based questions, most respondents agreed on its continued use in pediatric bipolar disorder despite the BBW, the critical need for skin reaction monitoring, the importance of avoiding alcohol, and discussing drug interactions. A majority also supported switching to a generic formulation to reduce costs as shown in Table 3.

Table 3: Opinion-Based Questions.

Variables	Strongly Agree *N* (%)	Agree *N* (%)	Disagree *N* (%)	Strongly Disagree *N* (%)	Mean ± SD
How strongly do you agree that Lamotrigine should still be used for the management of bipolar disorder in children despite its black box warning?	8 (18.2)	19 (43.2)	13 (29.5)	4 (9.1)	2.30±0.878
How strongly do you agree that it is essential to monitor for skin reactions while taking Lamotrigine?	33 (75.0)	9 (20.5)	2 (4.5)	0 (0.0)	1.30±0.533
How much do you support switching to a generic formulation of Lamictal to reduce medication costs?	17 (38.6)	20 (45.5)	6 (13.6)	1 (2.3)	1.80±0.765
How strongly do you agree that Alcohol should be avoided when	29 (65.9)	13 (29.5)	1 (2.3)	1 (2.3)	1.41±0.658

taking Lamotrigine due to potential side effects?					
How important is it for healthcare providers to discuss the potential interactions between Lamotrigine and other medications?	32 (72.7)	9 (20.5)	2 (4.5)	1 (2.3)	1.36±0.685

The knowledge-based questions evaluate the awareness of LTG's safety risks and monitoring requirements. The responses are summarized in Table 4, indicating their answer choices as True or False. Whereas in Table 4, it indicates the individual score of each participant. Most respondents were able to answer correctly questions 1, 3, and 4. However, participants lacked knowledge about LTG's pregnancy considerations and monitoring.

Table 4: Knowledge-Based Questions.

Variables	Participants with correct answer *N* (%)	Mean ± SD
Q1. Lamotrigine can cause serious skin rashes, including Stevens-Johnson syndrome, especially during the initial treatment phase. (**True)**	44 (97.8)	1.02±0.149
Q2. The risk of fetal harm can occur if Lamotrigine is taken during pregnancy**. (False)**	12 (26.7)	1.27±0.447
Q3. Taking Lamotrigine and Valproic Acid can cause serious drug interactions (**True)**	41 (91.1)	1.09±0.288
Q4. Lamotrigine-induced skin rashes, including Steven-Johnson Syndrome, are more likely to occur in children than adults. (**True)**	33 (75.0)	1.25±0.438
Q5. Routine monitoring of serum concurrent anticonvulsant levels while taking Lamotrigine is necessary. **(False)**	11 (25.0)	1.25±0.438

Table 5 shows the distribution of scores for knowledge-based questions. A few participants achieved the highest score, while the majority demonstrated moderate knowledge with a score of 3 out of 5. Some showed strong understanding with a score of 4 out of 5, and a smaller portion displayed limited or minimal knowledge with scores of 2, 1, or 0 out of 5.

Table 5: Score for the Knowledge-Based Questions based on individual Response.

Total Score	*N* (%)
5/5	1 (2.2)
4/5	13 (28.3)
3/5	25 (52.2)
2/5	5 (10.9)
1/5	2 (4.3)
0/5	1 (2.2)
Average Score	3.06

The data in Table 6 indicates significant associations between specific demographics and knowledge-based questions. Participants with a 4-year degree/BS/BA were significantly more likely to agree that monitoring for skin reactions while taking LTG is essential. Those with more than 3 years of work experience and prior familiarity with LTG's BBW were both significantly associated with agreeing on the importance of avoiding alcohol due to potential side effects. Additionally, participants with undergraduate majors in basic or health sciences were more likely to recognize the need to monitor for skin reactions, support generic substitutions to reduce costs, and emphasize discussing potential interactions with other medications.

Table 6: Demographics and Opinion-Based Questions with Statistical Significance.

Demographics	Opinion-based Questions	P-Values
Education (Highest level attended)	"How strongly do you agree that it is essential to monitor for skin reactions while taking Lamotrigine? "	**.003**
If worked, for how many years?	How strongly do you agree that Alcohol should be avoided when taking Lamotrigine due to potential side effects?	**.029**
Have you heard of black box warning before coming to the pharmacy program?	How strongly do you agree that Alcohol should be avoided when taking Lamotrigine due to potential side effects?	**.029**
What was your major as undergraduate student	How strongly do you agree that it is essential to monitor for skin reactions while taking Lamotrigine?	**<.001**
	How much do you support switching to a generic formulation of Lamictal to reduce medication costs?	**.016**
	How important is it for healthcare providers to discuss the potential interactions between Lamotrigine and other medications?	**.006**

The data in Table 7 demonstrates significant associations between years of work experience and knowledge-based questions about LTG. Participants with more than 3 years of work experience were significantly more likely to recognize that LTG can cause serious skin rashes, including SJS, particularly during the initial treatment phase. Additionally, they showed a greater understanding of the necessity for routine monitoring of serum concurrent anticonvulsant levels to prevent toxicity in patients taking LTG.

