Peripheral parenteral nutrition in protracted hyperemesis gravidarum – Report of two cases and a literature review

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Abstract

Hyperemesis gravidarum is defined as severe nausea and vomiting during the first trimester of pregnancy. It is characterized by dehydration, electrolyte imbalance, ketonuria and weight loss of more than 5% of body weight and it usually requires hospitalization.

Traditionally, total parenteral nutrition has been used when patients with hyperemesis gravidarum fail to respond to conservative measures, including dietary manipulation and antiemetics. Total parenteral nutrition has been shown to be an effective method of nutritional support during pregnancy but it is expensive and has potentially serious complications. Peripheral parenteral nutrition reduces the risk of complications, but caloric intake is limited. A small number of investigators have suggested using enteral nutrition as an alternative to total parenteral nutrition. Herein we report two cases of hyperemesis gravidarum successfully treated with an effective regimen of peripheral parenteral nutrition. (Acta gastroenterol. belg., **2008**, 71, **259-262**).

Key words : total parenteral nutrition ; hyperemesis gravidarum ; pregnancy.

Introduction

Nausea and vomiting commonly accompany the early stages of pregnancy, affecting 50-90% of pregnant women. These symptoms tend to develop early in pregnancy, peak around 9 weeks of gestation and rarely continue beyond 22 weeks of gestation (1). A much smaller subgroup suffers from hyperemesis gravidarum (HG), a condition characterized by intractable nausea and vomiting, which may occur in up to 2% of all pregnancies (2,3). The diagnosis of HG presumes exclusion of other causes of vomiting, such as gastroenteritis, cholecystitis, pyelonephritis, primary hyperthyroidism, primary hyperparathyroidism or liver dysfunction (4-6). Women with hyperemesis gravidarum are at high risk for malnutrition. They often experience weeks of diminished oral intake before hospitalization and the long-term effects of such nutritional disadvantage, including poor fetal outcome, may not be fully appreciated.

HG can be associated with substantial morbidity, including fluid and electrolyte imbalances, significant weight loss, nutritional deficiencies and retarded fetal growth (2,7,8). For these reasons, nutritional support of the mother is frequently required in cases of HG, with the use of enteral or parenteral nutrition.

Herein we report two severe cases of HG successfully treated with an effective regimen of peripheral parenteral nutrition.

Case report

Case 1

A pregnant twenty-seven-year old female patient was admitted to the Obstetrics Department due to HG and small degree of vaginal bleeding. She was at 10 weeks and 4 days of gestation. Physical examination was within normal limits and ultrasound examination of uterus and fetus was also normal and concordant to fetal age. The patient was treated with bed rest, intravenous administration of fluids, temporary discontinuation of oral intake and intravenous metoclopramide. Dimenhydrinate (histamine 1 receptor antagonist) was substituted for metoclopramide because of reported intolerance or allergy. After a few days she recovered, she had reduction of vomiting rate and she was discharged with dietary orders to avoid excessive amounts of food and fluids. A few weeks later, she was readmitted at 14 weeks and 5 days gestation due to severe exacerbation of HG with intractable vomiting, dehydration and exhaustion. She was unable to drink and keep in her stomach even small amounts of water or tea. Physical examination revealed weakness and malaise without any other specific findings. There was mild epigastric tenderness while bowel sounds were normal. Laboratory tests showed hematocrit 31.7 g/dl, white blood cells 4.59 k/μl with normal differential count, platelets 186 k/μl, ESR 27 mm at 1st hour, INR 1.2, glucose 99 mg/dl, urea 8 mg/dl, creatinine, 0.5 mg/dl, total bilirubin 1.2 mg/dl, direct bilirubin 0.28 g/dl, total proteins 6.2 g/dl, albumin 3.4 g/dl, aspartate aminostransferase 84 IU/L (Normal values < 40 IU/L), alanine aminotransferase 145 IU/L (NV < 40 IU/L), γGT 42 IU/L (NV < 32), alkaline phosphatase 68 IU/L (NV < 125), amylase 168 IU/L (NV < 90), LDH 480 IU/L (NV < 450), calcium 8.4 mg/dl, potassium 3.73 meq/L, sodium 136 meq/L, phosphate 4.2 mg/dl (NV 2.5-5), magnesium 1.61 meq/L

