

## Historical Perspective on the Progress of Chemotherapy-Induced Nausea and Vomiting Treatment in *Oncology Nursing Forum*

*Chemotherapy-induced nausea and vomiting (CINV) has been a priority symptom in the management of patients with cancer since the inception of chemotherapy. In the mid-1970s, the most effective agents available were the standard antiemetics used for gastrointestinal illnesses, postoperative nausea, and morning sickness. The Oncology Nursing Forum has documented the study of this symptom—causes, pathophysiology, and manifestations—in the past four decades as well as emerging treatment therapies. To date, CINV is fairly well controlled, but work still needs to be done, particularly in delayed and refractory management.*

**O**ncology Nursing Forum (ONF) published an article in its early newsletter format in 1977 entitled “Variables Affecting Nausea and Vomiting” (Mayer Scogna, 1977). That literature review provided an excellent analysis of the state of the art in the management of chemotherapy-induced nausea and vomiting (CINV) at that time. Healthcare providers knew that the vomiting center, chemoreceptor trigger zone (CTZ), and vagal afferents in the gastrointestinal (GI) tract were intimately involved in CINV and that multiple and varied chemoreceptors existed in the CTZ. Unfortunately, interventions lagged compared to the knowledge of the pathophysiology of the CINV process. Only 13 studies on the effectiveness of available antiemetics were published from 1964 to 1977, and no new agents had been developed since the 1950s (Mayer Scogna, 1977). That study investigated whether extrinsic factors, subjective attitude about effectiveness of chemotherapy, hours of sleep prior to treatment, activity level, or food intake affected CINV and found that they did not. Mayer Scogna (1977) recognized anticipatory nausea and vomiting, referring to this as a conditioned psychological component, and noted the lack of reliable tools to objectively measure nausea and vomiting.

The 1980s presented a particular challenge with the introduction of cisplatin, which is a very novel and effective agent, yet highly emetic. Maxwell (1982) published a special feature in *ONF* to express the frustration of the oncology field with not only the lack of well-performed antiemetic clinical trials, but the lack of effective antiemetics available. Maxwell also reviewed the current antiemetics with phenothiazines (i.e., prochlorperazine)

recommended as first-line treatment and cannabinoids and butyrophenones (i.e., haloperidol) and corticosteroids as second-line treatment. The difficulties associated with quantitatively measuring nausea and vomiting also presented a challenge. Gralla (1981) investigated the use of high-dose metoclopramide as an antiemetic for cisplatin-based chemotherapy. Although Gralla reported effective emetic control and safety, another study (Aapro, 1982) reported excessive central nervous system toxicity with high-dose metoclopramide.

Wickham (1989) published a state-of-the-art article in *ONF*, and the understanding of CINV broadened to include neurotransmitters involved with CINV, acute and delayed nausea and vomiting, and the emetic potential of various chemotherapeutic agents. Although, overall, the choice of antiemetics did not change, healthcare providers became more comfortable using high doses of metoclopramide and treating extrapyramidal side effects. Lorazepam was widely used as an amnesiac because the experience of nausea and vomiting was so unpleasant. Clinical trials with antiemetics revealed that prophylactic administration of antiemetics and combination antiemetics provided better emetic control. In addition, if acute nausea and vomiting were well controlled, delayed control was improved. Wickham (1989) also presented an assessment tool for nurses to use when caring for patients receiving chemotherapy.

### Difficult for Patients

As a nurse caring for patients receiving highly emetogenic chemotherapy at this time, it was extremely stressful for the patient experiencing significant nausea and vomiting when little could be done to improve the situation. Waves of nausea and vomiting came rhythmically with little control, and the nurse had to support the patient with a basin, cool wash cloth, and a cup of water to rinse (Rhodes, Watson, Johnson, Madsen, & Beck, 1987). Behavioral interventions also began to emerge as an adjunct to traditional antiemetics (Wickham, 1989). Relaxation techniques, distraction, exercise, guided imagery, and hypnosis were studied to establish their role in decreasing nausea and vomiting. Trials with acupuncture and acupressure applied to P6 (pericardium 6) were conducted to look at their effect on emesis (Price, Williams, & Sergiou, 1992).

The 1990s saw the emergence of a new class of antiemetics that would significantly impact CINV. The serotonin receptors of the 5-HT<sub>3</sub> type are located in both the CTZ and vagal afferent fibers of the gastrointestinal tract. Ondansetron, a 5-HT<sub>3</sub> receptor antagonist, was