

**Cochrane** Database of Systematic Reviews

# Systemic antibiotics for treating malignant wounds (Review)

Ramasubbu DA, Smith V, Hayden F, Cronin P	

Ramasubbu DA, Smith V, Hayden F, Cronin P. Systemic antibiotics for treating malignant wounds. *Cochrane Database of Systematic Reviews* 2017, Issue 8. Art. No.: CD011609. DOI: 10.1002/14651858.CD011609.pub2.

www.cochranelibrary.com



## [Intervention Review]

## Systemic antibiotics for treating malignant wounds

Darshini A Ramasubbu<sup>1</sup>, Valerie Smith<sup>2</sup>, Fiona Hayden<sup>3</sup>, Patricia Cronin<sup>2</sup>

<sup>1</sup>Dental Department, HSE, Dublin, Ireland. <sup>2</sup>School of Nursing and Midwifery, Trinity College Dublin, Dublin, Ireland. <sup>3</sup>Community Pharmacy, Lloyd's Pharmacy, Dublin, Ireland

**Contact:** Darshini A Ramasubbu, Dental Department, HSE, Kilbarrack Dental Clinic, Foxfield Crescent, Dublin, D5, Ireland. ramasubd@tcd.ie, darshini7@hotmail.co.uk.

Editorial group: Cochrane Wounds Group.

Publication status and date: New, published in Issue 8, 2017.

**Citation:** Ramasubbu DA, Smith V, Hayden F, Cronin P. Systemic antibiotics for treating malignant wounds. *Cochrane Database of Systematic Reviews* 2017, Issue 8. Art. No.: CD011609. DOI: 10.1002/14651858.CD011609.pub2.

Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

#### **ABSTRACT**

## **Background**

Malignant wounds are a devastating complication of cancer. They usually develop in the last six months of life, in the breast, chest wall or head and neck regions. They are very difficult to treat successfully, and the commonly associated symptoms of pain, exudate, malodour, and the risk of haemorrhage are extremely distressing for those with advanced cancer. Treatment and care of malignant wounds is primarily palliative, and focuses on alleviating pain, controlling infection and odour from the wound, managing exudate and protecting the surrounding skin from further deterioration. In malignant wounds, with tissue degradation and death, there is proliferation of both anaerobic and aerobic bacteria. The aim of antibiotic therapy is to successfully eliminate these bacteria, reduce associated symptoms, such as odour, and promote wound healing.

## **Objectives**

To assess the effects of systemic antibiotics for treating malignant wounds.

## Search methods

We searched the following electronic databases on 8 March 2017: the Cochrane Wounds Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL; the Cochrane Library, 2017, Issue 3), Ovid MEDLINE, Ovid Embase and EBSCO CINAHL Plus. We also searched the clinical trial registries of the World Health Organization (WHO) International Clinical Trials Registry Platform (apps.who.int/trialsearch) and ClinicalTrials.gov on 20 March 2017; and OpenSIGLE (to identify grey literature) and ProQuest Dissertations & Theses Global (to retrieve dissertation theses related to our topic of interest) on 13 March 2017.

## **Selection criteria**

Randomised controlled trials that assessed the effects of any systemic antibiotics on malignant wounds were eligible for inclusion.

## **Data collection and analysis**

Two review authors independently screened and selected trials for inclusion, assessed risk of bias and extracted study data. A third reviewer checked extracted data for accuracy prior to analysis.

## Main results

We identified only one study for inclusion in this review. This study was a prospective, double-blind cross-over trial that compared the effect of systemic metronidazole with a placebo on odour in malignant wounds. Nine participants with a fungating wound and for whom the smell was troublesome were recruited and six of these completed both the intervention and control (placebo) stages of the trial. Each stage lasted fourteen days, with a fourteen day gap (washout period) between administration of the metronidazole and the placebo.



The study, in comparing metronidazole and placebo, reported on two of this review's pre-specified primary outcomes (malodour and adverse effects of the treatment) and on none of the review's pre-specified secondary outcomes.

#### Malodour

The mean malodour (smell) scores for the metronidazole group was 1.17 (standard deviation (SD) 1.60) and the mean for the placebo group was 3.33 (SD 0.82). It is unclear if systemic antibiotics were associated with a difference in malodour (1 study with 6 participants; MD -2.16, 95% CI -3.6 to -0.72) as the quality of the evidence (GRADE) was very low for this outcome. The study was downgraded due to high risk of attrition bias (33% loss to follow-up) and very serious imprecision due to the small sample size.

## Adverse effects

No adverse effects of the treatment were reported in either the intervention or control group by the trial authors.

## **Authors' conclusions**

It is uncertain whether systemic metronidazole leads to a reduction in malodour in patients with malignant wounds. This is because we were only able to include a single study at high risk of bias with a very small sample size, which focused only on patients with breast cancer. More research is needed to substantiate these findings and to investigate the effects of systemic metronidazole and other antibiotics on quality of life, pain relief, exudate and tumour containment in patients with malignant wounds.

## PLAIN LANGUAGE SUMMARY

## Systemic antibiotics for treating malignant wounds

## **Review question**

We reviewed the evidence about the effect of systemic antibiotics on malignant wounds. We were looking for evidence relating to possible side effects of this treatment, and the impact on quality of life and other symptoms.

## **Background**

Malignant wounds occur in people who have advanced cancer. They usually develop in the last six months of life, at or near the site of a tumour. They occur when a tumour spreads and invades surrounding skin and blood vessels, causing them to break down. The area loses nourishment due to poor blood flow, and eventually the tissues die, resulting in a malignant wound. This type of wound can be very painful, can smell, and can bleed or ooze fluid. These symptoms can be very difficult for people with advanced cancer. Treatment for malignant wounds does not normally aim to heal the wound, but to limit symptoms that affect people's quality of life.

Antibiotics are medicines that fight bacterial infections. Systemic antibiotics affect the whole body. They can be given by mouth in tablet form, or in other ways such as via injections. We looked for evidence as to whether systemic antibiotics can prevent malignant wounds from getting worse, and help reduce the smell, pain and other complications associated with these wounds.

## **Study characteristics**

In March 2017 we searched for randomised controlled trials looking at the effects of systemic antibiotics on malignant wounds. We found only one trial, dating from 1984, which compared the effectiveness of the antibiotic metronidazole with a placebo (sugar pill) on six participants with malignant wounds resulting from breast cancer. The trial was a cross-over trial which means that participants receive both the treatment being tested and the comparison treatment, at different time-points, with a break between the treatments to ensure that the effects of the first treatment have worn off before the second treatment is taken. This is called the 'washout' period. In the one trial in this review, half the participants took the antibiotic first, for 14 days, and half took the placebo. Both groups then had 14 days with no medication before swapping over (cross-over) and trying the alternative treatment for 14 days.

## **Key results**

It is unclear if metronidazole reduces the smell of malignant wounds when taken orally (by mouth) in tablet form, without any side effects occurring. Its effectiveness in relation to other outcomes such as pain or quality of life was not measured in this trial. No change in the size or appearance of participants' tumours was reported.

## Quality of the evidence

It is uncertain whether metronidazole reduces the smell of malignant wounds when taken orally in tablet form because the quality of the evidence is very low. This evidence came from a very small study with serious study design flaws, and more research is needed involving more people with different types of cancer. Trials looking at how antibiotics can affect other outcomes, such as quality of life, pain relief and reducing any bleeding or ooze from the wound are also needed.

This plain language summary is up to date as of March 2017.