Journal Watch

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Title: Simon ST, Higginson IJ, Booth S, Harding R, Bausewein C. Benzodiapezines for the relief of breathlessness in advanced malignant and non-malignant diseases in adults. Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD007354. DOI 10.1002/14651858.CD003754.pub2.

Abstract: *Background:* Breathlessness is one of the most common symptoms experienced in the advanced stages of malignant and non-malignant disease. Benzodiazepines are widely used for the relief of breathlessness in advanced diseases and are regularly recommended in the literature. However, the evidence for their use for this symptom is unclear. *Objectives:* To determine the efficacy of benzodiazepines for the relief of breathlessness in patients with advanced disease. *Search strategy:* We searched 14 electronic databases up to September 2009. We checked the reference lists of all relevant studies, key textbooks, reviews, and websites. We contacted investigators and specialists in palliative care for unpublished data. *Selection criteria:* We included randomised controlled trials (RCTs) and controlled clinical trials (CCTs) assessing the effect of benzodiazepines in relieving breathlessness in patients with advanced stages of cancer, chronic obstructive pulmonary disease (COPD), chronic heart failure (CHF), motor neurone disease (MND), and idiopathic pulmonary fibrosis (IPF). *Data collection and analysis:* Two review authors independently assessed identified titles and abstracts. Three independent review authors performed assessment of all potentially relevant studies (full text), data extraction, and assessment of methodological quality. We carried out meta-analysis where appropriate. *Main results:* Seven studies were identified, including 200 analysed participants with advanced cancer and COPD. Analysis of all seven studies (including a meta-analysis of six out of seven studies) did not show a beneficial effect of benzodiazepines for the relief of breathlessness in patients with advanced cancer and COPD. Furthermore, no significant effect could be observed in the prevention of breakthrough dyspnoea in cancer patients. Sensitivity analysis demonstrated no significant differences regarding type of benzodiazepine, dose, route and frequency of delivery, duration of treatment, or type of control. *Authors' conclusions:* There is no evidence for a beneficial effect of benzodiazepines for the relief of breathlessness in patients with advanced cancer and COPD. There is a slight but non-significant trend towards a beneficial effect but the overall effect size is small. Benzodiazepines caused more drowsiness as an adverse effect compared to placebo, but less compared to morphine. These results justify considering benzodiazepines as a second or third-line treatment within an individual therapeutic trial, when opioids and non-pharmacological measures have failed to control breathlessness. Although a few good quality studies were included in this review, there is still a further need for well-conducted and adequately powered studies.

Strengths/uniqueness: This is the first systematic review of the effects of benzodiazepines on dyspnea in patients with advanced disease. Methodologically, it meets the high standards of a Cochrane systematic review, and represents a useful summary of current evidence.

Weaknesses: Although almost all the included studies were of high quality, the number of studies and patients was small. Also, the studies were heterogeneous e.g. with respect to treatment, comparator, and outcome assessment.

Implications for Palliative Care: This review indicates that the use of benzodiazepines for relief dyspnea in advanced disease is not supported by current evidence. As stated by the authors, further research in this area is warranted. Although they suggest that benzodiazepines could considered on a second or third-line basis, caution needs to be maintained regarding the deleterious effect of these drugs on cognitive function, which was not assessed in this review.