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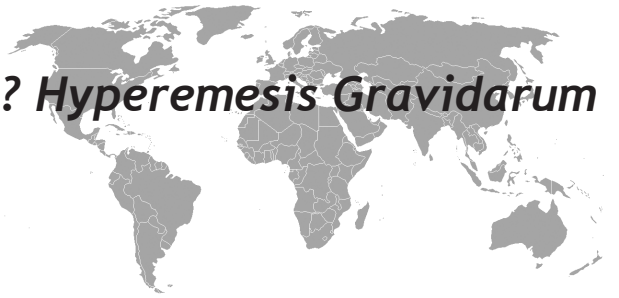
Review Article



Is it a Disease or a Symptom ? Hyperemesis Gravidarum

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ABSTRACT

Nausea and vomiting are common symptoms during early pregnancy. Although vomiting is the most obvious concerning symptom, persistent, debilitating nausea can severely adversely affect the woman's quality of life. It is namely Hyperemesis Gravidarum occurs in approximately 0.3-2.0% of pregnancies. The etiology is unknown but many risk factors have been determined as nulliparity, low maternal age, multiple gestation, previous pregnancy complicated by Hyperemesis Gravidarum. That remains a poorly understood condition and most likely involves a combination of hormonal, immunologic, and genetic factors. Data have shown increased levels of human chorionic gonadotropin in Hyperemesis Gravidarum , and proposed mechanisms include stimulation of secretory processes of the upper gastrointestinal tract and stimulation of the thyroid gland. In most women this condition is mild and self-limiting. While maternal morbidity is well documented, the effects of Hyperemesis Gravidarum on the fetus are less clear. A large majority (82.8%) reported that Hyperemesis Gravidarum caused negative psychosocial changes. Therefore, it is of great importance to treat this condition effectively to improve the quality of life for these women.

Key words: *Hyperemesis gravidarum, etiology, risk factors, treatment*

Hastalık mı Semptom mu ? Hiperemezis Gravidarum

ÖZET

Bulantı ve kusma erken gebelikte görülen en sık semptomlardır. İlerleyici bulantı ve şiddetli kusma kadının hayat kalitesini etkilemektedir. Hiperemesis Gravidarum olarak isimlendirilen bu durum yaklaşık olarak % 0.3-2.0 oranında görülmektedir. Etiyolojisi kesin olarak bilinmeyen Hiperemesis Gravidarum için nulliparite, küçük maternal yaş, çoğul gebelik, önceki gebeliğin hiperemesis ile komplike olması gibi bir çok risk faktörü tanımlanmıştır. Hormonal, immunolojik ve genetik faktörlerle ilişkilendirilen bu klinik durum halen gizemini korumaktadır. Human koryonik gonadotropinin artan serum miktarının üst gastrointestinal sistemde stimulasyona neden olması ve tiroid bezini stimule etmesi etiyopatogenezde suçlanmıştır. Bir çok kadında kendini sınırlayan ve şiddetli bir klinik sergilemeyen bu durumun maternal morbiditeye neden olduğu bilinmekte ancak fetal etkileri henüz tam olarak bilinmemektedir. Hiperemesis Gravidarum hastalarının büyük bir kısmında (% 82.8) negatif psikososyal değişimler tanımlanmıştır. Bu nedenle Hiperemesis Gravidarumun efektif olarak tedavi edilmesi hastanın yaşam kalitesinin iyileştirilmesinde oldukça önem arz etmektedir.

Anahtar kelimeler: *Hiperemesis gravidarum, etyoloji, risk faktörleri, tedavi*

INTRODUCTION

Nausea and vomiting are common symptoms during early pregnancy, affecting as many as 80% of pregnant women (1,2). Hyperemesis Gravidarum (HG) occurs in approximately 0.3–2.0% of pregnancies (2,3). It is characterized by continuous vomiting, dehydration, ketosis and muscle wasting. Some authors described that vomiting of pregnancy could be physiological symptom of the first trimester and frequent reason for consultation in emergency as well as hospitalization in the severe form as HG (4). Although there is inconsistency in the definition of this condition in the literature, (3) hyperemesis is most often characterized by severe nausea and vomiting that interferes with nutritional intake and metabolism, causes fluid and electrolyte imbalances, and may requires hospital management (5,6).

Nausea and vomiting during pregnancy which range from occasional is named morning sickness. Although popularly

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known as 'morning sickness', one study demonstrated that less than 2% of women experienced nausea only in the morning and 80% reported nausea throughout the day (7). But the most severe grade of nausea and vomiting during pregnancy often leads to HG. Many studies made to describe and determine pregnancy outcome in HG and also the effect of metabolic, biochemical, hematological and clinical indicators of disease severity on outcome.

Etiology and the Risk Factors

Hyperemesis Gravidarum has complex multifactorial aetiologies. Many of the previous studies of HG have been limited in their statistical power and generalizability as a result of being facility-based and relatively small in size (8). Many risk factors associated with hyperemesis have been reported. The risk factors include nulliparity, low maternal age, multiple gestation, fetal anomalies, previous pregnancy complicated by hyperemesis gravidarum, psychiatric conditions, and both high and low maternal preconceptional weight (5,6,9). Also female sex of fetus was associated with HG. It has been well established that pregnancies complicated by hyperemesis have altered sex ratios in favor of female offspring (10) and maternal hormonal levels associated with female offspring likely play a role in the occurrence of hyperemesis (11) In a study of Basso et al. (12) looked at the combined effect of gender and twin pregnancy on HG among subjects of more than 28 weeks of gestation. They found increased risks for all gender combinations among twin pregnancies compared with those with a singleton male (12). Although the exact mechanism is unknown but hyperthyroidism has been associated with HG (13). Increased human chorionic gonadotropin (hCG) levels were also accused especially in multiple gestations. The association between hCG levels and HG has been proposed by Goodwin (14). As a result of this association HG may appear in molar pregnancy and multiple pregnancy . A history of loss in the antecedent pregnancy may be risk factor for a subsequent pregnancy complicated by HG. On the other hand, smoking has been associated with reduced risk of HG (2).

