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[Intervention Review]

Interventions for the treatment of metastatic extradural spinal cord compression in adults

Reena George¹, Jenifer Jeba¹, Govindaraj Ramkumar², Ari G Chacko³, Prathap Tharyan⁴

¹Palliative Care Unit, Christian Medical College, Vellore, India. ²Department of Radiation Oncology, Royal Adelaide Hospital, Adelaide, Australia. ³Neurosciences, Christian Medical College, Vellore, India. ⁴Cochrane South Asia, Prof. BV Moses Center for Evidence-Informed Health Care and Health Policy, Christian Medical College, Vellore, India

Contact address: Reena George, Palliative Care Unit, Christian Medical College, Vellore, Tamil Nadu, 632004, India. reena.vellore@gmail.com.

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ABSTRACT

Background

Metastatic extradural spinal cord compression (MESCC) is treated with radiotherapy, corticosteroids, and surgery, but there is uncertainty regarding their comparative effects. This is an updated version of the original Cochrane review published in the *Cochrane Database of Systematic Reviews* (Issue 4, 2008).

Objectives

To determine the efficacy and safety of radiotherapy, surgery and corticosteroids in MESCC.

Search methods

In March 2015, we updated previous searches (July 2008 and December 2013) of the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, LILACS, CANCELIT, clinical trials registries, conference proceedings, and references, without language restrictions. We also contacted experts for relevant published, unpublished and ongoing trials.

Selection criteria

Randomised controlled trials (RCTs) of radiotherapy, surgery and corticosteroids in adults with MESCC.

Data collection and analysis

Three authors independently screened and selected trials, assessed risk of bias, and extracted data. We sought clarifications from trial authors. Where possible, we pooled relative risks with their 95% confidence intervals, using a random effects model if heterogeneity was significant. We assessed overall evidence-quality using the GRADE approach.

Main results

This update includes seven trials involving 876 (723 evaluable) adult participants (19 to 87 years) in high-income countries. Most were free of the risk of bias.

Different radiotherapy doses and schedules

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Two equivalence trials in people with MESCC and a poor prognosis evaluated different radiotherapy doses and schedules. In one, a single dose (8 Gray (Gy)) of radiotherapy (RT) was as effective as short-course RT (16 Gy in two fractions over one week) in enhancing ambulation in the short term (65% versus 69%; risk ratio (RR) was 0.93, (95% confidence interval (CI) 0.82 to 1.04); 303 participants; *moderate quality evidence*). The regimens were also equally effective in reducing analgesic and narcotic use (34% versus 40%; RR 0.85, 95% CI 0.62 to 1.16; 271 participants), and in maintaining urinary continence (90% versus 87%; RR 1.03, 95% CI 0.96 to 1.1; 303 participants) in the short term (*moderate quality evidence*). In the other trial, split-course RT (30 Gy in eight fractions over two weeks) was no different from short-course RT in enhancing ambulation (70% versus 68%; RR 1.02, 95% CI 0.9 to 1.15; 276 participants); reducing analgesic and narcotic use (49% versus 38%; RR 1.27, 95% CI 0.96 to 1.67; 262 participants); and in maintaining urinary continence (87% versus 90%; RR 0.97, 0.93 to 1.02; 275 participants) in the short term (*moderate quality evidence*). Median survival was similar with the three RT regimens (four months). Local tumour recurrence may be more common with single-dose compared to short-course RT (6% versus 3%; RR 2.21, 95% CI 0.69 to 7.01; 303 participants) and with short-course compared to split-course RT (4% versus 0%; RR 0.1, 95% CI 0.01 to 1.72; 276 participants), but these differences were not statistically significant (*low quality evidence*). Gastrointestinal adverse effects were infrequent with the three RT regimens (*moderate quality evidence*), and serious adverse events or post-radiotherapy myelopathy were not noted.

We did not find trials comparing radiotherapy schedules in people with MESCC and a good prognosis.

Surgery plus radiotherapy compared to radiotherapy

Laminectomy plus RT offered no advantage over RT in one small trial with 29 participants (*very low quality evidence*). In another trial that was stopped early for apparent benefit, decompressive surgery plus RT resulted in better ambulatory rates (84% versus 57%; RR 1.48, 95% CI 1.16 to 1.90; 101 participants, *low quality evidence*). Narcotic use may also be lower, and bladder control may also be maintained longer than with than RT in selected patients (*low quality evidence*). Median survival was longer after surgery (126 days versus 100 days), but the proportions surviving at one month (94% versus 86%; RR 1.09, 95% CI 0.96 to 1.24; 101 participants) did not differ significantly (*low quality evidence*). Serious adverse events were not noted. Significant benefits with surgery occurred only in people younger than 65 years.

