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Research Article

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Evaluation of Single-Agent Cisplatin versus Cisplatin and 5 Flouro Uracil Chemotherapy in Cervical Cancer Patients in India

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Abstract

Cervical cancer is the most common gynecological cancer in Indian women. We conducted this study to assess whether single-agent Cisplatin was better than Cisplatin and 5 flourouracil chemotherapy in cervical cancer patients in India.The aim was to assess tumor response of weekly injections of single-agent Cisplatin versus Cisplatin and 5 flouro uracil chemotherapy in women with carcinoma cervix with FIGO stages IB2 to IIIB. 54 patients were included in this study who completed the treatment. Disease was assessed prior to treatment by pelvic examination and contrast enhanced MRI of the abdomen and pelvis. Response was assessed 1 month after completion of treatment by physical examination and 3 months after also by MRI. There was a complete response rate of 88% after 3 months in patients getting Cisplatin and 5 flouro uracil chemotherapy compared to response rate of 80% in those getting only Cisplatin. The mean duration of treatment was 60 days. In conclusion, combination chemotherapy with cisplatin and 5 FU along with radiotherapy in patients with locally advanced squamous cell carcinoma of cervix was well tolerated and slightly better than single agent chemotherapy with Cisplatin alone.

Keywords: Cervical cancer, Chemoradiation, Cisplatin.

Abbreviations: 5-FU (5 flourouracil), locally advanced cervical cancer (LACC).

Introduction

Cervical cancer is the second most common cancer among women worldwide, and patients with locally advanced cervical cancer (LACC) have a poor prognosis [1]. The main curative treatment for patients with LACC has been radical. Radiotherapy in the past century. During the period of 1999 to 2002, four large randomized trials and two large Meta-analysis reported improved survival with cisplatin-based concurrent chemo radiotherapy (CCRT), making it the standard treatment for International Federation of Gynecology and Obstetrics (FIGO) Stage IB2-IVA cervical Cancer [2-7]. This approach involves the use of cisplatin 40 mg/m^2 weekly for 6 weeks along with standard radiation [8]. Even though concurrent chemo radiation is superior to radiation alone, five year overall survival rates continue to be low for patients with locally advanced cervical cancer [9]. Still many patients continue to fail in the pelvis (20-25%) and at distant sites (10-20%) and Persistent pelvic disease or loco-regional recurrence is the major cause of treatment failure. The presence of large and bulky primary tumor with hypoxic areas and the presence of malignant clones resistant to chemotherapy and/or radiation are possible reasons for treatment failure [10]. These facts have stimulated interests in exploring other concurrent combinations with potentially more clinical effect .The availability of new active drugs suggests the study of new combination regimens in this group of patients. Paclitaxel is active in cervical cancer either alone or combined with cisplatin [11-13]. In vitro, paclitaxel potentiates the antitumor activity of ionizing radiation and recruits cells in the most radiosensitive phase of the cell cycle, the G2/M [14,15]. The combination of weekly paclitaxel with carboplatin or cisplatin along with radiotherapy has been previously studied in head and neck cancer and in lung cancer, where it proved to be active [16-19].

Materials and Methods

Eligibility Criteria

Women with advanced cervical cancer of international federation of gynecology and obstetrics (FIGO) stage IIB (localized disease with parametrical involvement), stage III (extension of the tumor to the pelvic wall) or stage IV A (involvement of the bladder or rectal mucosa) were selected and then randomly allotted into two groups of 27 patients each.

Baseline and Treatment assessment

All patients underwent a complete physical examination including pelvic examination by a multidisciplinary team (gynecologic oncologist and radiation oncologist) to determine the clinical stage according to FIGO classification.Patients had chest-X-ray, MRI of abdomen and pelvic, complete hematology and chemistry tests and sigmoidoscopy or cystoscopy if necessary. Hematology and chemistry test was obtained before each chemotherapy injection. Radiation and chemotherapy was stopped if the WBC count was < 2,000/mm3, the platelet count < 100/000 mm3 or in the event of severe (grade4) radiation induced gastrointestinal and genitourinary toxicity. Blood transfusion had done if hemoglobin< 10gr 50% reduction of tumor size for 1 months after completion of radiotherapy. Progressive disease was defined as the appearance of any new lesion

during treatment of a > 25% increase in size of local tumor.

Treatment Plan

The first group was given weekly injections of Cisplatinand 5-FU and the other group was given only cisplatin. In the first group Cisplatin 50-75 mg/m^2 IV on day 1 plus5-flurouracil (5-FU) 1000 mg/m^2 continuous IV infusion over 24 h on days 1-4 (total dose 4000 mg/m^2 each cycle) every 3 wk plus radiation therapy, 1.8-2.0 Gy daily, for a total of three to four cycles was given. In the second group Cisplatin 40 mg/m^2 IV once weekly plus radiation therapy, 1.8-2 Gy daily per fraction, for six cycles was given. Both drugs were administered between 1 and 2 hour before radiotherapy. Radiotherapy was administered to the whole pelvic region in 25-28 fractions for a total of 50-50.4 Gy followed 1 or 2 weeks later for intracavitary brachytherapy.

Results

After one month of treatment, in clinical response evaluation 20 patients had complete response (74%) in group one and 19 patients had complete response (70 %) in group two. After three months of treatment, 24 patients had complete response (88%) in group one and 21 patients had complete response (80%) in group two assessed both clinically and by ultrasound and MRI imaging.

Discussion

Radiotherapy with concurrent cisplatin has become the standard treatment for cervical cancer. Recent studies have attempted to increase the efficacy of treatment in advanced cervical cancer by using other chemotherapeutic agents with or without cisplatin concurrent with radiation [20]. New combinations of chemotherapy given concurrently with radiotherapy can further improve the prognosis of these patients. A recent phase III trial demonstrated that concurrent chemo radiation with cisplatin and gemcitabine followed by adjuvant cisplatin and gemcitabine is significantly superior to chemoradiation with weekly cisplatin alone with regard to progression-free survival and overall survival. However, the toxicity of cisplatin/gemcitabine chemoradiation was found to be unacceptably high in other studies, indicating the need for less toxic regimens to be developed [21-31].

In our study we have found that combination therapy of cisplatin and 5-FU is slightly more effective in complete cure than cisplatin alone.

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