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(NV 1.3-2.1), TSH 1.64 μIU/ml (0.5-4.8). Abdominal ultrasound examination was normal but showed small amount of sludge in the gallbladder. Ultrasound examination of uterus and fetus was normal. Despite administering intravenous fluids and dimenhydrinate and discontinuing oral diet, the patient continued experiencing nausea and persistent vomiting. Epigastric pain became more severe. Gastroenterological consultation was obtained again and finally an upper endoscopy was performed, which revealed third degree esophagitis and erosive gastritis of the fundus. Those findings could be attributed to intractable vomiting. Ranitidine was introduced and peripheral parenteral nutrition was advised in the following regimen ; 1 lt (bag) of Clinomel N4-555 (Baxter Co) every twelve hours in slow intravenous infusion (2 bags per day). One of the bags was enriched with one ampoule of Cernevit (glutamine) to avoid villous atrophy.

The patient tolerated treatment exceptionally well and experienced a quick recovery ; in less than one day after introduction of peripheral parenteral nutrition the symptoms of HG subsided and the condition of the patient improved dramatically. A few days later, transaminase levels were significantly reduced to near normal. The patient received parenteral nutrition for 12 days and had no important problems in the next months of her pregnancy. She delivered vaginally a healthy female baby at 39 weeks of gestation with a body weight of 2860 g.

Case 2

A thirty-three-year old pregnant female patient was admitted to the Obstetrics Department with severe symptoms of HG. She was at 8 weeks and 3 days of gestation. She had unremarkable past medical history but two miscarriages 2 and 4 years ago. She also reported allergy or intolerance to metoclopramide. Physical examination, laboratory tests, ultrasound examination of her abdomen and fetus were within normal limits. Hemoglobin was 12.1 g/dl and hematocrit 35%. She was treated with discontinuation of oral intake, administration of intravenous fluids and dimenhydrinate (histamine-1 receptor antagonist). She also received intravenous solutions of aminoacids and glucose preparations via a peripheral vein without significant improvement of her symptoms. Nausea, epigastric discomfort and vomiting worsened. At 11 weeks and 5 days of gestation, after a gastroenterological consultation, peripheral parenteral solution with Clinomel N4-555 (Baxter Co) was introduced at the same regimen as in the previous case, with the addition of 500 ml of normal saline daily. As in the previous case, the patient experienced a quick recovery with amelioration of her symptoms and improvement of her nutritional status. She received peripheral parenteral nutrition with Clinomel for 14 days and a few days later she was discharged. She had no more significant problems during her pregnancy. She delivered vaginally a healthy female baby with a body weight of 3065 g at 39 weeks and 4 days of gestation. Unfortunately, a few days later the puerpernant developed a breast abscess that was successfully treated with antibiotics and local surgical drainage.

Discussion

Hyperemesis gravidarum (HG) is defined as severe nausea and vomiting during the first trimester of pregnancy. It is characterized by dehydration, electrolyte imbalance, ketonuria and weight loss of more than 5% of body weight and it usually requires hospitalization.

The etiology of HG is not well understood. Mechanisms proposed for this condition include thyroid imbalance, hyperparathyroidism, liver dysfunction, psychosomatic causes, gestational hormones, and nutritional deficiencies. The management for HG has changed little over the past few decades. The most common management is still gastric rest followed by simple carbohydrates. Other prescriptions and medical management have included glycerine vaginal suppositories to relieve cervical congestion, gastric lavage, starvation, thyroid hormone evaluation, psychotherapy and exercise (9). The mainstay of therapy continues to be fluid and electrolyte replacement, followed by slow reintroduction of a simple diet. Commonly used agents include pyridoxine alone or in combination with doxylamine, promethazine, metoclopramide and diphenhydramine. For patients who continue to vomit persistently and cannot tolerate oral feeding, parenteral nutrition has been used (3).

