Recent Advances in Management of Symptoms Other Than Pain in Palliative Care

Dr Lam Wai Man
Deputy Associate Consultant (Medicine), Haven of Hope Hospital
Correspondence: lamwm1@pacific.net.hk

After more than two decades of palliative care in Hong Kong, one of the challenges ahead is to have practices based on more research into pathogenesis and new therapeutics for refractory symptoms, existential and spiritual distress, and bereavement. In the following review, recent articles published between 2003 and 2006 of randomised controlled trials (RCT) and clinical trials which represented significant advances or would create an impact on the field of palliative medicine are selected and presented.

Cachexia

The cancer cachexia syndrome has been postulated to be due to persistent inflammatory response by the host producing inflammatory cytokines (e.g. TNF-α, IL1-β, INF-γ, IL-6) and tumour-specific catabolic factors produced by the tumour (e.g. PIF, LMF). A number of agents have been used to treat cancer cachexia including steroids, progestogens (megestrol acetate and medroxyprogesterone), non-steroidal anti-inflammatory agents, cannabinoids, eicosapentaenoic acid, fish oils, and pentoxyphylline. Only megestrol acetate has been confirmed by large-scale systematic reviews to improve appetite, weight gain, and possibly quality of life in cancer patients.2, 3

Thalidomide, an inhibitor of tumour-necrosis factor-α, has been shown in a double-blind RCT to attenuate loss of weight and lean body mass in patients with advanced pancreatic cancer.4 Thalidomide 200 mg or placebo was given daily to 50 patients with over 10% loss of body weight in the past six-months. At 4 weeks, patients taking thalidomide had a mean weight gain 0.37 kg while those on placebo lost 2.21 kg on average (p=0.005). The arm muscle mass increased by a mean of 1.0 cm³ in the thalidomide group while it decreased by a mean of 4.6 cm³ in the placebo group. (p=0.002). This significant improvement was also shown at 8 weeks post-treatment. The drug was well tolerated.

Fatigue

A double-blind RCT comparing patient-controlled Methylphenidate (5 mg every 2 hours as needed) with placebo in 112 cancer patients with moderate to severe fatigue (fatigue score of at least 4 in a scale of 0-10) showed a significant improvement in fatigue score and other symptoms as assessed by Edmonton Symptom Assessment Score (ESAS) in both groups, but no significant difference between the treatment and the placebo groups. The improvement achieved in both groups was postulated to be possibly related to the daily phone contact by the research nurse. No significant toxicity was observed.5

Dyspnoea

A locally relevant assessment tool, the Quality-of-life Concerns in the End-of-life, has been developed and validated by a collaborative effort of three hospitals for patients with advanced chronic obstructive pulmonary disease (COPD) and cancer.6

Oxygen supplement had been shown to be superior to air in a double-blind study by Bruera in 1993 to relieve dyspnoea in hypoxic terminal cancer patients. However, for advanced cancer patients without hypoxia who had moderate to severe dyspnoea, a double-blind crossover RCT comparing 5L oxygen versus air failed to show a significant improvement in dyspnoea, fatigue and distance walked.7

From a systematic review, systemic opioids were shown to improve sense of breathlessness while nebulized opioids did not.8 In a randomized, double-blind, placebo controlled crossover trial of predominantly COPD patients comparing 20 mg of sustained release morphine and placebo, participants reported significant improvement in dyspnoea scores when treated with morphine: an improvement of 6.6 mm on a 100 mm visual analogue scale (95% confidence interval 1.6-11.6 mm) in the morning (p=0.011) and of 9.5 mm (95% CI 3.0-16.1 mm) in the evening (p=0.006). No excessive sedation or respiratory depression was observed in the morphine group.9