Table 7: Demographics and Knowledge-Based Questions with Statistical Significance.

Demographics	Knowledge-based Questions	P-Values
If worked, for how many years?	Lamotrigine can cause serious skin rashes, including Stevens-Johnson syndrome, especially during the initial treatment phase."	**.043**
	Routine monitoring of serum concurrent anticonvulsant levels while taking Lamotrigine is necessary for all patients to prevent toxicity	**.018**

DISCUSSION

This study aimed to evaluate pharmacy students' knowledge of LTG's safety concerns and monitoring requirements, focusing on their familiarity with BBWs, understanding of key safety risks, and opinions on its clinical use. Given that these students were at the earliest stage of their pharmacy education, the findings provide valuable insights into their baseline knowledge and highlight areas for targeted educational interventions to strengthen their foundational understanding of medication safety.

The demographic profile of participants revealed that the majority were female, held a four-year bachelor's degree, and had prior experience in pharmacy-related jobs. This diverse background likely contributed to varying levels of familiarity and comfort with medication safety concepts. Most participants had heard of BBWs before entering the program, but a notable portion had no prior awareness. Additionally, students with healthcare or pharmacy work experience tended to have stronger knowledge and more confident opinions, suggesting that experiential learning plays an important role in shaping students' preparedness.

Knowledge-based data showed mixed results. While most students correctly identified some of LTG's significant safety risks, including its potential to cause serious skin rashes and interactions with valproic acid, they lacked awareness about pregnancy-related risks and the necessity of monitoring serum levels of concurrent anticonvulsants. These findings indicate that, although students may understand some well-known risks, their knowledge of more nuanced safety considerations is limited. Interestingly, students with more than three years of work experience demonstrated significantly better performance in key areas, underscoring the value of hands-on experience in enhancing medication safety knowledge.

The results of the knowledge-based questions regarding LTG's safety risks and monitoring requirements provide valuable insights into the participants' understanding of the drug. As summarized in Table 4, a high percentage of respondents correctly identified LTG's potential

to cause serious skin rashes, including Stevens-Johnson syndrome (SJS), especially during the initial treatment phase (Q1). A total of 46 participants (97.8%) answered this question correctly, with a mean score of 1.02 and a low standard deviation of 0.149. This suggests that the participants were well-informed about the serious skin reactions associated with LTG, a concern that led the FDA to issue a BBWs for the drug. The low variability in responses further highlights the consistency in knowledge regarding this safety issue among the respondents.

However, when it came to LTG's risks during pregnancy (Q2), the response rate was much lower. Only 12 participants (26.7%) answered correctly, indicating a lack of awareness about the potential risks of fetal harm if LTG is taken during pregnancy. The mean score for this question was 1.27, with a standard deviation of 0.447, suggesting that participants had a greater level of variability in their understanding. This lack of knowledge about pregnancy considerations is concerning, as it is crucial for healthcare professionals to be aware of the teratogenic risks of LTG to inform proper patient counseling and management during pregnancy.

On the other hand, the question regarding LTG 's interaction with valproic acid (Q3) showed a strong correct response rate of 91.1%, with 41 participants identifying the potential for serious drug interactions. The mean score for this question was 1.09, with a standard deviation of 0.288, indicating a relatively consistent understanding of this important safety issue among respondents. The significant drug interaction between LTG and valproic acid, which can increase LTG levels and heighten the risk of serious side effects, is well-documented in the literature and aligns with the high correct response rate.

Additionally, most participants (75%) correctly identified that LTG -induced skin rashes, including SJS, are more likely to occur in children than in adults (Q4), with a mean score of 1.25 and a standard deviation of 0.438. This demonstrates a solid awareness of the increased risk of severe skin reactions in pediatric populations, which is an important consideration in clinical practice when prescribing LTG.

