NEXTFRONTIERS TOCURECANCER2022
DE 22 A 25/06 - 100% ONLINE

A.C.Camargo Cancer Center
Especializado em Vida

Evaluation of the Role of Allantoin in Drug Resistance in Leukemia

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INTRODUCTION

Leukemia is a hematological cancer characterized by the exacerbated proliferation of cells of hematopoietic tissue. In the beginning of chemotherapy treatment, there may be the development of Tumor Lysis Syndrome (TLS) due to the large amount of intracellular content from lysis of tumor cells. For this, the treatment of TLS, carried out in parallel to the chemotherapy treatment, uses a recombinant urate oxidase enzyme. The enzyme is responsible for converting high serum uric acid levels into allantoin, which is more easily eliminated in the urine. However, there are no clinical studies that show the action of allantoin during chemotherapy treatment until its complete elimination by urine. Therefore, our objective was to investigate if allantoin interferes with the action of cisplatin, in vitro, in chronic myeloid leukemia cells.

METHODS

Sensitive and resistant chronic myeloid leukemia cells (K562 and Lucena-1 cells) were cultured in RPMI 1640 culture medium supplemented with 10% fetal bovine serum, 1% antibiotic, and maintained in a stove at 37°C and 5% CO_2. The cells were treated with cisplatin and allantoin at different concentrations. The cell viability assay was performed using the MTT assay and flow cytometry was used to analyze the induction of DNA fragmentation and efflux pump activity.

RESULTS

Our results show that allantoin does not induce cell death and cisplatin leads to decreased viability, in sensitive and resistant leukemia cells. We observed that in the presence of allantoin there is a reduction in death caused by cisplatin, allowing us to deduce that allantoin enhanced the survival of cells, preventing the efficient action of cisplatin. We also observed that allantoin does not interfere with the activity of efflux pumps of resistant cells.

- Viability of sensitive and resistant cells (K562 and Lucena-1 cells) treated with allantoin:

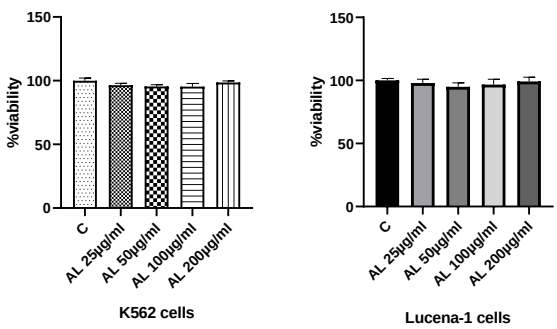

Figure 1: Allantoin does not reduce the viability of K562 and Lucena-1 cells.The cells were treated with allantoin for 48 hours and a MTT assay was performed to evaluate cell viability.

- Viability of sensitive and resistant cells treated with cisplatin:

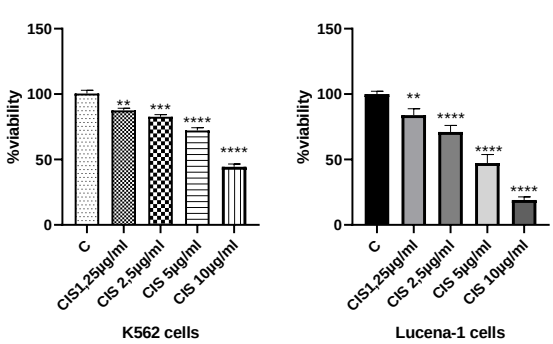

Figure 2: Cisplatin reduce the viability of K562 and Lucena-1 cells.The cells were treated with cisplatin for 48 hours and a MTT assay was performed to evaluate cell viability. **p<0.01, ***p=0.0001 and ****p<0.0001. Data with asterisk significantly differ from control.

RESULTS

- Viability of sensitive and resistant cells treated with cisplatin and allantoin:

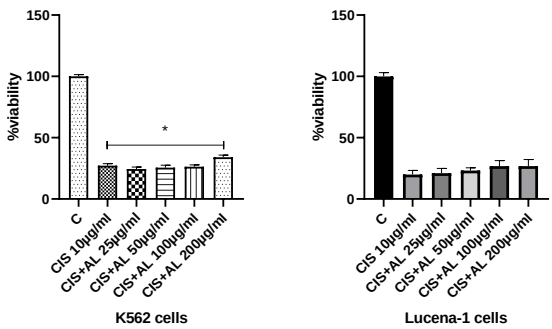

Figure 3: Allantoin induces a significant increase in cell viability of K562 cells treated with cisplatin. In Lucena-1 cells there was no significant increase in cell viability. MTT assay was performed to evaluate cell viability in the presence of cisplatin and allantoin.*p<0.05.

- DNA fragmentation of sensitive and resistant leukemia cells treated with cisplatin and allantoin:

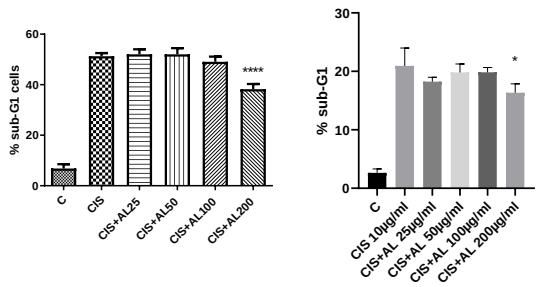

Figure 4: Allantoin reduces cisplatin-induced DNA fragmentation in K562 cells and Lucena-1 cells (preliminary result). Cells were treated with cisplatin and allantoin. Evaluation of DNA fragmentation by flow cytometry. Quantification of sub-G1 cell population by flow cytometry. *p<0.05 and ****p<0.0001

- Evaluation of the effect of allantoin on the activity of efflux pumps in resistant leukemia cells:

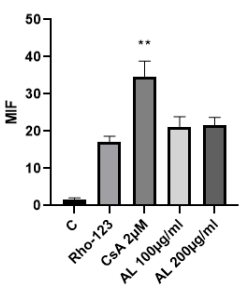

Figure 5: Effect of allantoin on efflux pump activity. Cells were treated with rhodamine 123 in the absence (Rho-123) and in the presence of cyclosporine A (CsA) and allantoin (AL 100 µg/ml and AL 200 µg/ml). MFI = mean fluorescence intensity. **p<0.01. Data with asterisk significantly differ from Rho-123 group.

CONCLUSION

Our study shows that allantoin interferes with the action of cisplatin, preventing the efficient action of cisplatin. But more experiments are needed to complete our study.

CONTACT

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