Effective Management of Severe Vomiting in Pregnancy

Vomiting is a very common pregnancy-associated symptom, but happens with a wide range of severity. In its most severe form, vomiting of pregnancy causes dehydration, ketosis and severe weight loss, and this is termed hyperemesis gravidarum. If untreated, or badly treated, the condition can be fatal. Typically admissions are prolonged and repeated, even though highly effective therapy has been recognised for well over a decade.

Given that hyperemesis gravidarum occurs with a very wide range of degrees of severity, a definition of "severe hyperemesis" is required. Severe intractable vomiting which prevents eating and produces more than 5% weight loss in early pregnancy has been recommended as a practical definition[1]. This serves to emphasise an important aspect of the condition in that it prevents normal eating, and malnutrition of mother and potentially of baby may occur. Women fulfilling this definition require expert, effective treatment. However, the definition must not be applied rigidly. For instance, once a woman has suffered severe hyperemesis in one pregnancy, it is highly likely to occur with greater severity in a subsequent pregnancy, and the diagnostic criteria can be relaxed to allow earlier effective treatment.

Clinical diagnosis of hyperemesis itself should present no particular problems. Some textbooks incorrectly describe hyperemesis as a condition of continuous vomiting of onset in the first twenty weeks of pregnancy, but in practice there is a sudden onset of symptoms most often in the first six weeks, and always before eight weeks of gestation. Severe vomiting of later onset is highly likely to have a different cause. In approximately one-third of women there will be a family history of severe vomiting in pregnancy affecting first-degree family members. The history of weight loss will be confirmed by the presence of wasting, especially of leg muscles. Abdominal discomfort on examination is that expected from severe prolonged vomiting of any cause. Should a doctor unwisely request thyroid function tests in a sick, vomiting person he or she will find that they are likely to be abnormal – the "sick euthyroid syndrome". This still causes confusion, and non-endocrinologists often are not aware that thyroid function tests are unreliable during any acute illness.

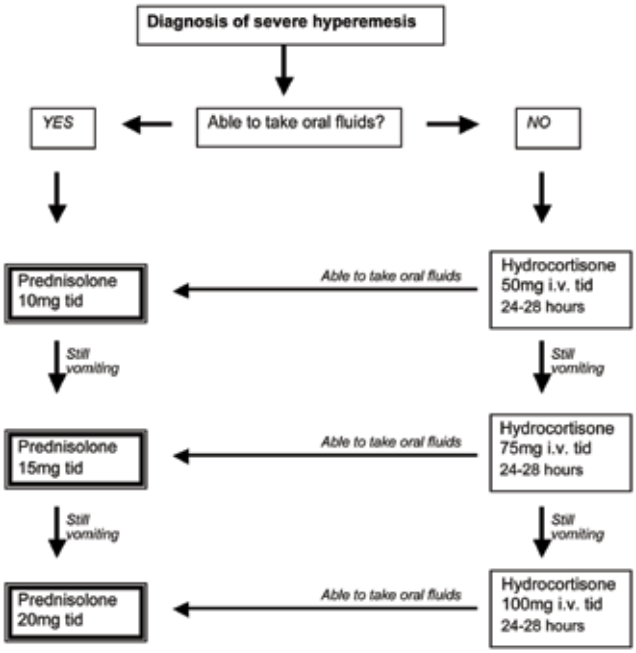
A close review of the symptoms is helpful as a background to diagnosis. Typically there is a very sudden onset of nausea between four and six weeks gestation, followed by vomiting which rapidly becomes intractable [2,3]. There is no diurnal pattern to the vomiting, quite unlike even troublesome morning sickness. Ptyalism is prominent in around half of all women. This apparent excess production of saliva relates to inhibition of the normal swallowing reflex, interrupting the usually subconscious swallowing of saliva. It is worth noting that the consistent spitting out of saliva elicits little sympathy from medical and nursing staff, who often label the behaviour as some form of pseudo-vomiting. The general lack of sympathy exhibited by healthcare staff not tuned into severe hyperemesis is in itself a helpful diagnostic feature. This relates in part to the erroneous description in standard textbooks of hyperemesis as being a "psychological condition reflecting rejection of pregnancy". Women who are overweight or obese before pregnancy are especially likely to have their malnutrition and weight loss disregarded, as they still have excess adiposity. The lack of sympathy from healthcare staff also reflects a lack of awareness of the wide range of severity of hyperemesis in pregnancy.

