Experience of use of endorectal high dose rate brachytherapy in neoadjuvant treatment of the locally advanced rectal cancer

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Abstract

Background: The aim of the present study is to assess the response rate and toxicity profile in patients with locally advanced rectal cancer using high dose rate endorectal brachytherapy (HDR-EBT) as a start component of the neoadjuvant treatment.

Material and methods: 28 patients with T3-4N0-2M0 rectal adenocarcinoma were included in the study. A novel approach using HDR-EBT is given in 4 fractions (4 Gy per fraction, 2 times a week) in combination with external beam radiotherapy (EBRT) 30,6 Gy (1,8 Gy per fraction). All patients received neoadjuvant chemotherapy during the course of irradiation consisting of Capecitabine 825 mg/m2 per os daily.

Results: The majority of patients were males (n=16; 57.1%), 12 (42.9%) – were females, their mean age was 60,6 years. All patients had a decrease in tumor size from average of 4,88 cm to 3,14 cm longitudinally. 21 of 28 patients (75%) had sphincter preserving surgery. 17 of 28 patients (60.7%) had a pathologic complete response of their primary tumors. Radiation therapy was well-tolerated. Acute GI and GU toxicity was limited to ≤ Grade 2 for all patients. Local recurrence in the observation group within 2 years was 3.6%.

Conclusions: The use of HDR-EBT as a start component of the neoadjuvant locally advanced rectal cancer treatment is an acceptable modality with high pathological response rate as well as an acceptable toxicity profile.

Key words: locally advanced rectal cancer, high dose rate, endorectal brachiotherapy.

Introduction

Neoadjuvant chemoradiotherapy with further rectal cancer surgery at the present day is a standard in the locally advanced rectal cancer (RC) treatment [1]. It is known that use of high dose rate endorectal brachytherapy (HDR-EBT) at the preoperative stage in the treatment of RC especially the low-localization tumors, leads to an improvement of a local control and possibility of the sphincter-saving procedure [2]. In spite of the resounding success of use of an intracavitary irradiation in complex curative or individual palliative therapy of RC, the problem of use of a contact gamma-therapy at this nosology is remote from a final solution. In particular, bright-line rules at the level of a cumulative doze (CD) from the present component of the radiotherapy, fractionating regimes and, in particular, an order of combination of HDR-EBT with other methods of the antineoplastic impact are absent.

The aim of the present study is to assess the response rate and toxicity profile in patients with locally advanced RC using HDR-EBT as a start component of the neoadjuvant treatment.

Material and methods

28 patients with the locally advanced primary unresectable RC of stage T3-4N0-2M0 were examined and they underwent a treatment due to the submitted regimen in 2011-2013 in Kherson Regional Oncological Dispensary.

Patients underwent HDR-EBT given in 4 fractions (4 Gy per fraction, 2 times a week) in combination with external beam radiotherapy (EBRT) 30,6 Gy (1,8 Gy per fraction). All patients on the first day of the radiotherapy received HDR-EBT session, in further HDR-EBT was conducted 2 times per week (Monday, Thursday), and EBRT was placed on days free of HDR-EBT.

EBRT was conducted with the use of device "Teragam K-01" (source activity 60Co 177 TBq, 1,17-1,33 MeV) per pelvis region. Lower limit of fields was situated 2 cm lower of an anal edge, upper limit - at the level L5-S1, lateral – 1 cm laterally of a bone pelvic ring. For the performance of 3D-planning on the system «PlanW 2000», axial plane CT series were used, that eventually led to the formation of the opposite fields 16–16 × 18–18 cm depending on the constitutional particulars of a patient.

HDR-EBT was conducted with the use of device «MultiSource» (source activity 60Co 70 TBq). Before the conduction of HDR-EBT a tumor size, a depth of the rectal wall invasion, a tumor prevalence were considered with the relation to the anal canal. Type and sizes of an applicator were chosen depending on a radiation area and anatomy of a patient. Planning was performed on the basis of MRI in a planning system «HDRplus 2.6».

Diagnosis of the underlying disease of all patients was morphologically verified. All tumors were an adenocarcinoma G2. All patients underwent radiotherapy with a Capecitabine radiosensitization with a daily doze of 825 mg/m2 per os.

