INTRAOPERATIVE RADIATION THERAPY IN THE TREATMENT OF BREAST CANCER

Spanish full text

ABSTRACT

Introduction: radiotherapy is an essential part of combined cancer treatment, with growing interest in recent decades in techniques that irradiate only the portion of the breast at greatest risk of developing local recidivation. The philosophy is to achieve higher and more effective doses of radiation without increasing the incidence of adverse effects, since sensitive structures are mobilised and shielded when radiation is administered. Such techniques include intraoperative radiotherapy (IORT), which seeks to enhance local control of the disease by administering a single dose of ionising radiation directly to the tumour bed, thereby enabling dosages to be increased and toxicity decreased through less irradiation of healthy tissue.

Objectives: to assess the effectiveness of IORT as adjuvant or replacement treatment for the current standard treatment of breast cancer, in terms of recurrence, survival, cosmetic results and impact on quality of life; and to ascertain the safety of this procedure, in terms of acute and late toxicity.

Methods: a search of the scientific literature was conducted, from January 2000 to January 2013, in the main biomedical databases: Centre for Reviews and Dissemination (Health Technology Assessment, Database of Abstracts of Reviews of Effectiveness, NHS Economic Evaluation Database), Cochrane Plus Library, Medline, Embase, ISI Web of Knowledge, CSIC-*Índice Médico Español*, Clinical Trials Registry, WHO International Clinical Trials Registry Platform and Current Controlled Trials. This process was completed by a general search of quality Internet web pages. Two independent reviewers selected the papers in accordance with pre-established inclusion and exclusion criteria, with any disagreements being resolved by consensus. Lastly, a manual review was performed of the bibliographic references cited in the papers selected. The data were then extracted and summarised in evidence tables. Study quality was assessed using the National Health and Medical Research Council scale.

Results: of the total of 77 studies selected for full-text appraisal, 44 met the inclusion criteria and comprised 1 systematic review, 1 meta-analysis, 1 clinical trial, 9 comparative case series and 32 case series, with the total number of patients included being 2310 in booster treatment and 5494 in monotherapy. IORT administered as an intraoperative booster dose registered a recurrence rate at 5 years of 6,5% (as the highest value and mainly at a local level) and survival rates of around 91% at 5 and 7 years. The cosmetic results obtained were good and/or excellent in over 90% of patients. Toxicity was of a moderate nature, reaching a maximum of grade III on the Radiation Therapy Oncology Group/European Organisation for Research and Treatment of Cancer (RTOG/EORTC) and Subjective, Objective, Management, Analytic/Late Effects Normal Tissue Task Force (SOMA-LENT) scales. The most frequent complications were development of fat necrosis (50%), seroma (48%) and skin toxicity (15%), with worse results being observed after IORT than with external radiation. Incidence of ulcers, fibrosis, oedema and lymphoedema was 5% and that of regular acute pain, 10%. Administration of IORT as the sole form of radiation yielded a recurrence rate ranging from 1,22% at 4 years to 7% at 10 years, slightly higher than that of conventional treatment, though without statistical significance. Overall survival was close on 90% at 10 years, with good

and/or excellent cosmetic results in 90% of patients. The complications registered indicated that patients treated with IORT presented with a higher incidence of ulceration, fat necrosis, infections (grade III), seromas and haematomas that required intervention than did patients who had been treated conventionally, with a lower incidence of pain, fibrosis and oedema, though in most cases these differences did not prove statistically significant. Administration of a single dose of IORT seemed to improve certain aspects of quality of life, such as daily and professional activity, or presence and intensity of pain, as compared to patients treated with an IORT booster dose or conventionally, though these differences again failed to prove statistically significant.

Discussion: the existence of a single randomised clinical trial (RCT) with certain methodological limitations, taken together with the fact that the remaining studies included were not only observational and descriptive in nature but also displayed certain limitations and possible conflicts of interest, amounts to a serious limitation when it comes to drawing firm conclusions.

Conclusions: the results of studies that assess IORT as an alternative to an external-radiation booster dose indicate that this combination does not amount to an increase in terms of effectiveness and overall survival, nor does it entail a significant reduction in terms of safety with respect to conventional external radiation treatment. These results are drawn from studies of little methodological rigour, and there are no clinical trials that would go to confirm them. Administration of a single dose of IORT is associated with an incidence of recurrences and metastasis comparable to that of conventional treatment, and, despite showing low toxicity, does not improve the toxicity of conventional treatment to any significant degree. This evidence is based on a single RCT with certain limitations and on observational and descriptive studies, something that considerably reduces the validity of these results. Indeed, the results of the studies included give rise to important doubts regarding the possible replacement of conventional external radiotherapy by intraoperative radiation as the treatment of choice in patients with breast cancer in the initial stages.

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avalia-t2013/xxx

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