Decreases in Pain at Rest and Movement-Related Pain during Zoledronic Acid Treatment in Patients with Bone Metastases due to Breast and Prostate Cancer: A Pilot Study.

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ABSTRACT

BACKGROUND: In patients with bone metastases, pain may be absent or moderate at rest, but may be exacerbated by different movements or positions. No study has evaluated separately pain at rest and on movement in patients with bone metastases undergoing treatment with zoledronic acid (ZA).

AIM: The aim of this prospective observational study was to evaluate the reduction in intensity of pain at rest and in movement-related pain after treatment with up to six infusions of ZA 4 mg every 28 days in patients with painful bone metastases due to breast or prostate cancer cared for at the Oncological Units and Pain Therapy and Palliative Care Unit of the NCI of Milano.

MATERIALS AND METHODS: Pain was assessed by a six-level verbal rating scale (0-5 score) at baseline and on each infusion as well as at follow-up visits (2 weeks after every infusion). The two main endpoints (estimated reduction in pain and movement-related pain) were defined as the difference between the baseline score and the average of all the post-treatment scores for each patient. To allow for the potential confounding effect of analgesic consumption, patients without any increase in analgesic consumption during zoledronic acid treatment were also analyzed as a separate subgroup.

RESULTS: Forty-eight patients with breast (34) or prostate cancer (14) were enrolled. At baseline, 100% of the patients had pain on movement, in 65% of them, the intensity ranged from moderate to very severe, in 61% of the patients, the intensity of pain on movement was higher than the intensity of pain at rest (average difference 0.89; 95% CI, 0.5-1.30). The estimated mean intensity reduction of pain at rest and on movement was: (a) 0.62 (95% CI, 0.28-0.98) and 0.79 (95% CI, 0.43-1.14), respectively, during the first 90 days of ZA treatment; (b) 0.59 (95% CI, 0.23-0.96) and 0.86 (95% CI, 0.49-1.23), respectively, during the entire treatment and follow-up period. Analgesic consumption decreased or was stable on average in 31 and 27%, respectively, of available follow-up data. In the 14 patients with decreased or stable analgesic consumption, pain reduction was 0.61 and 1.01, respectively.

CONCLUSIONS: In this study, at baseline, all the patients with painful bone metastases experience movement-related pain, and during zoledronic acid treatment, a decrease for both pain at rest and on movement was obtained.

STRENGTHS: The eligibility criteria for both inclusion and exclusion of participants were well-illustrated. The study had a relatively long follow-up period.

WEAKNESS: This was an uncontrolled pilot study. The absence of a control group does not allow for any comparison with placebo or other modalities of treatment, including other bisphosphonates. The allocation i.e administration of zoledronic acid was not concealed creating a potential source of bias. Other potential sources of bias in this study include non-randomization and the selection process used in recruiting participants.The completion rate was also low.

Of note, 21(44%) of the participants had previously received radiotherapy to the bone. It would have been worthwhile to determine the site that was irradiated was also the site of the ongoing pain. Some participants also underwent chemotherapy and hormonal therapy and the potential for these interventions to confound the findings was not adjusted for in the data analyses.

RELEVANCE TO PALLIATIVE CARE: This study represents the first time that the effectiveness of zoledronic acid in movement-related pain will be studied. Breakthrough pain, including incidental or movement-related pain is common in patients with metastatic bone lesions. It provides us with clinical and statistical evidence of the benefits of zoledronic acid in bone pain.

One of the challenges in palliative care is in determining an appropriate dosage schedule for bisphosphonate use without causing any untoward side-effects. Osteonecrosis of the jaw which has been reported more frequently in previous studies in patients receiving zoledronic acid was not shown in the study.