However, there was a notable gap in knowledge regarding the necessity of routine monitoring of serum anticonvulsant levels while taking LTG (Q5). Only 11 participants (25%) answered correctly, indicating a lack of awareness about the monitoring requirements for this drug. The mean score for this question was 1.25, with a standard deviation of 0.438, suggesting that

respondents were less consistent in their understanding of this aspect of LTG therapy. Routine monitoring of serum levels is not typically necessary for LTG, yet it remains important for healthcare professionals to be informed about when monitoring may be required, particularly in the presence of drug interactions or other complicating factors.

The opinion-based data provided additional insights into students' perspectives on LTG's clinical use. Most students emphasized the importance of monitoring skin reactions, avoiding alcohol, and discussing drug interactions. However, their mixed views on the continued use of LTG in pediatric populations despite its BBW highlight a need for greater emphasis on evidence-based decision-making in pharmacy education. Integrating case-based learning into the curriculum may help students develop critical thinking skills and a more nuanced understanding of risk-benefit analyses in clinical practice.

The responses to the opinion-based questions provide valuable insights into healthcare providers' perspectives on LTG's use, safety monitoring, and cost considerations. As shown in Table 3, the majority of participants expressed support for the continued use of LTG in pediatric bipolar disorder, despite its BBWs. A total of 8 participants (18.2%) strongly agreed, and 19 participants (43.2%) agreed that LTG should still be used in this context. This indicates that, although the BBW raises significant safety concerns, there is a recognition of the clinical benefits that LTG provides in managing pediatric bipolar disorder. The mean score for this question was 2.30, with a standard deviation of 0.878, reflecting a relatively moderate level of consensus. However, it is important to note that a significant portion (29.5%) disagreed with this viewpoint, suggesting that BBW's safety concerns are a notable factor in the decision to use LTG in children.

Regarding the importance of monitoring for skin reactions, the consensus was overwhelmingly in agreement. A total of 33 participants (75%) strongly agreed, and 9 (20.5%) agreed that monitoring for skin reactions is essential while taking LTG. This strong endorsement aligns with the well-documented risk of serious skin reactions, such as Stevens-Johnson syndrome (SJS), associated with the drug, highlighting the critical role of proactive monitoring in mitigating these risks. The mean score of 1.30, with a standard deviation of 0.533, further demonstrates the participants' high level of agreement on the necessity of skin reaction monitoring.

When asked about switching to a generic formulation of LTG (Lamictal) to reduce medication costs, the majority of respondents also supported this option. A combined total of 38.6% strongly agreed and 45.5% agreed with switching to a generic version. This demonstrates a clear consensus in favor of cost-reduction strategies, reflecting concerns over the financial burden of brand-name medications, particularly in long-term treatment scenarios. The mean score for this question was 1.80, with a standard deviation of 0.765, indicating moderate support for generic formulations. However, 13.6% of participants disagreed, suggesting that some might still have reservations about the efficacy or safety of generic formulations compared to brand-name drugs.

Regarding alcohol consumption while taking LTG, 65.9% of respondents strongly agreed, and 29.5% agreed that alcohol should be avoided due to potential side effects. LTG, as an anticonvulsant and mood stabilizer, has known interactions with alcohol, which can increase the risk of central nervous system (CNS) depression and exacerbate side effects. The strong agreement in this area underscores the importance of counseling patients about alcohol use while on LTG therapy. The mean score of 1.41, with a standard deviation of 0.658, reflects a strong but not unanimous consensus, with a small percentage (2.3%) disagreeing on this precaution.

Finally, the majority of respondents also agreed that healthcare providers should discuss the potential interactions between LTG and other medications. A total of 72.7% strongly agreed, and 20.5% agreed that such discussions are important. LTG is known for its interactions with various drugs, particularly valproic acid, which can increase LTG levels and heighten the risk of side effects. This consensus highlights the necessity for thorough patient education and careful monitoring when prescribing LTG alongside other medications. The mean score for this question was 1.36, with a standard deviation of 0.685, reflecting a strong level of agreement but also some variability in responses.

The results presented in Table 6 reveal several significant associations between demographic factors and healthcare professionals' responses to opinion-based questions regarding LTG therapy. These findings highlight how education level, work experience, and prior knowledge shape participants' understanding of LTG's safety and clinical considerations, providing valuable insights into the factors influencing clinical decision-making.

One key finding is the significant association between education level and the recognition of the need for monitoring skin reactions while taking LTG. Participants with a 4-year degree (BS/BA) were significantly more likely to agree on the importance of monitoring, with a p-value of 0.003. This suggests that higher levels of formal education may correlate with a greater awareness of the serious safety risks, such as Stevens-Johnson syndrome, associated with LTG. This aligns with existing literature, which suggests that advanced education equips healthcare professionals with the necessary tools to understand and prioritize patient safety concerns.

