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Review

Nausea and vomiting in advanced cancer

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ABSTRACT

Nausea and vomiting are very common symptoms in cancer both treatment and non-treatment related. Many complications of advanced cancer such as gastroparesis, bowel and outlet obstructions, and brain tumors may have nausea and vomiting or either symptom alone. In a non-obstructed situation, nausea may be more difficult to manage and is more objectionable to patients. There is little research on management of these symptoms except the literature on chemotherapy induced nausea where guidelines exist. This article will review the etiologies of nausea and vomiting in advanced cancer and the medications which have been used to treat them. An etiology based protocol to approach the symptom is outlined.

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1. Introduction

Nausea is a common complaint in advanced cancer and the effect on quality of life can be severe (Harris, 2010; Dunlop, 1989). 20–30% of people with advanced cancer suffer from nausea −70% in the last week of life (Conill et al., 1997). Studies have shown that treatment strategies can be effective but many patients continue to suffer unnecessarily (Stephenson and Davies, 2006; Davis and Hallerberg, 2010).

The National Cancer Institute defines nausea as a disorder characterized by a queasy sensation and/or the urge to vomit (National Cancer Institute, 2010). Vomiting is characterized by the reflexive act of ejecting the stomach contents through the mouth (National Cancer Institute, 2010). Retching resembles vomiting, but without stomach expulsion.

Some clinicians use a therapeutic strategy based on the likely cause and neurotransmitters involved (Bentley and Boyd, 2001; Lichter, 1993; Stephenson and Davies, 2006), while others base management on single drug trials (Bruera et al., 1996; Pereira and Bruera, 1996; Skinner and Skinner, 1999). To date, there are no trials comparing these two strategies.

Chemotherapy related nausea and vomiting is beyond the scope of this article. We will review the etiologies of nausea and vomiting in advanced cancer and suggest treatment strategies.

2. Etiology

In the etiologic approach, it is important to understand the neurotransmitters involved (Carpenter, 1990) in nausea to select the correct drug class. The chemoreceptor trigger zone (CTZ) is on the floor of the fourth ventricle. Significantly, it is outside the blood brain barrier and vulnerable to metabolic and chemical triggers. It contains various receptors: acetylcholine, dopamine, serotonin, cannabinoid and opioid (Cameron, 1990; Davis and Walsh, 2000). In contrast, the vomiting center is within the blood brain barrier and the medulla oblongata. It has acetylcholine, dopamine, gamma amino butyric acid (GABA) and serotonin receptors (Davis and Walsh, 2000). It also receives afferent neural fibers from the CTZ, the glossopharyngeal and splanchnic and vagal nerves. Within the GI tract there are dopamine receptors which affect gastric motility. There are also stretch mechanoreceptors which signal distention and organomegaly through the vagus nerve (Harris, 2010).

To improve the treatment, efforts have been made to identify etiology based guidelines (Bentley and Boyd, 2001; Glare et al., 2004; Lichter, 1993; Stephenson and Davies, 2006). The rationale is that by identifying the mechanism, treatments can be individualized. In most, a primary etiology can be identified (Bentley and Boyd, 2001). However, the multifactorial nature of nausea in advanced cancer had led others to advocate a systematic protocol to be used after reversible causes have been excluded (Gupta et al., 2013).

2.1. Medications

Of those with a reversible cause for nausea and vomiting 51% were drug related and of these 83% were due to opiates (Bentley and Boyd, 2001). This is related to multiple factors including gastroparesis, CTZ stimulation and sensitization of the labyrinth (Laugsand et al., 2011). Opioid rotation or dose reduction is effective in many to reduce symptom burden. Numerous other drugs commonly prescribed to cancer patients may cause nausea and should be stopped if possible. Drug induced nausea and vomiting is mediated through the chemoreceptor trigger zone through 5-HT_3 and dopaminergic receptors.

2.2. Central nervous system causes

2.2.1. Elevated intracranial pressure (ICP)

ICP causes nausea through mechanisms not clearly understood, but perhaps to pressure transmitted through the 4th ventricle to the vagal ganglion. Typically, in slowly progressive tumors nausea is less common; sudden occlusion of the collecting system may cause acute headache and nausea (Alomar, 2010). Both primary and metastatic lesions can elevate ICP. Tumors of the brainstem may also cause nausea from direct stimulation of the nausea and vomiting centers. Those with symptoms from leptomeningeal disease are less responsive to drug therapy and may benefit from CSF drainage.

2.2.2. Vestibular

The vestibular apparatus controls the sensation of rotation, and can trigger nausea. Tumors affecting this area can cause both nausea and vertigo (Abraham and Fowler, 2009). The vestibular system acts through cholinergic muscarinic receptors on the vomiting center provoking nausea and vomiting (Takeda et al., 1993).

2.2.3. Emotional

Patients can experience anticipatory nausea prior to events like chemotherapy (Roscoe et al., 2011) or procedures due to anxiety. Anxiety itself can cause nausea as can depression or pain (American Gastroenterological Association, 2001). These cortical functions cause nausea through GABA receptors.

2.3. Gastrointestinal causes

2.3.1. Motility

Impaired gastric motility can be caused by medications (including opiates, acid suppressing medications and tricyclic antidepressants) and autonomic dysfunction. Peristalsis may also be impaired by direct tumor invasion of the bowel wall. Organomegaly can cause nausea through stretched visceral capsules like hepatomegaly which causes vagal stimulation and in turn delayed gastric emptying (Abraham and Fowler, 2009).

2.3.2. Constipation

Constipation can lead to a sense of fullness and perhaps nausea (Larkin et al., 2008). As it is generally easily reversible it should be ruled out in all cases.

2.3.3. Obstruction

Malignant bowel obstruction occurs in 3–15% of cancer patients (Tuca et al., 2012). It is more common in ovarian (20–50%) and