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Review

Nausea and vomiting of pregnancy - What's new?

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ABSTRACT

Nausea and vomiting of pregnancy (NVP) is one of the most common disorders of pregnancy. The symptoms occur predominantly during the first trimester, although in a subgroup of patients they can continue throughout the entire pregnancy and can affect the woman's quality of life. A small percentage of women develop a severe form of NVP called hyperemesis gravidarum (HG) that if left untreated may lead to significant maternal morbidity and adverse birth outcomes. Overall, the morbidity in pregnant women with NVP is significant, although it tends to be underestimated. The pathogenesis of NVP remains unclear, but there is consensus that the disorder is multifactorial and that various genetic, endocrine and infectious factors may be involved. The treatment of NVP can be challenging as the optimal targets for therapy are not known. Currently, the therapy used depends on the severity of the disorder and it is focused on improving the symptoms while minimizing risks to mother and fetus. Therapies range from dietary changes, pharmacologic treatment or hospitalization with intravenous fluid replacement and nutrition therapy. The aims of this review are 1) to provide an overview of NVP, 2) to present possible links between the most important factors associated with the pathogenesis of NVP and 3) to discuss the effectiveness and safety of the pharmacologic and non-pharmacologic options available to treat this disorder.

Contents

Abbreviations: NVP, Nausea and vomiting of pregnancy; HG, Hyperemesis gravidarum; PUQE, Pregnancy-Unique Quantification of Emesis scoring; TNF-a, Tumor necrosis factor alpha; IL-1, Interleukin 1; IL-6, Interleukin 6; hCG, Human chorionic gonadotrophin; *H. pylori*, *Helicobacter pylori*.

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1. Nausea and vomiting of pregnancy

Nausea and vomiting of pregnancy (NVP) is a very common disorder reported in 70–80% of all pregnant women (Flaxman and Sherman, 2000; Lacroix et al., 2000; O'Brien and Zhou, 1995; Pepper and Craig Roberts, 2006). Symptoms usually begin 2–4 weeks after fertilization, peak between 9 and 16 weeks of gestation and generally resolve by 22 weeks gestation (Brandes, 1967; Broussard and Richter, 1998; Gadsby et al., 1993; Hasler et al., 1995; Klebanoff et al., 1985; Lee and Saha, 2011; Zur, 2013). Up to 10% of women have a prolonged course with symptoms extending until the time of delivery (Hasler et al., 1995). NVP persists throughout the day in as many as 98% of women with NVP (Hasler et al., 1995); therefore, the popular term “morning sickness” doesn't properly reflect this condition (Lacroix et al., 2000; Zur, 2013).

Although NVP tends to be treated as a normal part of pregnancy (Brandes, 1967; Tierson et al., 1986), it can significantly reduce the quality of life of the pregnant woman. Women with NVP have significantly increased odds for high blood pressure and preeclampsia compared with symptom-free pregnant women (Chortatos et al., 2015). In addition, in 10–35% of patients the symptoms of NVP lead to increased feelings of depression, and may cause a negative impact on employment, household duties, parenting and family relationships (Attard et al., 2002; Mazzotta et al., 2000a, 2000b; Niebyl, 2010; O'Brien and Naber, 1992; Smith et al., 2000). Even more concerning is the observation that women with mild NVP have also reported experiencing the same psychosocial problems as women with severe symptoms (Mazzotta et al., 2000a). These data suggest that morbidity in pregnant women with NVP is significant although these issues tend to be overlooked. In addition, NVP also exerts a large economic impact on patients, caregivers and society. In 2012 the total economic burden of NVP was estimated to be $1.77 billion in the United States (Piwko et al., 2013).

In contrast to the burden that NVP can be for the pregnant woman, most studies have found that mild NVP is associated with favorable outcomes for the fetus including reduced odds for low birth weight and small for gestational age (Brandes, 1967; Chortatos et al., 2015; Little, 1980; Medalie, 1957; Milkovich and van den Berg, 1976; Petitti, 1986; Tierson et al., 1986), reduced risk of preterm delivery (Brandes, 1967; Jarnfelt-Samsioe, 1987; Klebanoff et al., 1985; Koren et al., 2014; Medalie, 1957; Milkovich and van den Berg, 1976; Petitti, 1986; Tierson et al., 1986) and reductions in the likelihood of miscarriage (Jarnfelt-Samsioe, 1987; Klebanoff et al., 1985; Koren et al., 2014; Medalie, 1957; Milkovich and van den Berg, 1976; Petitti, 1986; Weigel and Weigel, 1989).

