Raised serum human chorionic gonadotrophin concentrations in hyperemesis gravidarum

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Summary and conclusions

Serum human chorionic gonadotrophin (HCG) concentrations were determined by radioimmunoassay with an antiserum specific to HCG beta-subunit in 42 patients with hyperemesis gravidarum and 115 women with normal pregnancies. Mean concentrations (±SE of mean) were higher in the women with hyperemesis gravidarum at 7-8 weeks (40·8±5·2 IU/ml v 22·1±1·4 IU/ml; P<0·001), 9-11 weeks (38·1±2·3 IU/ml v 27·1±2·1 IU/ml; P<0·0025), and 12-14 weeks of gestation (35·9±4·2 IU/ml v 25·1±1·7 IU/ml; P<0·005), but there was no difference between the two groups at 15-20 weeks of gestation. In the hyperemesis gravidarum group primigravid women had a higher (P<0·005) mean HCG concentration (41·8±4·0 IU/ml) than multigravid women (32·2±2·3 IU/ml).

The results suggest a causal relation between a high serum HCG concentration and hyperemesis gravidarum.

Introduction

A high serum human chorionic gonadotrophin (HCG) concentration is characteristic of hydatidiform mole[1] and twin pregnancy,[2] both of which are commonly accompanied by hyperemesis gravidarum.[3] Hence there may be a correlation between increased circulating HCG and hyperemesis gravidarum. Various bioassay techniques used to measure urinary gonadotrophic hormones in hyperemesis gravidarum have resulted in increased,[4 5] normal,[6] and low[7] values.

Serum gonadotrophin concentrations were either above[8] or within the normal range.[6] The discrepancy between these results may have been due to methodological weaknesses of the techniques used, which were further unable to distinguish between placental and pituitary gonadotrophins.

Specific measurement of serum HCG in the presence of luteinising hormone (LH) is now possible with radioimmunoassay using an antiserum raised against the β-subunit of HCG.[9] We have used this assay to evaluate further the role of HCG in hyperemesis gravidarum.

Patients and methods

Forty-two women with single pregnancies were admitted to hospital between seven and 17 weeks of gestation because of hyperemesis gravidarum. All had profuse vomiting, weight loss of at least 5%, and acetonuria. Their mean age was 26·2 years (range 19-38) and parity 2·0 (range 1-7). Eighteen were primigravid. The control series comprised 115 healthy women with single pregnancies admitted for therapeutic abortion between six and 20 weeks of gestation.

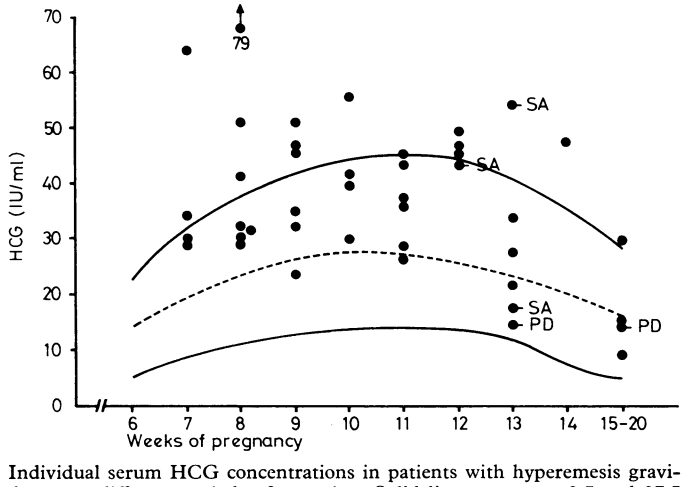
The duration of pregnancy was calculated from the date of the last menstrual period. A peripheral venous blood sample was taken on the second or third hospital day. Patients with hyperemesis gravidarum received intravenous fluid and electrolytes at least for 24 hours before sampling. Serum was separated by centrifugation and stored at −20°C until assayed.

Serum HCG was measured with a kit for measuring HCG β-subunit, essentially as described by Vaitukaitis *et al.*[9] Samples were diluted 1/50 with phosphate-buffered saline (pH 7·3) containing 1% bovine serum albumin. Diluted serum (50 µl) in duplicate was taken for assay. Standards (2nd international standard, World Health Organisation) were prepared in male serum diluted as above. Sensitivity of the assay with the above sample dilution was about 0·4 IU/ml. Over this concentration no cross-reactivity with physiological amounts of LH (in male, female midcycle, and postmenopausal plasma) was observed.

The between-assay coefficient of variation was below ±5% and the interassay coefficient of variation ±13%. The 95% normal range in uncomplicated early pregnancy was calculated according to Herrera.[10] The Mann-Whitney U test was used to test differences.

