Clinical Digest

Pulmonary Disease

Pilot Study for Patients With Chronic Obstructive Pulmonary Disease

In a recent pilot study, a researcher from Case Western Reserve University in Cleveland, Ohio, investigated whether selected cytokines vary between rest and activity periods in critically ill patients with chronic obstructive pulmonary disease (COPD). The study had 2 specific aims: (1) to examine the serum levels of interleukin (IL)-6 and IL-10 in hospitalized patients while at rest, and (2) to compare "at rest" serum IL-6 and IL-10 levels with those obtained immediately after a period of therapeutic activity.

The observational, exploratory study examined 17 patients, and was conducted in the medical intensive care unit and the medical stepdown unit of a teaching hospital in Cleveland, Ohio. Each patient had a diagnosis (established by a physician prior to the patient's admission to the hospital) of "exacerbation of COPD" with or without pneumonia. To ensure that patients included in the study were safely able to oxygenate, only patients with a fraction of inspired oxygen greater than 0.6 (regardless of profile/trajectory ratio) were included.

The participants were observed during sequential periods of rest and activity, where the initial period (rest or activity) was assigned randomly according to a coin toss. Rest periods had durations of 60 minutes (which provided baseline serum cytokine values), while the goal was 20 minutes for duration of activity. Serum was collected immediately after each period (rest and activity). The total observation time lasted approximately 90 minutes per patient (60 minutes of rest, 20 minutes of activity, and 10 minutes of data collection). A similar set of observations was conducted on a second day to determine whether the data on the participants varied day-to-day.

In the study, activity was defined as therapeutic mobility purposefully initiated by the nurse, bedside clinician (physical therapist, occupational therapist, or assistive staff member), or patient to maintain joint range and muscle strength. "Early" mobility was defined as occurring within 72 hours of admission. Activity was measured via direct observation and actigraphy. Activity included turning (patients move to a lateral, supine, or prone position from a baseline lateral, supine, or prone position), range of motion (patients repetitively position an extremity around a joint with or without muscular activation), dangling (patients sit with legs hanging over the side of the bed, with or without foot, back, and arm support for a defined period), chair sitting (patients transfer from bed to chair), and ambulation (patients walk with or without aid or an assistive device).

The researchers say that "The hospitalized patients in this study exhibited elevated serum IL-6 values similar to those of patients with COPD, with resting IL-6 averaging 10.8 pg/mL over both days." Values for IL-10 averaged 32 pg/mL at rest on day 1 and 16.9 pg/mL on day 2. These values were significantly elevated compared with IL-10 values in patients without COPD.

The researchers say the results indicate that it is safe to allow a critically ill patient with COPD exacerbations to engage in activity for about 20 minutes, even early in the hospitalization. Further, activity can progress safely over 2 days in an intensive-care unit or stepdown unit setting. They note that for this study, physical activity was low in intensity. No significant differences were evident between serum inflammatory biomarkers at rest vs after activity in this small sample. However, trend-related data indicate that low-intensity activity has the potential to alter the inflammatory profile of hospitalized patients with COPD.

Source: *Heart Lung*. 2010;39(4):319–330. doi:10.1016/jhrtlng.2009.09.004.

Palliative Care

Treating Symptoms Other Than Pain

According to researchers from the VA Pittsburgh Healthcare System and the University of Pittsburgh, both in Pennsylvania, limited information currently exists on nonpain symptoms (such as constipation/fecal impactions, cough, nausea/vomiting, fever, and diarrhea) and their appropriate treatment in the long-term care setting at the end of life. As such, in a recent study, the researchers sought to evaluate the prevalence of undertreatment of nonpain symptoms in older nursing home hospice patients and palliative care patients.

