CARDIAC RISK ASSOCIATED WITH PHARMACODYNAMIC INTERACTIONS BETWEEN ANTIDEPRESSANTS AND TYROSINE KINASE INHIBITORS USED IN THE TREATMENT OF LUNG CANCER.

Machado, J.S.[1,2*]; Ribeiro, A.C.A.[2]; Silva, M.P.[1,2]; Ribeiro, K.C. [1,2]
[1]*Faculty of Pharmacy, Federal Fluminense University, Rua Miguel de Frias, 9, Niterói, Rio de Janeiro, Brazil.*
[2]*Federal Hospital da Lagoa, Rua Jardim Botânico, 1.001, Lagoa, Rio de Janeiro, Brazil.*
**jessicamachado@id.uff.br of the author for contact.*

Introduction

Depression is the most common psychiatric disorder among cancer patients, affecting between 20% and 30% of this population, with a higher prevalence in lung cancer patients[1,2] . Lung cancer has the highest prevalence among cancer types[2], often related to its unfavorable prognosis. Disease progression, symptom severity, and concerns about the finitude of life are associated with the development of depression; it is common for patients to experience depressive states and require additional medications beyond chemotherapy. Both therapies can be essential for the comprehensive recovery of the patient. Given this context, this study aimed to investigate the interactions between these antidepressants and tyrosine kinase inhibitors used in the treatment of metastatic lung cancer.

Material and Methods

To identify the interactions between antidepressants and tyrosine kinase inhibitors, the Micromedex®[3] database was used. The methodology included a systematic search of each antidepressant from the following classes: unicyclic, tricyclic, tetracyclic, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, 5-HT receptor modulators, and serotonin-norepinephrine reuptake inhibitors, in combination with tyrosine kinase inhibitors (including both nonspecific active ingredients and biospecific isoforms for the MET and ALK/ROS1 mutations) used in the treatment of metastatic lung cancer[4]. The reported interactions were evaluated, considering their severity and clinical relevance[3].

Results and Discussion

The results showed that the main interactions occurred between selective serotonin reuptake inhibitors, tricyclic antidepressants, and selective norepinephrine reuptake inhibitors, notably with the tyrosine kinase inhibitors osimertinib (n:12) and crizotinib (n:14). The identified interactions were pharmacodynamic (n:26), exhibiting an additive effect between the drugs that altered the QT interval in electrocardiogram tests. This can lead to serious reactions and increase the risk of adverse cardiac events, including torsades de pointes.

Conclusion

The coadministration of these medications is not recommended; if substitution is unfeasible, it is necessary to monitor the electrocardiogram and adjust the dosage of the antidepressants according to the recommendations for each active ingredient. To maintain antidepressant therapy, the prescriber should prioritize antidepressants that do not present interactions, such as amoxapine, duloxetine, escitalopram, levomilnacipran, maprotiline, nortriptyline, protriptyline, and vortioxetine.

Acknowledgments

The authors would like to express their sincere appreciation for the financial support from the residency scholarship provided by the Ministry of Health and the Federal Fluminense University, responsible for the residency program in Hospital Pharmacy. We also thank the Clinical Pharmacy Service of the Training Service Unit at the Hospital Federal da Lagoa, which made this work possible.

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