Symptom Clusters: The New Frontier in Symptom Management Research

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Significance of the Problem
- Patients with cancer experience a variety of symptoms
  - Disease-related symptoms
  - Treatment-related symptoms
- Symptoms are a major problem for patients and FCs
  - Require self-management
- Unrelieved symptoms have deleterious effects on patient outcomes
  - Functional status
  - QOL

Prevalence of Multiple Symptoms
- Development of the MSAS
  - Oncology inpatients and outpatients (n=218)
- Prevalence of symptoms
  - Lack of energy – 73.4%
  - Worrying – 72.4%
  - Feeling sad – 67.4%
  - Pain – 63.1%
  - Feeling nervous – 59.7%
  - Dry mouth – 55.3%
  - Difficulty sleeping – 52.8%

Prevalence of Multiple Symptoms
Walsh, et al. Supportive Care in Cancer, 2000
- Oncology patients on admission to a palliative care unit (n=1000)
- Prevalence of symptoms
  - Pain – 84%
  - Easy fatigue – 69%
  - Weakness – 66%
  - Anorexia – 66%
  - Lack of energy – 61%
  - Dry mouth – 57%
  - Constipation – 52%
  - Early satiety – 51%
  - Dyspnea – 50%
  - > 10% weight loss – 50%
  - Sleep problems – 49%
  - Depression – 41%

Descriptive and Intervention Studies
- Traditional approach
  - Perform detailed assessments of individual symptoms
  - Develop and test interventions for individual symptoms
- Clinical experience suggests that oncology outpatients present with multiple symptoms or perhaps symptom clusters

Symptom Cluster Research
- Symptom clusters and their effect on functional status (Dodd, Miaskowski, & Paul, ONF 28(3):465-470, 2001)
- Symptom clusters in elderly patients with lung cancer (Gift et al., ONF 31(2):203-209, 2004)
Definition – Symptom Cluster

A symptom cluster is three or more concurrent symptoms that are related to each other.

(Dodd, Miaskowski, & Paul, ONF 28(3):465-470, 2001)

Symptom Clusters and Their Effect on Functional Status - 1

(Dodd, Miaskowski, & Paul, ONF 28(3):465-470, 2001)

- Determine the effect of the symptom cluster of pain, fatigue, and sleep insufficiency on functional status during 3 cycles of CTX
- 93 oncology outpatients
- Two-stage hierarchical multiple regression analysis
  - KPS at end of CTX was the dependent variable
  - Step 1 – KPS at baseline
  - Step 2 – age and symptom cluster

Symptom Clusters and Their Effect on Functional Status - 2

(Dodd, Miaskowski, & Paul, ONF 28(3):465-470, 2001)

- Model explained 48.4% of the variance in functional status
- After KPS at baseline was partialled out from the KPS at end of CTX
  - Age explained 11.8%
  - Pain explained 10.7%
  - Fatigue explained 7.3%
  - Sleep insufficiency (only 1%)
- Symptom clusters appear to influence functional status

Symptom Clusters in Elderly Patients with Lung Cancer

(Gift et al., ONF 31(2):203-209, 2004)

- Identify the number, type, and combination (cluster) of symptoms experienced by patients with lung cancer (n=220 newly diagnosed)
- Factor analysis revealed that the following symptoms formed a cluster: fatigue, nausea, weakness, appetite loss, weight loss, altered taste, vomiting
- Predictors of symptoms included: initial stage of disease, number of comorbid conditions, CTX treatment

Symptom Clusters in Patients with Lung Cancer

(Gift et al., Nursing Res 52(6):393-400, 2003)

- Symptom cluster – fatigue, weakness, wt loss, appetite loss, nausea, vomiting, altered taste
- Did the symptom cluster identified at the time of diagnosis remain at 3 and 6 months (n=112)
- Cluster of 7 symptoms had internal consistency and remained at 3 and 6 months
- Mean number and severity of symptoms decreased over time
- Stage of cancer diagnosis was most predictive of the number of cluster symptoms reported

Approaches for Symptom Cluster Studies

- Cluster symptoms
  - Administer a comprehensive symptom inventory
  - Factor analysis approach
- Cluster patients
  - Identification of high risk groups
  - Choose symptoms
  - Cluster analysis
Study Purposes

- Can subgroups of oncology outpatients be identified based on symptom clusters (i.e., pain, fatigue, sleep disturbances, and depression?)
- Do patients in different symptom cluster groupings differ in outcomes (i.e., functional status and QOL)?

