Bimodal Treatment for Triple-Negative Breast Cancer by Combining Optical and Gamma Radiation

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Abstract: Triple-negative breast cancer is resistant to chemo and radiation therapy. Light-based technologies have been reported as promising allies to cancer treatment. Herein, we combined photodynamic and gamma therapies to verify their potential to treat TNBC. © 2022 The Author(s)

1. Introduction

Breast cancer is the most common cancer for women worldwide. According to the World Health Organization, it is considered the 5th leading cause of death from cancer [1]. Triple-negative breast cancer (TNBC) is a subtype of this disease that represents around 20% of all breast cancer, has a high mortality rate, and it is resistant to conventional treatments, such as exposure to ionizing radiation (IR) [2]. Conversely, photodynamic therapy (PDT) mediated by photosensitizing drugs has been reported as a potential therapy against cancer, however, few studies combine therapies to improve the TNBC treatment [3]. Thus, our goal in this work was to associate PDT and gamma teletherapy in the treatment of TNBC.

2. Methodology

MDA-MB-231 cells were submitted to PDT using the TMPyP porphyrin at a concentration of 30 µM, a red LED (660 ± 11 nm) with an irradiance of 57.3 mW/cm^2 delivering radiant exposures of 20 or 50 J/cm^2. Immediately after PDT, cells were divided into groups non-treated (control), only IR (IR_5 or $IR_{2.5}$) and PDT associated with IR (PDT_{50}+$IR_{2.5}$ and PDT_{20}+IR_5) and then, exposed to IR using a ^{60}Co source with a dose of 5 or 2.5 Gy. Past 24-h of the PDT session, we assessed the cell viability through the MTT assay, clonogenicity, and oxidative stress by glutathione assay (GSH/GSSG ratio). All data were submitted to ANOVA One-Way and numerical values are presented as mean ± standard error of the mean. Statistically significant differences were considered when $p < 0.05$.

3. Results

IR did not affect the mitochondrial activity of TNBC cells (Fig.1a). Indeed, cell viability was similar for control and IR groups regardless of the dose used. On the other hand, PDT was able to reduce around 35% of cell viability when combined with IR, even though no statistically significant differences were noticed between radiant exposures. Clonogenicity was evaluated by the relative survival displayed in Fig.1b. It is possible to observe that the control and $IR_{2.5}$ groups exhibited similar behavior, however, the IR_5 group showed a significant survival reduction (approximately 45%) over the control group. In contrast, the PDT_{50}+$IR_{2.5}$ and PDT_{20}+IR_5 groups presented a more pronounced decrease (around 70%) when compared to the control. Besides, statistically significant differences were also observed between groups IR and PDT+IR. The GSH/GSSG ratio, which is related to antioxidant balance, exhibited different behavior according to the protocol (Fig.1c). As expected, the control group showed a GSSG level higher than GSH, suggesting a pathological condition that causes oxidative stress. $IR_{2.5}$ and PDT appear to influence the redox balance since levels of GSH are higher than GSSG. The IR_5 group showed similar levels of GSH and GSSG.

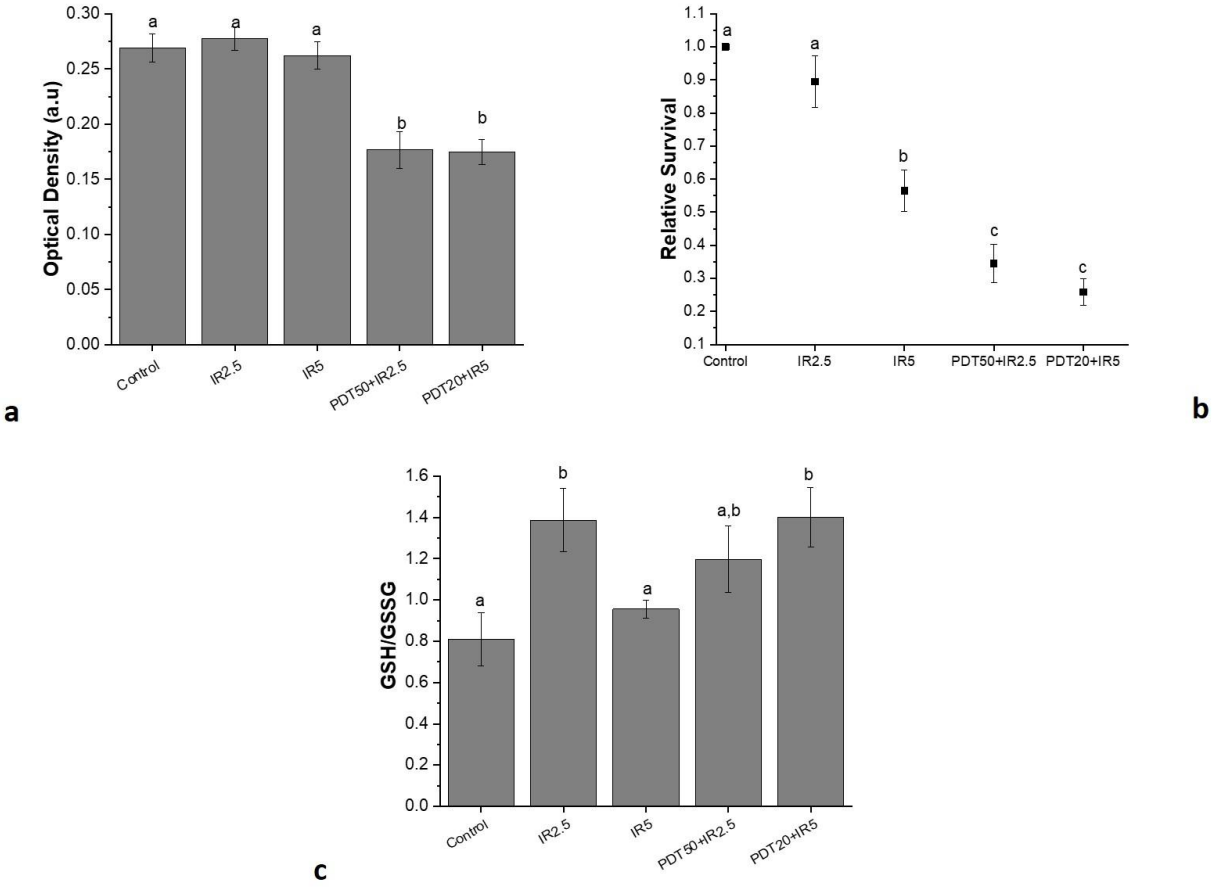

Figure 1- Mean values ± SEM of the Cell viability (a); Relative survival (b); and GSH/GSSG ratio for TNBC cells submitted to PDT and IR. Different letters mean statistically significant differences between groups.

4. Conclusions

Taken together, our results suggest that PDT could be a new ally to radiotherapy of TNBC. Further *in vivo* studies are warranted to pursue the best protocol.

5. References

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