High dose corticosteroids compared to moderate dose or no corticosteroids

Data from three small trials suggest that high-dose steroids may not differ from moderate-dose or no corticosteroids in enhancing ambulation (60% versus 55%; RR 1.08, 95% CI 0.81 to 1.45; 3 RCTs, 105 participants); survival over two years (11% versus 10%; RR 1.11, 95% CI 0.24 to 5.05; 1 RCT, 57 participants); pain reduction (78% versus 91%; RR 0.86, 95% CI 0.62 to 1.20; 1 RCT, 25 participants); or urinary continence (63% versus 53%; RR 1.18, 95% CI 0.66 to 2.13; 1 RCT, 34 participants; *low quality evidence*). Serious adverse effects were more frequent with high-dose corticosteroids (17% versus 0%; RR 8.02, 95% CI 1.03 to 62.37; 2 RCTs, 77 participants; *moderate quality evidence*).

None of the trials reported satisfaction with care or quality of life in participants.

Authors' conclusions

Based on current evidence, ambulant adults with MESCC with stable spines and predicted survival of less than six months will probably benefit as much from one dose of radiation (8 Gy) as from two doses (16 Gy) or eight doses (30 Gy). We are unsure if a single dose is as effective as two or more doses in preventing local tumour recurrence. Laminectomy preceding radiotherapy may offer no benefits over radiotherapy alone. Decompressive surgery followed by radiotherapy may benefit ambulant and non-ambulant adults younger than 65 years of age, with poor prognostic factors for radiotherapy, a single area of compression, paraplegia for less than 48 hours, and a predicted survival of more than six months. We are uncertain whether high doses of corticosteroids offer any benefits over moderate doses or indeed no corticosteroids; but high-dose steroids probably significantly increases the risk of serious adverse effects. Early detection; and treatment based on neurological status, age and estimated survival, are crucial with all treatment modalities. Most of the evidence was of low quality. High-quality evidence from more trials is needed to clarify current uncertainties, and some studies are in progress.

PLAIN LANGUAGE SUMMARY

Interventions for the treatment of spinal cord compression due to the spread of cancer

Metastatic extradural spinal cord compression (MESCC) due to cancer from other parts of the body affecting the spine and causing compression of the spinal cord often results in pain, impaired functioning including reduced ability to walk, incontinence, and shortened

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survival. Radiation is the mainstay of treatment, but surgery, and corticosteroids are also used to treat people with MESCC. This update of a previous review published in 2008 evaluates the clinical trial evidence up to 3 March 2015 to determine how effective radiotherapy, surgery and corticosteroids are in improving functioning and survival, and in reducing pain; and how well tolerated they are in adults with MESCC.

We found seven studies conducted in high-income countries including 876 adults (aged 19 to 87 years) with MESCC. Follow-up ranged from one month to three years, and the number evaluated in each varied from 29 to 303. Two studies compared different doses of radiation, two compared surgery before radiation versus radiation alone, and three small trials evaluated the effects of high-dose corticosteroids versus moderate-dose steroids or placebo.

The key results are: 1. For different doses of radiation: one dose of radiation was as effective as two doses and two doses were as effective as eight doses of radiation in adults with spinal cord compression with stable spines who are expected to live for less than six months. Adults with a better prognosis may require the longer radiation course to prevent local cancer recurrence, but the immediate benefits of shorter courses might be important for people with MESCC who have only a short time to live. No serious adverse events were noted, and the incidence of diarrhoea, nausea and vomiting was low and no different with the different radiation doses. 2. For surgery before radiation: removing part of the vertebra to enlarge the spinal canal (laminectomy) before radiation offered no advantages over radiation alone. Direct decompressive surgery (directly accessing and removing affected parts of the vertebrae and, if required, fixing the spines using bone grafts and instruments) followed by radiation treatment was more effective than radiation alone in carefully selected adults younger than 65 years. Surgery plus radiation did not cause more harmful effects than radiation alone. 3. For high dose steroids: beneficial effects were not significantly different with high-dose versus moderate-dose steroids or placebo, but serious adverse effects were more frequent with high-dose steroids.

None of the studies reported on satisfaction with care or quality of life. We also did not find trials comparing different radiation doses in adults with MESCC with a good prognosis. We lacked full confidence in many results since they came from single trials or a few small trials. Also, in the study of decompressive surgery, some of the adults given radiation alone had cancers that were only moderately sensitive to radiation, and a third of patients in both intervention arms had unstable spines. In usual clinical practice, surgery, not radiation, is the preferred option in such instances. The overall GRADE quality of evidence was *moderate* for all outcomes for the comparisons of different radiation doses and for the adverse effects of high doses of corticosteroids, indicating reasonable confidence in the results, though future research could alter the estimates in this review and our confidence in the estimates. The GRADE quality of evidence was *very low* for all outcomes in the comparison of laminectomy, and *low* for the outcome of local tumour recurrence with different radiation doses, for all outcomes in the comparison with decompressive surgery, and for the efficacy outcomes in the comparison of high-dose corticosteroids. This indicates less confidence in these results, and acknowledges that future research is likely to alter the estimates in this review. More studies are required to clarify these uncertainties and some are in progress.