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Local Application of Cisplatin Soaked Gauge in Neck Intraoperatively in Head and Neck Cancers – Short Term Outcome.

KEYWORDS: Head and neck cancer, cisplatin

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ABSTRACT Local delivery of chemotherapeutic drugs has long been recognized as a potential method for reaching high drug doses at the target site while minimizing systemic exposure. Cisplatin is one of the most effective chemotherapeutic agents for the treatment of various tumors; however, its systemic toxicity remains the primary dose-limiting factor Based on the randomized double-blinded phase III trial to determine the effectiveness of cisplatin plus epinephrine in injectable gel form in treating patients who have recurrent or refractory head and neck cancer at U.S. National Institutes of Health we performed a study of local application of cisplatin intraoperatively in the neck& the margins of excised head and neck malignancy and to evaluate its effect.

INTRODUCTION

Head and neck cancers in India are emerging as major public health problems. In India nearly 80,000 oral cancers are diagnosed every year [1] Buccal mucosa is common site of involvement . Most of Head and Neck cancers have local reccurance after treatment, that too within two years. In Head and neck cancers Cisplatin is widely used for the treatment of testicular, bladder, head and neck, small-cell and non-small-cell lung cancers, but it also possesses substantial side effects, such as nephro-, neuro-, and myelotoxicity[2-4]. Cisplatin may be used locally as Polymer-based cisplatin-loaded drug delivery systems such as liposomes[5] polymeric micelles[6] hydrogels [7] polymeric gels [8] and implants[9] provide an opportunity to deliver high, localized doses of drugs for a prolonged period directly into a tumor or at agent in the cavity created by the tumor removal provides high local concentration of the drug, killing the surviving malignant cells. This may also prevent the systemic side effects of chemotherapy that is normally associated with intravenous administration. Debulking of large tumors prior to the surgery can be done by exposing the tumor to large concentrations of the drug[10]

MATERIALS & METHODS

After discussion in Tumor Board Meeting with medical and radiation oncologist, uniform standards were decided. Patient admitted in our ward with age between 18 year and 65 year , previously untreated, performance status: KPS more 70%, haematological parameters within normal range, serum creatinine normal, no hypersensitivity to cisplatin, no uncontrolled local infection at treatment sites, no medical or psychiatric condition that would preclude informed consent, no pregnant or nursing women, adequate contraception required of fertile patients, histologically confirmed squamous cell carcinoma of the head and neck were included in our study. Patients who have already received some form of chemotherapy, presence of metastatic disease,operated cases, presence of any uncontrolled systemic illness like diabetes, tuberculosis and hypertension were excluded from study. An informed consent was taken from the patients explaining them the whole procedure and aim behind conducting the study. Fifty patients received cisplatin in a dose of 20ml soaked in a gauge for local application and placed the neck and in the operated site after doing MRND . Patient was followed in postoperative period for the local side effects and was followed for a period of one year to evaluate for various variables local recurrence. .In postoperative period, patient did not have nausea and vomiting, routinely blood counts were done which donot show significant change, no signs of systemic absorbtion of cisplatin was seen. patient tolerated well.

Patients were followed in postoperative period. Forty patients had skin flap necrosis without any pus culture was negative in most of patients, debridment of the flap was done wound healed with secondary intention , in five patients debridment and skin grafting was done in one patient whole of PMMC flap got infected and necrosed so it was debrided and revised with Latissimus Dorsi flap

DISCUSSION

In our study incidence buccal mucosa lesion was more common in male patients between age group of 40-49 years who were tobacoo chewer. Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. cisplatin concentration is 1,000-fold and 100-fold greater within treated tumors and tumor-draining lymphatics, respectively, compared with that in plasma after intratumoral injection. Damage of DNA and inhibition protein and rRNA synthesis occurs with cisplatin.[11,12] Cisplatin causes its effect by binding to DNA, creation of interstrand cross-links, and formation of intrastrand bidentate N-7 adducts at d(GpG) and d(ApG).[13] Cisplatin is cell cycle phase nonspecific and is eliminated

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via renal excretion.[12] In human patients, cisplatin is used to treat many solid tumors including squamous sarcomas in the head and neck areas, lymphomas, and small cell and non-small cell lung, testicular, ovarian, gastric, esophageal, and pancreatic cancers. Cisplatin is used to treat solid tumors, including osteosarcomas, carcinomas, and sarcomas in companion animals.[12-14] Cisplatin administration causes nephrotoxicosis (renal tubular inflammation and necrosis), leukopenia, nausea, anemia, and chronic neurotoxicosis and ototoxicosis[14-15] As peak plasma cisplatin concentration increases, the risk for systemic toxic effects increases but the therapeutic effects against the targeted tumor remain relatively stable.[14] Cisplatin can be used as metronomic chemotherapy and local injection of cisplatin into affected tissues so as to minimize peak plasma cisplatin concentration and to decrease the side effects specifically nephrotoxicity.[14-]

In our study due to local toxicity of cislpatin wound dehiscence and flap necrosis occurred in most patients.

TABLE 1: COMPLICATIONS

Complications	Number of Patients
Skin Flap Necrosis	40
Wound Dehiscence	13
Increase in Hospital Stay	20days
Average Delay in Adjuvant Treatment	1month

CONCLUSION

In our surgical audit skin flap necrosis and infection was in 15%-20% of operated head and neck cancer which increased to 80% after use of cisplatin locally leading to increase in hospital stay and delay on adjuvant treatment, rest parameters were same, probably local cisplatin was the cause.

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