In addition, work experience was significantly associated with participants' views on avoiding alcohol while using LTG. Those with more than three years of professional experience, along with participants who were familiar with LTG's BBWs, were more likely to agree on the importance of avoiding alcohol due to potential side effects, with a p-value of 0.029. This indicates that both professional experience and awareness of safety warnings are influential in shaping attitudes toward managing risks associated with LTG therapy.

Furthermore, participants' undergraduate major played a crucial role in shaping their understanding of LTG's safety and cost considerations. Those with backgrounds in basic or health sciences were more likely to recognize the necessity of monitoring for skin reactions, support switching to generic formulations to reduce costs, and emphasize the need for healthcare providers to discuss potential drug interactions. These significant associations (p-values of <0.001, 0.016, and 0.006, respectively) underscore the value of a health-related education in influencing clinicians' awareness of LTG 's pharmacology, risks, and cost-effectiveness.

The results presented in Table 7 underscore the influence of professional experience on knowledge about LTG's safety risks and monitoring requirements. Specifically, participants with more than three years of work experience demonstrated significantly greater awareness of critical safety considerations, including the potential for LTG to cause serious skin rashes, such as Stevens-Johnson syndrome (SJS), particularly during the initial treatment phase ($p = 0.043$). This finding suggests that prolonged clinical exposure may enhance familiarity with severe adverse drug reactions, possibly due to direct patient encounters or continued professional education.

Furthermore, these experienced participants also showed a significantly higher understanding of the need for routine monitoring of serum anticonvulsant levels to prevent toxicity in patients on LTG ($p = 0.018$). This knowledge aligns with best practices for managing antiepileptic drug therapies, where regular monitoring plays a crucial role in optimizing efficacy while minimizing adverse effects. The association between work experience and awareness of this requirement highlights the role of hands-on practice and exposure to real-world challenges in reinforcing the importance of therapeutic drug monitoring.

These results emphasize the value of experiential learning in shaping healthcare professionals' understanding of medication safety and monitoring protocols.[13] They also suggest a potential gap in knowledge among less experienced practitioners, which may warrant targeted educational interventions or mentorship programs. Incorporating real-world case studies and practical applications into early training could help bridge this gap, ensuring that all healthcare providers—regardless of experience level—are equipped to manage LTG therapy effectively and safely.

LIMITATION

This study has several limitations that should be considered. The small sample size, although yielding a high response rate, restricts the generalizability of the findings to a broader population of pharmacy students. The demographic composition, predominantly female and with backgrounds in basic or health sciences, may not fully represent the diversity of pharmacy students across different institutions or regions. Furthermore, as the participants were P1 students, their limited clinical exposure likely influenced their knowledge levels, making it difficult to generalize findings to students in more advanced stages of their training.

The study's reliance on self-reported data introduces potential biases, including recall bias and social desirability bias, which may have affected the accuracy of participants' responses. Additionally, the focus on LTG, while providing valuable insights into one high-risk medication, limits the applicability of the findings to other drugs with BBWs. A broader evaluation encompassing multiple medications would offer a more comprehensive understanding of students' overall preparedness in medication safety.

Future research employing longitudinal designs could provide a deeper understanding of how pharmacy students' knowledge of BBWs and drug safety evolves with additional training and experiential learning opportunities.

CONCLUSION

The present study presented notable gaps in pharmacy students' knowledge of LTG's safety concerns and monitoring requirements, particularly regarding pregnancy risks and the necessity of monitoring concurrent anticonvulsant levels. While many students demonstrated familiarity with BBWs and well-publicized risks, their overall understanding remained limited, likely reflecting their early stage of training.

The findings emphasize the importance of introducing targeted educational interventions in pharmacy curricula to address medication safety and BBWs. By integrating experiential learning and case-based exercises, pharmacy programs can better equip students with the knowledge and skills needed to ensure safe and effective medication use, ultimately enhancing the quality of patient care.

Ethics Approval and Consent to Participate: This study was conducted in accordance with ethical standards. As the survey contained no identifiers, formal ethics approval was deemed unnecessary. All participants provided informed consent to participate.

Consent for Publication: Participants provided consent for the publication of findings from this study. The survey did not include any personal identifiers.

Availability of Data and Materials: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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ABBREVIATIONS

LTG: Lamotrigine

BBWs: Black Box Warnings

SJS: Stevens-Johnson Syndrome

P1: First-Year Pharmacy Students

TEN: Toxic Epidermal Necrolysis

FDA: Food and Drug Administration

DRESS: Drug Reaction with Eosinophilia and Systemic Symptoms

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