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[Intervention Review]

Adjuvant chemotherapy after concurrent chemoradiation for locally advanced cervical cancer

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ABSTRACT

Background

Current standard treatment for patients with cervical cancer who have locally advanced stage disease (International Federation of Gynecology and Obstetrics (FIGO) stage IIB to IVA) is concurrent chemoradiation therapy (CCRT). However, less than two-thirds of patients in this group survive for longer than five years post treatment. Adjuvant chemotherapy (ACT) can be given in an attempt to improve survival by eradicating residual disease in the pelvis and treating occult disease outside the pelvic radiation field. However, inconsistency in trial design, inclusion criteria for participants, interventions and survival benefit has been noted among trials of ACT after CCRT for locally advanced cervical cancer (LACC).

Objectives

To evaluate the effect of adjuvant chemotherapy (ACT) after concurrent chemoradiation (CCRT) on survival of women with locally advanced cervical cancer compared with CCRT alone.

Search methods

We searched the Cochrane Gynaecological Review Group Trial Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE and conference proceedings to March 2014. We handsearched citation lists of relevant studies.

Selection criteria

Randomised controlled trials (RCTs) comparing CCRT alone versus CCRT plus ACT were included. Patients were diagnosed with cervical cancer FIGO stage IIB to IVA with a histopathology of squamous cell carcinoma, adenosquamous cell carcinoma, adenocarcinoma or undifferentiated carcinoma.

Data collection and analysis

Two review authors (ST, KK) selected relevant trials, extracted data, assessed risk of bias independently, compared results and resolved disagreements by discussion.

Main results

We identified two RCTs involving 978 women with cervical cancer stage IIB to IVA. As the trials were significantly different clinically, we did not perform meta-analyses. One industry-funded trial involving 515 women compared CCRT (cisplatin) versus CCRT (cisplatin and gemcitabine) plus ACT (two additional cycles). This trial reported significant improvement in progression-free survival (PFS) and overall survival (OS) in women who were given CCRT plus ACT compared with those treated with CCRT alone: Three-year PFS was 74.4% versus 65.0% (hazard ratio (HR) 0.68, 95% confidence interval (CI) 0.49 to 0.95, P value 0.027), and three-year OS was 80% versus 69% (HR 0.68, 95% CI 0.49 to 0.95, P value 0.022). However, as the CCRT chemotherapy differed between the two arms, we considered the findings to be at high risk of bias.

The second trial was a four-arm study from which we extracted data on 463 women in two study arms receiving CCRT (intravenous mitomycin C and oral 5-fluorouracil (5-FU)) or CCRT plus ACT (oral 5-FU for three cycles). The HR for OS in women who received ACT after CCRT compared with the HR for OS in those who were given CCRT alone was 1.309 (95% CI 0.795 to 2.157), and the HR for disease-free survival (DFS) was 1.125 (95% CI 0.799 to 1.586).

Haematological adverse events were more common in the ACT arms of both trials. Quality of life (QoL) was not reported in either trial.

Authors' conclusions

With limited data from only two trials, we found insufficient evidence to support the use of ACT after CCRT. Future large trials are required to demonstrate efficacy, toxicities and QoL.

PLAIN LANGUAGE SUMMARY

Can additional chemotherapy after initial treatment for locally advanced stage cervical cancer reduce recurrence and extend life?

The issue

Standard treatment for locally advanced stage cervical cancer (stage IIB to IVA) is 'concurrent chemoradiation' when anticancer drugs are given during the same treatment period as pelvic radiotherapy (radiation therapy to lower abdomen). However, the tumour may remain (residual cancer) or may come back (recurrent cancer) after this standard treatment. This review evaluated whether giving additional anticancer drugs (ACTs) after standard treatment could help women with locally advanced cervical cancer to live longer compared with standard treatment alone.

How we conducted the review

We searched the literature to March 2014 and identified two randomised controlled trials comparing standard treatment versus standard treatment plus ACT in women with locally advanced cervical cancer. Two review authors assessed these studies and collected data independently.

Findings

The two studies were very different; therefore we could not pool their data. One trial conducted internationally between 2002 and 2004, involving 515 women, found that cancer took longer to return in women receiving ACT (cisplatin and gemcitabine), and more women in the ACT group were alive after three years than in the standard treatment group (80% versus 69%). We considered the findings to be at high risk of bias in this trial, as women were given different drugs during standard treatment, and so the overall effect of the study treatment could not be attributed to the ACT alone. The other trial, which was conducted in several hospitals in Thailand between 1988 and 1994, involved 463 women. ACT (5-fluorouracil) did not improve the length of survival or the time taken for cancer to return in women in this trial. A trend towards increased side effects was reported in the ACT arms of both studies.

Conclusions

We found insufficient evidence to support giving additional anticancer drugs to women who have received standard treatment for locally advanced cervical cancer, as currently only limited data are available from two very different trials.