Finally, the severity of symptoms for NVP range from mild to moderate nausea and vomiting to pathologic cases of women with a severe form of NVP called hyperemesis gravidarum (Lee and Saha, 2011).

2. Hyperemesis gravidarum

Hyperemesis gravidarum (HG) is characterized by severe nausea and excessive vomiting starting before the end of the 22nd week of gestation (World-Health-Organization, 2016). HG affects 0.3–2% of pregnant women and if left untreated or if treatment is unsuccessful it may lead to significant maternal morbidity and adverse birth outcomes (Dodds et al., 2006; Lee and Saha, 2011; Munch, 2002; Verberg et al., 2005; Zur, 2013). In fact, women with HG have a lower health-related quality of life (Munch et al., 2011). The condition interferes with liquid and food intake and may lead to dehydration, electrolyte and acid-base imbalance, nutritional deficiency, ketonuria and loss of more than 5% of body weight (Bashiri et al., 1995; Fejzo et al., 2009; Golberg et al., 2007; Goodwin, 1998; Grooten et al., 2015a; Verberg et al., 2005). In addition, women with HG also can have excess salivation (Godsey and Newman, 1991), vitamin B1 and mineral deficiencies (Koch and Frissora, 2003), gastroesophageal reflux symptoms and abnormal liver function tests (Lee and Saha, 2011). HG is associated with morbidity such as acute kidney injury (Machado et al., 2012), liver dysfunction (Shekhar and Diddi, 2015), pneumomediastinum (Gorbach et al., 1997; Liang et al., 2002), ruptured esophagus (Buchanan and Franklin, 2014), and Wernicke's encephalopathy (Berdai et al., 2016; Giugale et al., 2015). In addition, a recent case-control study found that psychological distress was a direct consequence of HG (Aksoy et al., 2015), which is in accordance with previous reports of increased risk of cognitive, behavioral, and emotional disorders in this population (Poursharif et al., 2008; Zur, 2013). Even more, the complications associated with HG can result in termination of an otherwise wanted pregnancy (Poursharif et al., 2007; Trogstad et al., 2005). The long-term consequences of HG on mothers are still undetermined, although several studies suggest increased rates of depression, post-traumatic stress disorder, and various neurological disorders (Goodwin, 2008; Grooten et al., 2015a).

HG is the most common reason for hospitalization in the first half of the pregnancy and second only to preterm labor throughout the whole of pregnancy (Gazmararian et al., 2002). In the United States over 285,000 women are admitted to the hospital and over 26,077 are admitted to the Emergency Department each year due to HG (Piwko et al., 2013; Zur, 2013). The cost of care is estimated to be $47,351 per HG patient (Piwko et al., 2013). Although uncommon in contemporary practice, several maternal deaths have also been reported secondary to HG (Daaloul et al., 2012; Kantor et al., 2014; Knight et al., 2014; MacGibbon et al., 2015). These fatalities illustrate the importance of rapid diagnosis, preventative vitamin supplementation, and electrolyte monitoring and correction (MacGibbon et al., 2015).

Some studies have also found an association of HG with poor neonatal outcomes like low birth weight, preterm birth, fetal death and small for gestational age (Dodds et al., 2006; Grooten et al., 2015a; Lee and Saha, 2011; Veenendaal et al., 2011; Zhang and Cai, 1991). HG is also associated with poor adult health for the offspring like decreased insulin sensitivity and increased risks of psychological and behavioral disorders (Mullin et al., 2011; Veenendaal et al., 2011). Besides, infants born to women with HG and low pregnancy weight gain were more likely to have low birth weight, have a 5-minute Apgar score of <7 and have increased blood pressure (Dodds et al., 2006; Grooten et al., 2015a; Lee and Saha, 2011).