Benzodiazepines and the Management of Dyspnea in Palliative care Patients

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Disclosure Statement

I have no relevant financial relationships to disclose

Background

- Dyspnea is a common symptom in palliative care patients
- Opioids proven to relieve dyspnea
- Benzodiazepines (BZD) relieves anxiety associated with dyspnea – not conclusive evidence
- Role of BZD in management of dyspnea evolving
  - Midazolam + Morphine > Morphine alone
  - Midazolam = Morphine
  - Lorazepam + Morphine = safe & effective

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Simon et al., *Cochrane review*, 2010(1):CD007354
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Specific Aims

- To describe current practice regarding BZD use for palliative care inpatients with dyspnea
- To examine whether BZD alone or BZD in conjunction with opioids are effective for dyspnea

Methods : Subjects

- Retrospective chart review: 5 years
  - 2005 – 2010
- Inpatients with dyspnea at the initial evaluation by the Palliative Care Service (PCS) and a second assessment by the PCS within 24 hours

Methods : Data

- Dyspnea, pain and anxiety assessed by PCS using categorical scale
  - 0=none, 1=mild, 2=moderate, 3=severe
  - Clinically meaningful improvement = 1-point change
- Chart review for:
  - BZD and opioid dose, diagnosis, demographics, Charlson Co-morbidity Index (CCI)

Methods: Statistics

- Descriptive statistics
- Bivariate analysis (chi square, ANOVA)
  - Factors determining BZD used
  - Clinically meaningful improvement at 24 hours

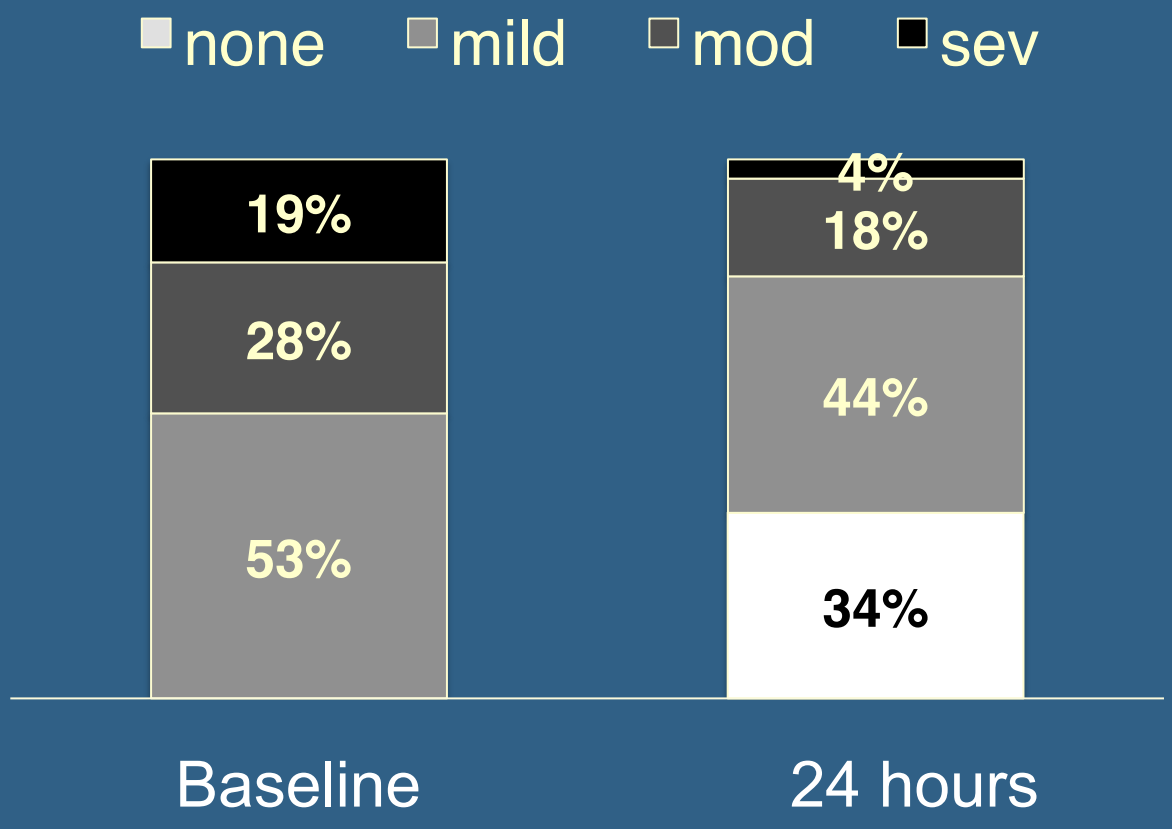
- Factors with significant association at $p<0.10$ were included in multivariate logistic regression

