ABSTRACT

Objective: Radiotherapy induces the formation of oxygen free radicals that subsequently causes damage to cell DNA. These oxygen free radicals attack cells in all phases of the cell cycle (figure 1), but are most effective in targeting cells in the growth phase (G1 and G2). Cells in the G0 or dormant phase are affected to a much lesser extent.

Xerostomia is a common complication after radiation in the head and neck. Many therapeutic options have been proposed but to date there is no optimal preventive or curative therapy.

Study design: Randomized blinded prospective animal experiment with control.

Methods: The study consists of 19 CD rats, 3 sacrificed at baseline; the remaining 16 rats were divided in two groups and randomized within each group. Group A consisted of 8 rats, injected on day 0 and sacrificed on day 14; 5 received sham injection, 3 received Botox® injection. Group B was randomized and injected similarly, but sacrificed on day 28. After sacrifice, glands were stained with Ki-67 which stains positive for all cells except those in G0.

Results: Our study did not show a difference in mitotic rate among treatment arms in those subjects who were sacrificed at 14 days. It did however show a trend towards decreased mitotic rate of salivary glands treated with Botox® when compared to those treated with sham solution for the group that was dissected on day 28.

Conclusion: Our study shows a trend towards decreased mitotic rate in salivary glands treated with Botox® after 28 days. This decreased mitotic rate could potentially have a protective effect for salivary glands in patients receiving radiotherapy.

INTRODUCTION

Radiotherapy induces the formation of oxygen free radicals that subsequently causes damage to cell DNA. These oxygen free radicals attack cells in all phases of the cell cycle (figure 1), but are most effective in targeting cells in the growth phase (G1 and G2). Cells in the G0 or dormant phase are affected to a much lesser extent.

Xerostomia is a common complication after radiation in the head and neck. Many therapeutic options have been proposed but to date there is no optimal preventive or curative therapy.

We believe that by decreasing salivary gland mitotic rate and keeping the cells in the G0 phase while patients undergo radiotherapy, we can protect glands from the ill effects of radiation. Studies have shown that by increasing stimulation to salivary glands, either electically or chemically, the glandular cell mitotic rate increases significantly. The relationship between gland inhibition and decreased mitotic rate has yet to be studied, and is the primary focus of our pilot project. Botox® inhibits the pre-synaptic release of acetylcholine. Studies have demonstrated that it is effective in decreasing salivary gland mitotic rate. We hypothesized that Botox® will decrease parasympathetic stimulation of salivary glands, thus keeping them in the G0 phase of the cell cycle.

METHODS AND MATERIALS

For this study, we received 19 CD rats, 3 sacrificed at baseline; the remaining 16 divided into two groups and randomized within each group. Group A consisted of 8 rats, injected on day 0 and sacrificed on day 14; 5 received sham injection, 3 received Botox® injection. Group B was randomized and injected similarly, but sacrificed on day 28. After sacrifice, glands were stained with Ki-67 which stains positive for all cells except those in G0.

RESULTS

Thirty-two salivary glands were collected and examined in each group, 16 parotid and 16 submandibular glands. Laterality was not segregated as treatment was constant in both sides. The results from both pathologists were averaged to result in one number for every subject. Figures 5 and 6 show the results for mitotic rate at day 14 and 28 respectively. We see a trend towards decreased mitotic rate in the Botox group at 28 days, most notable in the parotid gland. None of the results reached statistical significance, which is expected being a pilot study with low power. Subject health was evidenced by a constant increase in weight gain from day 1 to day 28 as seen in figure 7.

CONCLUSIONS

This is an innovative approach to a well-known and unresolved clinical problem in head and neck cancer. Further research along these lines could have tremendous implications in decreasing functional morbidity after radiation.

REFERENCES