At least laboratory investigations such as thyroid function tests, electrolytes, haematocrit, hepatic viral markers, transaminases, bilirubin, and urinary tests should be performed for differantial diagnosis. In addition, ultrasonography should be performed in order to exclude multiple pregnancy, abortion, trophoblastic disorders and the other neoplasias (15).

Management of Hyperemesis Gravidarum

Women presented with HG suffer not only physically but also psychologically, which has been documented in a number of studies. A large majority (82.8%) reported that HG caused negative psychosocial changes, consisting of socioeconomic changes, for example, job loss or difficulties, attitude changes including anxiety regarding future pregnancies and psychiatric sequelae, for example depression some continued postpartum (16). Therefore, it has great importance to treat this condition effectively to improve the quality of life for these women. Beside this before administrating any treatment, it is important to exclude other causes of nausea and vomiting such as urinary tract infection and thyrotoxicosis. Assessment of severity with checking for ketones is essential as severity should be change the management. Maintaining hydration is more important than nutrition in the short term (17). At first some recommendations could be given. The common dietary advices are drinking and eating small amounts with several times, avoiding being hungry that means avoiding having an empty stomach, before get out of bed eating a biscuit or hardtack, avoiding fatty, rich or spicy foods. Other helpful strategies may include eating bland, dry and high- protein foods. Ginger and acupuncture have beneficial effect throughout the pregnancy. These nonpharmacologic aproches provide the regression of symptoms 90% of women (18).

Many authors review different classes of antiemetics used to treat this condition and discuss that some have better safety profiles than others, but most appear to be safe to use in pregnancy. Generally antiemetic medication is the first choice. Anti-emetic medication appears to reduce the frequency of nausea in early pregnancy. There is some evidence of adverse effects, but there is very little information about effects on fetal outcomes from randomised controlled trials (7). Standart anti-emetics are ineffective and as yet there is no consensus on effective therapy (16). Antihistamine H1 receptor blockers, phenothiazines, prokinetic agent metoclopramide, benzamine, ondansetron have been shown to be safe and successful in treating refractory cases. Vitamin B_6 (pyridoxine) can be used as a single agent or with doxylamine (an antihistamine) and should be considered a first-line treatment. Useage of pryidoxine in every 8 hours with 10-25 mg and doxilamine (Unisom) 25mg at night, 12.5mg at afternoon and 12.5 mg at morning were supported in randomized trials. These combination can result 70% reduction in nausea and vomiting (17,18).

The second choice may be steroid therapy. Steroid therapy for hyperemesis was first reported almost 50 years ago and more recent small case series have reported benefit, the place of steroid therapy has remained contentious (19). Teratogenic evidence for corticosteroids is lacking. Early concerns from animal work of a possible relationship between oral facial clefts and cortisone has not been borne out by recent case-controlled studies (20). In a recent prospective observational study, severe disease requiring repetetive courses of betamethasone was associated with significant reduction in head circumference and birthweight in prematurely delivered infants (21,22). The maternal side-effects of long-term steroid therapy are well documented, including osteopenia, prevention of gastric ulcer healing and psychiatric morbidity. However, the most common steroid side-effect in pregnancy is gestational diabetes (19). Nelson et al. (20) advertised steroid treatment to women with severe HG in abolishing vomiting and restoring nutrition, allowing recovery of muscle mass and muscle strength. This treatment also enabled return to normal social functioning. The treatment protocol should be flexible, the major aim is controlling the symptoms using the minimum steroid dose. Oral prednisolone 10 mg 8 hourly can be prescribed or initial stabilization with intravenous hydrocortisone 50 mg 8 hourly for the patients who unable to tolerate tablets because of vomiting. When the dosage would be reduced, it must be done step by step. Typically, dosage would be decreased within 5 weeks to 15 mg daily. If vomiting recurred after a dosage reduction treatment dosage must be return to previous dosage (19,20).

Patients with HG those are not controlled with pharmacotherapy require intravenous hydration and nutrition supplement in hospital-based treatment. Fluid replacement with multivitamines, especially thiamine should be given. Total parenteral nutrition should be thougth for patients whose body weigth decreased more than 5%. Because it can cause severe side effects as steatohepatitis and sepsis (8,10,18).

Conclusion

Having one affected pregnancy increases the likelihood of the next pregnancy requiring hospitalization for hyperemesis, over 80% of these women did not require hospitalization for hyperemesis in the subsequent pregnancy (17). Because women with severe hyperemesis might avoid subsequent pregnancy. On the other hand woman who had vomiting is keep away ownself from the harmful nutrition, cigarette and alcohol in preconceptional period. Because of the maternal morbidity causes negative psychosocial and socioeconomic changes it is very important to manage carefully and also look after for the complications as dehydration, vitamin and metabolic disturbances, coagulopathy and peripheral neuropathy. Firstly nonpharmacological treatment should be advised. Antiemetic and steroid treatment should be considered latter. The vomiting in pregnancy can occured with gastroenteritis, appendecitis, intestinal obstruction, acute cholecystitis, pacreatitis, pneumonia, acute pyelonephritis. Therefore the other causes must be searched for differential diagnosis (2,6,7).

At the last, besides the studies, it is possible that the factor causing hyperemesis gravidarum has not been identified yet, hyperemesis gravidarum could have a multifactorial cause or might be the end result of various unrelated conditions.

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