Traditionally, total parenteral nutrition has been used when patients with hyperemesis gravidarum fail to respond to conservative measures, including dietary manipulation and antiemetics (10-17). Successful outcomes can be achieved in obstetric patients requiring parenteral nutrition. The complication rate for centrally inserted central catheters was reported significantly higher (50%) than that for peripherally inserted central catheters (9%) (15). Although effective in meeting fluid, electrolyte, and nutritional needs, this approach carries considerable disadvantages, including potential complications such as pneumothorax, infection, venous thrombosis, intrahepatic cholestasis, and fatty infiltration of the placenta (18). Indeed, at least one case of maternal-fetal death has been reported as a result of total parenteral nutrition in a patient with HG (19). Moreover the cost is high for prolonged therapy. Interestingly, Ogura *et al.* reported on their experience with the use of peripherally inserted central catheters during pregnancy in 52 cases (20). These authors reported a higher risk of complications (50%) than that reported by Russo-Steiglitz *et al.* (15), although many of the patients treated had other diagnoses than HG. Most of the complications were related to infection. Peripheral parenteral nutrition reduces the risk of complications, but caloric intake is limited (2).

Other approaches have also been used for pregnants with HG. In one study, a short course of medical treat-

ment with oral methylprednisolone for one month, starting with 48 mg per day was effective in ameliorating symptoms of HG without any adverse effects on pregnancies outcome (21). In this study, 17 of 18 patients (94%) were free of vomiting and able to tolerate regular diet within three days. Four of the 6 patients who were receiving total parenteral nutrition had also a complete response to methylprednisolone within three days. Another randomized, double-blind, placebo-controlled trial of corticosteroids for the treatment of HG supported a beneficial role for steroids in severe hyperemesis, but did not validate the hypothesis that they lead to rapid and complete remission of symptoms (22). Side effects of corticosteroids in patients with HG are infrequent and self-limited (23,24).

Other authors used enteral feeding to provide sufficient nutritional support. By these means, nasogastric enteral feeding offers an attractive alternative to total parenteral nutrition (2). Enteral nutrition has less potential for serious complications and is cheaper than total parenteral nutrition. The reported experience showed that enteral nutrition was well tolerated and safe after correction of any fluid and electrolytes imbalance. In a study, seven pregnant women with HG had an excellent response to nasogastric enteral feeding within a few days (2). The mechanisms by which enteral feedings alleviate HG are unclear. Clinical experience suggests that enteral feeding is most successful for patients in whom nausea and vomiting are linked to the consumption of food (25). Tactile sensation in the oral cavity and smell are factors that might promote symptoms of nausea and vomiting. Other authors used a blindly placed nasojejunal tube for enteral nutrition in two patients with HG (9). That method was well tolerated and cost effective. Both mothers were given nutritional support at home, had normal subsequent pregnancies and delivered normal babies.

Others performed endoscopic gastrostomy or jejunostomy to alleviate symptoms of intractable nausea and vomiting while providing adequate caloric and nutritional intake for the pregnants (11,26). The reported cases had an excellent outcome. In spite of that, one should take into account that these methods involve a small but not negligible risk of complications, e.g. leakage from the site of the puncture, peritonitis and sepsis that may require surgical intervention (27,28).