Results

Of the 42 patients with hyperemesis gravidarum, 15 (36%) had serum HCG concentrations above the 97·5 percentiles for normal pregnancy, and only 8 (19%) had values below the median for normal pregnancy (see figure). Mean concentrations at 7-8, 9-11, and 12-14 weeks of gestation were significantly higher in the hyperemesis gravidarum group than among the controls (table). Primigravid women with hyperemesis gravidarum had higher (P<0·005) HCG concentrations (mean 41·8±SE of mean 4·0 IU/ml) than multigravid women in the group (32·2±2·3 IU/ml).



Individual serum HCG concentrations in patients with hyperemesis gravidarum at different periods of gestation. Solid lines represent 2·5 and 97·5 percentiles, and dotted line median HCG concentrations in normal early pregnancy. SA=Spontaneous abortion. PD=Preterm delivery.

Mean serum HCG concentrations (±SE of mean) in hyperemesis gravidarum and normal pregnancy at various times up to 20 weeks of gestation

Weeks of gestation	Hyperemesis gravidarum		Normal pregnancy		P
	No of women	HCG (IU/ml)	No of women	HCG (IU/ml)	
7-8	11	40·8±5·2	38	22·1±1·4	<0·001
9-11	16	38·1±2·3	39	27·1±2·1	<0·0025
12-14	11	35·9±4·2	25	25·1±1·7	<0·005
15-20	4	17·2±4·5	6	17·9±3·9	<0·05

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The course and outcome of pregnancy was not correlated with the serum HCG value. The mean concentrations in 29 patients admitted once (35·9±2·8 IU/ml) and 13 patients admitted twice or more (33·4±3·1 IU/ml) were similar. Moreover, individual values in patients with subsequent spontaneous abortion (three cases) or preterm delivery (two) were not noticeably different from those in other patients (figure).

Discussion

Patients with hyperemesis gravidarum had serum HCG concentrations significantly higher than normal between seven and 14 weeks of gestation. Haemoconcentration could be ruled out because packed cell volume and potassium and sodium concentrations in the same samples were within normal limits.

Endocrine and emotional factors are often suggested as important in the aetiology of hyperemesis gravidarum. However, the secretion of adrenocorticotrophic hormone and cortisol[11]; concentrations of growth hormone, prolactin, and pituitary gonadotrophins[12]; and progesterone and oestrogens concentrations as reviewed by Fairweather,[3] were similar in vomiting and non-vomiting women. Furthermore, attitudes to pregnancy, delivery, marriage, family, children, and spouse showed no difference between healthy and vomiting women.[13] We cannot be certain whether the high concentration of HCG in serum is a primary factor in the aetiology of hyperemesis gravidarum or a secondary change. The association of HCG and hyperemesis gravidarum is supported by the observation that hyperemesis gravidarum begins concomitantly with the rising concentration of HCG; maximum values occur at 10-12 weeks of gestation, when hyperemesis is most common. We postulate that the hypothalamic vomiting centre is sensitive to HCG and that vomiting begins when the individual vomiting threshold concentration of HCG is reached.

The kit used for measuring the β-subunit of HCG was provided by courtesy of NIAMDD, National Institutes of Health, Bethesda, Md, USA.

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Reduction of catheter-associated sepsis in parenteral nutrition using low-dose intravenous heparin

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Summary and conclusions

To assess whether adding low-dose heparin to the infusate of patients receiving parenteral nutrition reduced the incidence of septic complications related to the central venous catheter, 80 consecutive patients requiring intravenous feeding were studied. Half of these patients received heparin 1 unit/ml of infusate, while in the remaining 40 (controls) an equal volume of physiological saline was added to the infusate. Strict criteria for the management of the indwelling CVC were observed. The catheter tips were cultured after removal: only one was infected in the heparin group compared with nine in the control group. This significant reduction may have been due to the heparin preventing a fibrin sleeve from forming around the catheter tip.

It is recommended that, as well as observing the usual aseptic precautions in managing the cannula, 500 units of heparin are added to each 500 ml of fluid infused to reduce the incidence of catheter-associated sepsis.

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Introduction

The commonest serious complication of parenteral feeding is infection associated with the indwelling central venous cannula,[1] the reported incidence of infection of the catheter tip varying from 0% to 41%.[2 3] While this may be minimised by using a careful, aseptic technique when inserting the cannula, regularly inspecting the entry site into the skin, changing the giving set daily, and proscribing the catheter as a route for giving or taking blood or administering drugs, occasional infections will still occur.[4] As heparin given via a peripheral venous cannula at a dose of 1 unit/ml of infusate reduces the incidence of thrombophlebitis associated with the cannula, I designed this trial to assess whether a reduction in catheter-associated sepsis could be achieved in patients receiving parenteral nutrition using a similar regimen.

Patients and methods

I studied 80 consecutive patients who required intravenous feeding. The only criterion for entry into the trial was that I inserted or supervised the insertion of the central venous catheter. The catheter was inserted with full sterile precautions, the operator wearing a mask and sterile gloves. The skin was prepared with povidone-iodine solution, and the catheter when inserted was securely sutured to the skin to prevent movement at the entry site. The area of entry was then sprayed with povidone-iodine aerosol, covered with a sterile gauze