

Sphincter Preservation and Pathologic Response in Rectal Cancer Undergoing Neoadjuvant Chemoradiation with and without Oxaliplatin According to Thymidilate Synthase (TS) Expression

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ABSTRACT

Background

Oxaliplatin (OX) significantly enhanced the antitumor activity of 5-FU in patients with advanced colorectal cancer and recently some phase II trials have evaluated the feasibility and efficacy of oxaliplatin in neoadjuvant setting for treatment of locally advanced rectal cancer. On the other hand various studies have demonstrated that the overexpression of thymidylate synthase (TS) can induce resistance to 5-FU in colorectal carcinoma. The aim of this study was to assess the value of TS expression as a predictive factor in the efficacy of neoadjuvant chemoradiation with and without oxaliplatin in rectal cancer.

Materials and Methods

This study was performed in 61 patients (that ultimately 50 patients had including criteria) with locally advanced rectal adenocarcinoma that inferior margin of the tumor had to be located no farther than 6 cm from the anal verge. Preoperative radiotherapy was delivered to the pelvis with CO 60 to 50/4 Gy. All patients received simultaneous chemotherapy: 5-fluorouracil (5-FU), 300 mg/square meter i.v. 24 h infusion during radiotherapy on days 1-5 every week. Thirty patients received oxaliplatin 50-60 mg /square meter weekly during radiotherapy. TS expression was assessed by immunohistochemical staining technique in pretreatment specimen, and the patients were categorized into TS (+) and TS (-) groups.

Results

A total of 23 of 50 tumors showed TS positive status at biopsy (46 %). Overall 36 patients (72%) achieved pathologic response (40% complete and 32% partial) that was significantly better in the TS (-) group than in the TS (+) group (85.1 vs 56.5%, $p=0.024$) and in the OX (+) group than in the OX (-) group (86.6 vs 50%, $p=0.005$). Among TS (-) patients there was no difference in pathologic response (88.2 vs 80%, $p=0.561$) or sphincter preservation (76.4 vs 80%, $p=0.831$) as a result of whether oxaliplatin therapy was carried out or not. But among the TS (+) patients there was a significant gain in pathologic response (84.6 vs 20 %, $p=0.002$) and sphincter preservation (84.6 vs 40 %, $p=0.026$) in favor of oxaliplatin group.

Conclusions

Our study indicate that oxaliplatin can improves poor outcome of TS positive rectal cancer and TS expression may be used for selecting patients for oxaliplatin containing neoadjuvant chemoradiation protocols that can have major role in the tumor down staging and preservation of sphincter and ultimately better quality of life.

Keywords: Rectal cancer, Oxaliplatin, TS, Pathologic response

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INTRODUCTION

Colorectal cancer is the third most common cause of cancer and the second leading cause of