There were men 57.1% (n=16) and women – 42.9% (n=12) under investigation. Age of patients varied within the range of 39-77 years (on average 60.6). Tumors of the rectal lower ampulla were present in 12 (42.9%) and the rectal middle ampule – in 16 (57.1%) cases. Pain was present in 20 (71.4%) of patients before treatment given. Chronic rectal bleeding was present in 13 (46,4%) of patients. 9 (32,1%) of patients suffered from a constipation at the beginning of the treatment. Distance between an anus and a distal pole of a tumor before therapy amounted to 2-9 cm (on average 5,55 cm). Extension of a primary tumor along the length of a rectum amounted from 2 to 10 cm (on average 4,88 cm).

Results and discussion

Total pain relief after the treatment given was reached in 12 (42.9%), partial pain relief – in 8 (28.6%) of patients. Chronic rectal bleeding was negated in 92.9% of cases. Constipation disappeared for the moment of the treatment termination in all cases. Distance between an anus and a distal pole of a tumor after therapy increased on average to 1,35 cm, extension of a primary tumor diminished to 3,14 cm (on 35.6%).

Some studies showed that combined radiotherapy is more effective in rectal tumor downstaging than EBRT alone and achieves a significant improvement in sphincter-saving procedure up to 76% in T2-T3 RC [3]. RC downstaging into a resectable stage was evaluated during a control examination in 4-6 weeks after completion of a radiotherapy (MRI, edoscopy) in our study, and amounted to 96.4% of cases (27 patients). 6 (21.4%) of patients were not candidates for sphincter-saving procedures. The number of the sphincter-saving procedures amounted to 21 (75%). Surgery was not performed in 1 (3.6%) patient. Reason of rejection of a surgery treatment was unresectable tumor. In the post-surgery period 1 case of sigmoidoproctostomy deficiency and 1 postoperative urinary bladder atony were noticed that amounted to 3.6% (total number of the postoperative complications didn't exceed 7.2%, which is comparable with statistical number of the postoperative complications in Ukraine and in the world).

It is known that HDR-EBT has advantages in the tumor destruction, but it also has disadvantages which are associated with the risk of complications [4]. During the whole course of a radiotherapy any undesirable effects were absent for 6 (21.4%) patients. One undesirable effect was noticed in 19 (67.9%) patients, simultaneously two — in 3 (10.7%) patients. Three and more undesirable effects were not registered. Absence of the toxic reactions of grade III and grade IV was detected. Intensity of the general complications in all cases corresponded to grade I according to the CTCAE 4.0.

El Sayed (2014) et al. and Hacker-Prietz (2015) reported cases of grade III proctitis post- HDR-EBT [5, 6]. In our study radiation proctitis of grade I and grade II developed with the same frequency, 5 (17.9%) cases. The cases of grade III proctitis were not registered.

There was only grade I radiation cystitis noticed in 3 (10.7%) patients. Grade I radiation epidermis was noticed in 1 (3.6%) patients in our study. El Sayed (2014) et al. reported no patients developed grade III cystitis, but grade III dermatitis in that study was seen in 12% of patients [5].

Anaemia developed in 1 (3.6%) patient, leucopenia – in 6 (21.4%) patients. Granulocytopenia, lymphopenia and thrombocytopenia were not detected. General type reaction (weakness, ailment, inappetency, low-grade fever) was noticed in 3 (10.7%) patients. Vomiting was not observed, sicchasia was registered in 1 (3.6%) patient, in this case this toxicity didn't exceed grade I.

Complete pathological response was noticed in 17 (60.7%) patients, pathological partial response was registered in 10 (35.7%), absence of pathologic changes was noticed in 1 (3.6%) case. Our results are hopeful because not numerous research of HDR-EBT effectiveness for RC treatment showed complete pathological response up to 33% [6] and 47% [5].

Local recurrence developed within 2 first years of monitoring in 1 (3.6%) patient. No case of a distant metastasis during the whole period of monitoring was detected. 2 (7.1%) fatal cases were registered. The cause of death of both died persons was a pathology unrelated to cancer (in one case was an injury, in the second one – a heart failure).

Conclusions

The use of HDR-EBT as a start component of the neoadjuvant locally advanced rectal cancer treatment is an acceptable modality with high pathological response rate as well as an acceptable toxicity profile.

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