Herein, we used an effective and safe regimen of peripheral enteral nutrition via a peripheral large vein, providing full nutritional support in female pregnant patients with HG. In one of the cases, another regimen of peripheral parenteral nutrition had failed. The demonstrated regimen was simple to use and did not require specialized knowledge and expertise of parenteral nutrition, since it was well standardized, but a general knowledge of the principles and the means of parenteral nutrition was desirable. Clinomel is a well-balanced solution including all the appropriate nutrients for complete parenteral nutritional coverage. It contains 3 compartments, the first one with aminoacids and electrolytes, the second one with glucose and calcium and the third one with fat. The three compartments are easily mixed just before the administration and the patient receives a well-balanced solution of parenteral nutrition that provides full nutritional support. The peripheral vein used for nutrition should be changed every three days to avoid local complications. A short course of the used parenteral solution, Clinomel, provided very good nutritional support and ameliorated symptoms of HG in less than one day. Despite the fact that the patients' condition improved quickly, we administered peripheral parenteral nutrition for 12-14 days in order to treat any nutritional deficiencies and to prevent recurrence of symptoms. Full term healthy babies were finally born in the described cases without any adverse effects or undesirable events during the rest of the patients' pregnancy. On the one hand, the patients did not face the risk of complications via a centrally inserted catheter for parenteral nutrition, while one the other hand they did not have to tolerate a nasogastric feeding tube, which additionally might not have prevented vomiting. The regimen with Clinomel was easy to use, cheaper than central total parenteral nutrition and provided adequate and full nutritional support. Excellent pregnancy outcomes were achieved.

In conclusion, treatment of refractory cases of HG can be achieved with a short course of a standardized commercial regimen of peripheral parenteral nutrition, with excellent efficacy and safety and minor disturbance of the pregnant and the obstetrician.

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References

1. MALAGELADA J.R., MALAGELADA C. Nausea and Vomiting. *In* : FELDMAN M.F., L.S., BRANDT L.J. (ed). Sleisenger and Fordtran's Gastrointestinal and Liver Disease. Vol. 1. Philadelphia : Saunders Elsevier, 2006 : 143-158.
2. HSU J.J., CLARK-GLENA R., NELSON D.K., KIM S.H. Nasogastric enteral feeding in the management of hyperemesis gravidarum. *Obstet. Gynecol.*, 1996, **88** : 343-346.
3. ABELL T.L., RIELY C.A. Hyperemesis gravidarum. *Gastroenterol. Clin. North Am.*, 1992, **21** : 835-849.
4. KALLEN B. Hyperemesis during pregancy and delivery outcome : a registry study. *Eur. J. Obstet. Gynecol. Reprod.*, 1987, **26** : 291-302.
5. TSANG I.S., KATZ V.L., WELLS S.D. Maternal and fetal outcomes in hyperemesis gravidarum. *Int. J. Gynaecol. Obstet.*, 1996, **55** : 231-235.
6. HIROI H., KOGU K., HOSHINO H., KOZUMA S., TAKETANI Y. Hyperemesis gravidarum associated with thyrotoxicosis and a past history of an eating disorder. *Arch. Gynecol. Obstet.*, 2001, **265** : 228-230.
7. GROSS S., LIBRACH C., CECUTTi A. Maternal weight loss associated with hyperemesis gravidarum : a predictor of fetal outcome. *Am. J. Obstet. Gynecol.*, 1989, **160** : 906-909.
8. QUINLA J.D, HILL D.A. Nausea and vomiting of pregnancy. *Am. Fam. Physician*, 2003, **68** : 121-128.
9. PEARCE C.B., COLLETT J., GOGGIN P.M., DUNCAN H.D. Enteral nutrition by nasojejunal tube in hyperemesis gravidarum. *Clinical Nutrition*, 2001, **20** : 461-465.