They used information derived from the resident file of the 2004 National Nursing Home Survey in their cross-sectional study. All patients were aged 65 years and older and were assigned to a bed on a hospice specialty unit or were receiving services from a special program for hospice, palliative, or end-of-life care. Facility staff determined nonpain symptoms and used medical

records to answer questions about their facility's residents. Medication-use data were obtained from medication administration records. For the study, undertreatment was defined as "the omission of a necessary medication for a specific nonpain symptom" and, it was evaluated as a dichotomous variable (yes = the nonpain symptom was not treated with a medication; no = the nonpain symptom was treated with a medication). The researchers conducted bivariate analyses using χ^2 and regression coefficient tests to determine factors potentially associated with undertreatment of nonpain symptoms.

Of the 303 patients included in the study group, 82 had 1 or more nonpain symptoms. The most common nonpain symptoms were constipation/fecal impaction (35 patients), cough (34 patients), nausea/vomiting (26 patients), fever (11 patients), and diarrhea (9 patients). Of those 82 patients, 47 were undertreated. Undertreated patients had significantly more problems with bed mobility, mood, and pressure ulcers than treated patients. Moreover, patients in the undertreated group had a significantly greater number of secondary diagnoses ($P = .004$) but, interestingly, a shorter length of stay than patients in the treated group.

The researchers say that although the prevalence of nonpain symptoms was low in older nursing home hospice and palliative care patients, medication undertreatment of nonpain symptoms was seen in more than half of these patients. The researchers note that while medication intake generally increases with age, the medical literature shows that underuse of medications or the omission of drug therapy that is indicated for the treatment or prevention is an important issue. They acknowledge that in some cases, debilitated patients may not communicate their symptoms or staff may have misperceptions about patients' degree of discomfort. Patients with depressive symptoms may also be less likely to report nonpain symptoms or to request medications. With regard to the shorter length of stay, the researchers say it is possible that patients who stay longer simply get more treatment.

Source: *Am J Geriatr Pharmacother.* 2010;8(3): 225–232. doi:10.1016/j.amjopharm.2010.05.002

NEUROLOGY

Migraine Raises Stroke Risk

Observational studies have suggested there is a link between migraine headache and ischemic stroke. As such, in a recent meta-analysis, researchers from McGill University and Jewish General Hospital, both in Montreal, Canada, and Johns Hopkins University in Baltimore, Maryland, aimed to quantitatively summarize the strength of the association between migraine and ischemic stroke risk.

For the meta-analysis, the researchers systematically searched electronic databases (including MEDLINE and EMBASE) for relevant published reports, from the beginning of indexing for each database through February 2009. Using article titles, abstracts, and full texts, pairs of reviewers independently evaluated articles for selection criteria. Twenty-one of 35 studies met the selection criteria, resulting in a total of 622,381 participants. For the association between any migraine and ischemic stroke, the pooled adjusted odds ratio was 2.3 (95% confidence interval [CI], 1.91–2.76). The pooled adjusted effect estimates for studies that reported relative risks and hazard ratios, respectively, were 2.41 (95% CI, 1.81–3.2) and 1.52 (95% CI, 0.99–2.35). The overall pooled adjusted effect estimate was 2.04 (95% CI, 1.72–2.43).

The researchers found that a history of migraine headache doubles the risk of ischemic stroke, and that the risk might be further increased in migraineurs with aura, although this risk was "unlikely to be significant." The risk was also potentially higher in women, although no direct comparison of effect estimates between men and women could be made because no studies presented data separately by gender. The researchers also note that while migraine is more common among women, it is difficult to say whether women have a true increased risk, given the many potential confounders (such as pregnancy, oral contraceptive use, and postmenopausal hormone use). Higher estrogen levels, the researchers note, might raise the risk of stroke via their effect on endothelial function, coagulation factors, and inflammation. They add that vasoactive medications used to treat migraine may predispose patients to ischemic stroke.

As migraine headache was shown to be independently associated with increased ischemic stroke risk, the researchers say their findings underscore the importance of identifying high-risk migraineurs with other modifiable stroke risk factors. Further study may be warranted to assess the effects of migraine control and modifiable risk factor reduction on stroke risk in migraineurs.

Source: *Am J Med.* 2010;123(7):612–624. doi:10.1016/j.amjmed.2009.12.021