

Perbandingan efektivitas terapi antara radiasi dan gabungan radiasi dengan mitomycin-c pada kanker leher rahim stadium lanjut local (analisis fraksi pertumbuhan tumor yang dinyatakan dengan ekspresi antigen Ki-67 sebagai predictor respons tumor)

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Abstrak

Respons tumor terhadap radiasi dipengaruhi oleh berbagai faktor yang dapat digolongkan ke dalam faktor intrinsik yang bersifat genetik dan faktor-faktor lingkungan mikro (microenvironment) yang disebut faktor epigenetik. Faktor intrinsik dapat ditunjukkan dengan 'predictive assay' yang dapat memperlihatkan sensitivitas individual tumor. Faktor epigenetik terdiri dari berbagai faktor termasuk hipoksia, vaskularisasi dan fraksi pertumbuhan. Dan berbagai penelitian dapat ditunjukkan hubungan antara beberapa faktor itu dengan respons tumor, maupun antara ketiga faktor tersebut. Dapat diasumsikan bahwa faktor hipoksia, vaskularisasi dan fraksi pertumbuhan merupakan indikator-indikator lingkungan tumor yang dapat merupakan prediktor terhadap respons radiasi pada jaringan tumor tersebut. Pada penelitian ini, fraksi pertumbuhan tumor akan diteliti kaitannya dengan respons tumor dan pemanfaatannya dalam pengobatan gabungan untuk meningkatkan respons pada tumor yang mempunyai prognosis buruk. Berdasarkan asumsi bahwa tumor dengan fraksi pertumbuhan rendah relatif hipoksik, maka dilakukan pengobatan gabungan radiasi dengan MMC, suatu sitostatika yang bekerja efektif dalam keadaan hipoksik pada kelompok-kelompok tumor yang sudah digolongkan ke dalam fraksi pertumbuhan yang rendah dan yang tinggi. Pemilahan pasien berdasarkan besarnya fraksi pertumbuhan dilakukan dengan pemeriksaan imunohistokimia pada jaringan biopsi segar penderita kanker leher rahim menggunakan antibodi monoklonal Ki-67. Penderita KLR yang diteliti adalah penderita stadium lanjut lokal (stadium II b sampai III b menurut FIGO) yang datang ke Sub Bagian Onkologi Bagian Obstetri dan Ginekologi FKUI/RSCM dan kemudian dikirim ke Sub Bagian Radioterapi Bagian Radiologi FKUI/RSCM

<hr>Response of tumors toward radiation is affected by various factors that can be classified as intrinsic factors, which are genetic, and epigenetic factors, which are micro environment. The intrinsic factors can be demonstrated through a "predictive assay" which can show the sensitivity of individual tumor.

Epigenetic factors consist of many factors including hypoxia, vascularization, and growth fraction. From results of many studies, can' be shown that there is a relation between these last factors with response of tumor. There is also relation among these three factors. We can assume that hypoxia, vascularization and growth fraction are indicators of tumor's environment which can also be predictors of response to radiation in tumor tissue.

In this study, the rate of tumor growth will be studied in it's relation to tumor's response and the uses in combined treatment to increase the response of tumors with bad prognosis.

Based on an assumption that tumors with low growth fraction are relatively hypoxic, combination of radiation with MMC is used, a cytostatic agent that effectively work on hypoxic condition in groups of

tumors which have been classified as having low growth fraction. Patients grouping were performed based on the growth fraction as seen in immunohisto chemistry examination on fresh biopsy tissue of patients with cancer of cervix, using Ki-67 monoclonal antibody. Those patients of cancer of the cervix included in this study were patients in locally advanced stages (stage IIb - IIIb by FIGO classification), who came to Oncology Sub Department of the Department of Obstetric and Gynecology Faculty of Medicine University of Indonesia/Dr. Cipto Mangunkusumo Hospital, and referred to Radiotherapy Sub Department of the Department of Radiology at the same institute.

After going through inclusion and exclusion criteria, 146 patients were found to be suitable for evaluation with the prescribed protocol. The patients were sorted into 4 groups according the growth fraction and type of treatment to be performed. Group I and Group II were patients with Ki-67 index less than 40% with a difference that Group I underwent radiation therapy only, while Group II was treated with combination of radiation therapy and MMC. Group III and IV were patients with Ki-67 index 40% or higher, with a difference that Group III underwent radiation therapy only, while Group IV was treated with combination of radiation therapy and MMC. The 40 % Ki-67 criterion was determined based on results of preliminary study which set the level around 40%.

The radiation therapy consisted of external radiation to the pelvis area in 28 sessions with a dose of 180 cGy per sessions or 5040 cGy total dose given in around 5.5 weeks. After a 1 - 2 week rest, radiation therapy were continued in the form of intra cavitory radiation using High Dose Rate (HDR) system in 2 sessions, 1 week apart, each in a dose of 850 cGy, giving a total dose of 1700 cGy. A small number of patients (42 patients) were given with Low Dose Rate (LDR) intra cavitory system in similar session and interval with those patients with HDR system. The dose was 1300 cGy per session or total dose of 2600 cGy being equal to the total dose of 1700 cGy in HDR system. Mitomycin-C was given in the combined treatment groups, with a dose of 15 mg/m², as a bolus injection intravenously, at the first day of external radiation and the first intracavitory insertion.

Routine blood examinations were performed to each patient before treatment and once a week until the radiation therapy were completed. Liver function tests were performed before treatment, at the end of external radiation and after all radiation therapy completion.