Research Team

- Christine Miaskowski, RN, PhD, FAAN
- Marylin Dodd, RN, PhD, FAAN
- Brad Aouizerat, PhD
- Kathryn Lee, RN, PhD, FAAN
- Claudia West, RN, MS
- Bruce Cooper, PhD
- Steven Paul, PhD
- Maria Cho, RN, PhD
- Alice Bank, RN, MS

Funding

- Oncology Nursing Society
- National Cancer Institute
- National Institute of Nursing Research

Design and Methods

- Descriptive, cross-sectional study
- Four outpatient settings in Northern CA
- Inclusion criteria:
  - Over 18 years of age
  - Receiving active treatment in an outpatient setting
  - Able to read, write, understand English

Study Procedures

- Informed consent was obtained
- Patients completed a number of self-report questionnaires
  - General sleep disturbance scale (GSDS)
  - Lee Fatigue Scale (LFS)
  - Center for Epidemiological Studies – Depression Scale (CES-D)
  - Numeric rating scale for worst pain intensity
- Mailed completed questionnaires to the research office

Demographic Characteristics – 1 (n=191)

<table>
<thead>
<tr>
<th></th>
<th>Mean (S.D.)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>60.8 (12.4)</td>
</tr>
<tr>
<td>Education (years)</td>
<td>15.4 (2.8)</td>
</tr>
<tr>
<td>KPS score</td>
<td>79.0 (14.5)</td>
</tr>
</tbody>
</table>
Demographic Characteristics – 2 (n=191)

% F 54.9
Lives alone 29.0
Married/partnered 58.1
Caucasian 89.6

Cancer Diagnoses (n=191)

% Breast 25.2
Ovarian 6.8
Lung 10.2
Colon 5.8
Prostate 14.6
Head and neck 5.3
Other 32.1

Current Cancer Treatment (n=191)

% Chemotherapy 60.0
Radiation therapy 38.5
Hormonal therapy 14.1
Biotherapy 4.4

Mean Scores on Symptom Scales

Mean (S.D.)

CES-D (depression) 13.6 (10.2)
LFS (fatigue) 3.7 (2.2)
GSDS (sleep) 54.2 (21.1)
NRS worst pain 6.9 (2.2)

Cluster Analysis

- A methodology to identify subgroups of patients based on symptom intensity
- Hierarchical cluster analysis
  - Scores for pain, fatigue, sleep disturbance, depression were standardized on their ranges
  - Placed measures on the same scale but retained their variances in the analysis
  - Linkage method was weighted average clustering
  - Squared Euclidean distances used in the proximities matrix
- Used the Harabasz and Duda and Hart stopping rules
- Clusters confirmed using STATA Version 8 and SAS Version 9.1

Two Cluster Solution

LOW TO MODERATE ON ALL SYMPTOMS
N = 163
85.3%

HIGH ON ALL SYMPTOMS
N = 28
14.7%
Three Cluster Solution

LOW PAIN & HIGH FATIGUE
N = 68
35.6%

LOW TO MODERATE ON ALL SYMPTOMS
N = 95
49.7%

HIGH ON ALL SYMPTOMS
N = 28
14.7%

Four Cluster Solution

LOW PAIN & HIGH FATIGUE
N = 68
35.6%

HIGH ON ALL SYMPTOMS
N = 28
14.7%

LOW ON ALL SYMPTOMS
N = 67
35.0%

HIGH PAIN & LOW FATIGUE
N = 28
14.7%

Differences in Demographic and Treatment Characteristics Among the Four Subgroups

- Patients in the HIGH subgroup were significantly younger (54.4 years) than patients in the LOW subgroup (62.4)
- Patients in the HIGH subgroup were significantly less likely to be married/partnered (35.7%) than the LOW (72.7%) or the HIGH PAIN & LOW FATIGUE (59.3%) subgroups
- No differences in any of the disease or treatment characteristics were found among the four subgroups
Conclusions

1. Oncology outpatients can be grouped into subgroups based on severity of symptoms
2. ~65% of the patients reported moderate to high levels of one or more symptoms
3. ~30% of the patients (56/191) reported pain
4. ~66% of those in pain (56/85) reported pain in the severe range
5. ~76% of patients reported moderate levels of sleep disturbance
6. ~31% of patients reported CES-D scores of >16
7. ~29% of patients reported fatigue scores of >5
8. Patients in the HIGH subgroup reported the lowest QOL scores (35.8% difference between the HIGH and LOW subgroups)
9. Moderate levels of fatigue, sleep disturbance and depression with or without pain resulted in similar outcomes
Implications for Future Research

- Longitudinal studies are needed with specific patient populations and specific treatments
  - Changes in the patterns of symptoms
  - Relationships among symptoms
- Further delineation of subgroups of patients using cluster analysis
  - Evaluate changes over time
  - Evaluate for a common mechanism or different mechanisms

Challenges/Issues in Symptom Cluster Research

- Definition of terms
- Nature and prevalence of symptom clusters
- Assessment of symptom clusters
- Intervention studies for symptom clusters
- Additional considerations
- Approaches to advance the science of symptom cluster research