10. HASBUN J., CHARLIN V., VON MULHENBROCK R., MUNOZ H., YURI C. Total parenteral nutrition in severe hyperemesis gravidarum. *Rev. Chil. Obstet. Ginecol.*, 1994, **59** : 378-382.
11. GODIL A., CHEN Y.K. Percutaneous endoscopic gastrostomy for nutrition support in pregnancy associated with hyperemesis gravidarum and anorexia nervosa. *JPEN J. Parenter. Enteral. Nutr.*, 1998, **22** : 238-241.
12. GREENSPOON J.S., ROSEN D.J., AULT M. Use of peripherally inserted central catheter for parenteral nutrition during pregnancy. *Obstet. Gynecol.*, 1993, **81** : 831-834.
13. LEVINE M.G., ESSER D. Total parenteral nutrition for the treatment of severe hyperemesis gravidarum : maternal nutritional effects and fetal outcome. *Obstet. Gynecol.*, 1988, **72** : 102-107.
14. MACCARONE G., FARAGUNA D., CANDUSSO M., MONTEROSSO A. Total parenteral nutrition in pregnancy. *Minerva Ginecol.*, 1998, **50** : 185-189.
15. RUSSO-STIEGLITZ K.E., LEVINE A.B., WAGNER B.A., ARMENTI V.T. Pregnancy outcome in patients requiring parenteral nutrition. *J. Matern. Fetal. Med.*, 1999, **8** : 164-167.
16. WIEDNER L.C., FISH J., TALABISKA D.G., JENSEN G.L. Total parenteral nutrition in pregnant patient with hyperemesis gravidarum. *Nutrition*, 1993, **9** : 446-450.
17. ZIBELL-FRISK D., JEN K.L., RICK J. Use of parenteral nutrition to maintain adequate nutritional status in hyperemesis gravidarum. *J. Perinatol.*, 1990, **10** : 390-395.
18. KUSCU N.K., KOYUNCU F. Hyperemesis gravidarum : current concepts and management. *Postgrad. Med. J.*, 2002, **78** : 76-79.
19. GREENSPOON J.S., MASAKI D.I., KURZ C.R. Cardiac tamponade in pregnancy during central hyperalimentation. *Obstet. Gynecol.*, 1989, **73** : 465-466.
20. OGURA J.M., FRANCOIS K.E., PERLOW J.H., ELLIOTT J.P. Complications associated with peripherally inserted central catheter use during pregnancy. *Am. J. Obstet. Gynecol.*, 2003, **188** : 1223-1225.
21. SAFARI H.R., ALSULYMAN O.M., GHERMAN R.B., GOODWIN T.M. Experience with oral methylprednizolone in the treatment of refractory hyperemesis gravidarum. *Am. J. Obstet. Gynecol.*, 1998, **178** : 1054-1058.
22. NELSON-PIERCY C., FAYERS P., DE SWIET M. Randomised, double-blind, placebo-controlled trial of corticosteroids for the treatment of hyperemesis gravidarum. *Br. J. Obstet. Gynaecol.*, 2003, **108** : 9-15.
23. CHAN G.C., WILSON A.M. Complications of the use of corticosteroids for the treatment of hyperemesis gravidarum. *Br. J. Obstet. Gynaecol.*, 1995, **102** : 507-508.
24. SUNBRAMANIAM R., SOH E.B., DHILLON H.K., ABIDIN H.Z. Total parenteral nutrition (TPN) and steroid usage in the management of hyperemesis gravidarum. *Aust. N. Z. J. Obstet. Gynaecol.*, 1998, **38** : 339-341.
25. BOYCE R.A. Enteral nutrition in hyperemesis gravidarum : a new development. *J. Am. Diet Assoc.*, 1992, **92** : 733-736.
26. SERRANO P., VELLOSO A., GARCIA-LUNA PP., PEREIRA JL., FERNANDEZ Z., DUCTOR M.J., CASTRO D., TEJERO J., FRAILE J., ROMERO H. Enteral nutrition by percutaneous endoscopic gastrojejunostomy in severe hyperemesis gravidarum : a report of two cases. *Clinical Nutrition*, 1998, **17** : 135-139.
27. ARVANITAKIS M., BALLARIN A., VAN GOSSUM A. Ethical aspects of percutaneous endoscopic gastrostomy placement for artificial nutrition and hydratation. *Acta Gastroenterol. Belg.*, 2006, **69** : 317-20.
28. OZUTEMIZ O., TEKIN F., ORUC N. An unusual complication of percutaneous endoscopic gastrostomy. *Acta Gastroenterol. Belg.*, 2007, **70** : 309.