Evaluation of Hypercalcemia of Malignancy Management

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Background: Cancer-related hypercalcemia typically occurs in stage IV malignancies with a prevalence up to 2.74% per year and is associated with a poor prognosis. The primary treatment goal is to manage the underlying malignancy and provide additional calcium-reducing pharmacologic therapies. First-line options include intravenous fluids and bisphosphonates, while calcitonin or denosumab may be used as the situation warrants. Treatment approaches are variable and consensus recommendations are lacking, necessitating research to evaluate clinical response and efficacy of treatment. Evaluation of trends may help identify opportunities to improve practice and add to current literature.

Objective:
To evaluate clinical efficacy and response of varying treatment options used for hypercalcemia of malignancy to develop appropriate use criteria and identify areas to improve current practice

Methods: This was an IRB-approved, multicenter, retrospective chart review of patients with hypercalcemia of malignancy admitted between July 1, 2016 and June 30, 2021. Patients included were ≥ 18 years old and diagnosed with hypercalcemia and had an active malignancy. Patients were excluded if diagnosed with hyperparathyroidism. The primary endpoint was time in days to corrected calcium < 10.5 mg/dL or discharge based on initial severity of hypercalcemia (mild, moderate, and severe) and initial treatment option. Secondary endpoints included hypercalcemia-related symptom resolution, incidence of observed treatment related adverse effects, and patient disposition.

Results: Overall, 97 patients were included in this study. Sixty-eight percent of patients presenting with hypercalcemia had solid tumor malignancies and the most common hematologic malignancy in 18% of patients was multiple myeloma. Fifty-four percent of patients presented with metastatic disease and 56% of patients were classified as having severe hypercalcemia of malignancy at baseline. The most common initial agent for all severities of hypercalcemia was zoledronic acid. The most common subsequent agent administered in both moderate and severe hypercalcemia was calcitonin followed by zoledronic acid, and no subsequent agents were administered in mild hypercalcemia. The median time to corrected calcium < 10.5 mg/dL or discharge for mild, moderate, and severe hypercalcemia was 3.5 days, 5 days, and 5 days, respectively. The median time to corrected calcium < 10.5 mg/dL or discharge based on the initial agent used was shortest at 2 days for cinacalcet and longest at 5.5 days for pamidronate. Nausea and vomiting resolved following treatment in 88% of patients, dystonic reactions resolved in all patients, altered mental status resolved in 77.5% of patients, and no resolution of bradycardia was observed following treatment. The most common treatment related adverse effect was bone pain, which was associated with bisphosphonates in combination with calcitonin, calcitonin, pamidronate, and zoledronic acid. The median length of stay was 8 days, and the mortality rate was 66%.

Conclusion: These results may serve as an opportunity to develop appropriate use criteria to guide initial treatment options based on severity. Opportunities for improvement include reinforcing the need for symptoms resolution documentation and considering future studies evaluating efficacy and safety of cinacalcet. Ultimately, given the lack of consensus guidelines, this study may provide additional literature for hypercalcemia of malignancy management.