Effects of a Mu-Opioid Agonist and Antagonist on Head and Neck Cancer Cells

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ABSTRACT

Background: Previous studies have suggested that the mu-agonist, morphine, promotes the growth of breast and lung cancer cells, possibly contributing to recurrence of these cancers. This study aims to determine if exposing head and neck cancer cell lines to either a mu-agonist (morphine) or a mu-antagonist (naloxone) affects cancer cell growth with the hypothesis that morphine will increase cell growth and naloxone will inhibit growth.

Methods: Three human head and neck squamous cell cancer (SCC) tissue cell lines were each separately exposed to 10, 25, 50, 75 and 100 ng/mL of morphine with a media-only control using a 96 well plate. Resorufin reduction assays (alamarBlue) were used to monitor cell viability at 24, 48 and 72 hours. Parallel assays were performed using the same concentrations of naloxone. Triplicate experiments were performed for each condition.

Results: SCC-12 (laryngeal SCC) cells showed no change in growth when exposed to morphine relative to untreated controls. Exposure of SCC-12 cells to naloxone showed a significant decrease in growth at all concentrations except for 10 ng/mL (p <0.001). Morphine and naloxone did not significantly affect growth in the other two cell lines.

Conclusion: This data suggests an inhibitory effect of opioid antagonists on laryngeal squamous cell carcinomas. If indeed there is inhibition of growth from mu-antagonism, it is possible that other mu-agonists, such as nalbuphine, may be indicated as an analgesic and therapeutic option in this group of cancer patients. Further investigations are warranted.

METHODS AND MATERIALS

• SCC-12 laryngeal SCC, SCC-49 lateral oral tongue SCC, and SCC-74a base of tongue SCC cell lines were obtained from the University of Michigan SPORE bank laboratory and cultured in the University of Utah Surgical Laboratory.

• Resorufin reduction assays (alamarBlue) were used to monitor cell growth at 24, 48 and 72 hours when exposed to concentrations of morphine and naloxone separately, at 10, 25, 50, 75 and 100 ng/mL with a media-only control.

RESULTS

Figure 4. Comparison of growth of laryngeal SCC cells as compared to the control at 24, 48 and 72 hours when exposed to morphine and naloxone, separately.

• Exposure to naloxone showed a significant decrease in growth with all concentrations except for the lowest, 10 ng/mL (p <0.001). The greatest inhibition was found at 48 hours.

• Morphine showed an increase in growth as shown in Figures 4 and 5, but the results were not of significant value.

Figure 5. Comparison of morphine and naloxone exposed laryngeal SCC cell growth as compared to control values at 48 hours with increasing concentrations of the respective drug.

DISCUSSION

• Our preliminary data suggests that opioid receptor antagonism may have direct effects on laryngeal SCC cells.

• There was significant inhibition of growth of laryngeal SCC when exposed to naloxone (mu-opioid antagonist).

Future studies:

• Nalbuphine, which is a mu-antagonist, exerts its analgesic effects by being an agonist to the kappa receptors. If found to have similar inhibitory properties, the results would serve as key step in suggesting nalbuphine as not only an effective peri-operative analgesic, but also a therapeutic drug in laryngeal SCC patients.

• Perform in-vivo experiments with an animal model to take into account the other mu-opioid receptor modulator properties that affect the immune system and angiogenesis.

• The results of further studies will provide valuable information to surgeons and anesthesiologists about appropriate peri-operative analgesia in patients with laryngeal squamous cell carcinoma.

CONCLUSIONS

• Naloxone (mu-opioid antagonist) shows a significant inhibition of growth in laryngeal SCC cell lines.

• Should mu-antagonism continue to show inhibitory effects in head and neck cancer cells with future experiments using other mu-agonists, new therapeutic and analgesic options can be offered to these patients.

REFERENCES