Results

- Reviewed 94% (309/333) of eligible cases
- Mean age: 66 years old
- Women: 48%
- Primary diagnosis
  - Cancer outside lung (32%)
  - Primary lung cancer (23%)
  - Heart failure (12%)
  - COPD (7%)
- Disposition: 47% died, 25% hospice, 17% home

Results: Dyspnea

Percent of patients categorized by severity of dyspnea



57% improved
36% same
7% worse

Results: Opioids use

- 49% (151/309) already received opioids at baseline
  - median dose 52 mg/day *
  - 87% (132/151) also received opioids at follow up
    - median dose 60 mg/day *
- Among 51% (158/309) of patients not on opioids at baseline
  - 41% (64/158) received opioids at follow up
    - median dose 22 mg/day *
- Overall 64% (196/309) received opioids at follow up
  - Median dose 41.5 mg/day *

* Oral morphine equivalent

Results: BZD use

- At the follow up
  - Overall 24% (75/309) received BZD at follow up
  - 22 % (68/309) received BZD and Opioid
  - Only 7 patients recived BZD alone
    - median dose 1 mg/day*

* Oral lorazepam equivalent

Results: Factors Associated with Receiving BZD at Follow Up

Factors	Model 1 OR, (95%CI)	Model 2 OR (95%CI)
Age	0.97 (0.96, 0.99)*	0.98 (0.97, 1.0)
Baseline anxiety	1.8 (1.0, 3.1)*	1.4 (0.7, 2.7)
Metastatic cancer	1.7 (0.9, 3.2)	1.9 (0.9, 4.0)
Baseline BZD	-	14.3 (6.2, 32.7) *
Baseline opioids	-	0.8 (0.4, 1.7)
Follow up opioids	-	6.4 (2.4, 16.2) *

* significant at $p < 0.05$

Results: Factors Associated with Dyspnea Improvement at Follow up

Factors	OR, (95%CI)
Age	1.01 (1.0, 1.03)
Co-morbidity Index	0.9 (0.8, 0.98)*
Baseline dyspnea	
- Mild	1.0
-Moderate	4.1 (2.3, 7.5)*
-Severe	4.5 (2.2, 9.0)*
BZD & opioids at baseline	1.3 (0.5, 3.2)
BZD & opioids at follow up	**2.1 (1.0, 4.2)***

* significant at $p < 0.05$

Conclusion

- Most patients have improvement in dyspnea at about 24-hour follow up
- 64% received opioids
- 24% received BZD
- 22 % Opioid BZD
- Only BZD and opioids together associated with significant improvement in dyspnea

Discussion

- In our study, opioids alone, not associated with relief of dyspnea
  - High mortality rate: slowing of respiratory rate near death so patient may not receive continued or increased doses of opioids
  - Simultaneous treatments; difficult to document
  - Unlikely to be due to under-dosing
- Patients who received both opioids and BZD may have been those who did not improve with other interventions

Limitations

- Single site, referral-based palliative care service
- Confounding by indication and unmeasured confounders
- Chart review limited in describing temporal relationships and measures of dyspnea

Implications for Research, Policy, and Practice

- Results support the BZD as adjuvant for patients with dyspnea where opioids alone were not sufficient
  - Low-dose BZD seem sufficient
- Our results should not dissuade people from using opioids as the first-line treatment
- Role of BZD alone in management of dyspnea needs further study

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