This lack of awareness of doctors, midwives and nurses of the existence of severe hyperemesis and the existence of effective therapy is reflected dramatically on patients' websites. Very graphic descriptions of lack of sympathy and even treatment by termination of pregnancy can be read on patients' blogs on the internet. The Hyperemesis Education and Research Foundation website is a good resource (www.helpher.org), although it suffers from the usual malady of patient- generated websites that all treatments ever suggested are listed, from copper bracelets through ginger biscuits to steroid therapy.

Therapy for hyperemesis should follow normal sound lines of clinical management. Dehydration requires to be managed with rapid intravenous rehydration. If vomiting has been preventing food intake for more than two weeks, then vitamin B1 (thiamine) replacement therapy is very important to avoid the possibility of Wernicke's encephalopathy. Thiamine, normally given in the UK as the intravenous preparation (Pabrinex) must be given before any carbohydrate is provided. However once (and only once) thiamine has been replaced, there is a major advantage in provision of calories as intravenous 10% dextrose, as each litre provides 400 kilocalories. This will allow suppression of ketone production. The repeated vomiting frequently causes significant heartburn, and this requires treatment with Ranitidine, initially intravenously and with oral follow-up. Antiemetics can be prescribed, although there is only a small chance of useful response. One of the most important components of therapy is rarely discussed: the symptoms of hyperemesis are markedly exacerbated by moving around, and also by smells of cooking. Bed-rest will temporarily assist with suppressing the symptoms of hyperemesis. In many women, a single admission with rehydration will suffice to control their condition. The observation that vomiting recurs after discharge home is often interpreted as indicating some psychological problem at home rather than a normal reaction to resuming activities. However, if more than 5% weight

loss has already occurred in comparison with reported pre-pregnancy weight, or if there have been previous similar admissions, then definitive therapy must be considered.

For women in this defined group of severe hyperemesis, therapy with prednisolone will be effective in all cases, if necessary preceded by intravenous hydrocortisone. A full algorithm for therapy has been published[3] and this is reproduced as Figure 1. The usual starting dose would



Newcastle guideline for management of steroid dose in severe hyperemesis[3]

be hydrocortisone 50mg TID if intravenous therapy is required. This would be continued until eating was able to be resumed, whereafter treatment with prednisolone of 20mg TID can be commenced. Approximately one in five women will require a higher dose of steroid, and stepwise increases to hydrocortisone 75mg then 100mg TID, or prednisolone 15mg or 20mg TID are necessary at approximately 48-hour intervals. Care must be taken to achieve complete control of the hyperemesis prior to discharge, otherwise the journey home in the car is likely to precipitate recurrence of symptoms as discussed above. Subsequent prednisolone dosage depends upon the individual response, but in general the initial suppressive dose which is successful should be continued for two weeks, followed by a decrease of approximately 5mg per week with the proviso that if severe vomiting recurs the dose should be increased. Awareness of the natural history of hyperemesis is important. In 80% of women the hyperemesis will persist until 18-22 weeks (known as remitting hyperemesis) and during this time it has been observed that average daily prednisolone requirements are 15mg per day. When the disease has run its course, the individual woman is never in doubt that the feeling of continuous nausea has lifted, and that steroid therapy can be rapidly tailed off and stopped. Unfortunately this self-limiting form of hyperemesis is not universal, and around 20% of women have full-term hyperemesis – which remits with dramatic suddenness as soon as the placenta is delivered.

The decision to commence prednisolone therapy requires careful discussion with the individual patient. The critical point is that steroid therapy has been used for severe asthma and inflammatory bowel disease in pregnancy for over sixty years and many studies have identified no evidence of harmful effect upon the foetus [4-6]. The transplacental passage of prednisolone is only around 10%[7]. On the other hand, untreated severe hyperemesis is likely to bring about a baby smaller than expected for dates, and malnutrition during pregnancy is not without consequences. Unfortunately potentially misleading information about steroid use and cleft lip or cleft palate is in circulation, relating to use of steroids any time from before pregnancy to late pregnancy[8]. One of the largest studies has found no association at all (Czeizel 1997). Another reported an increase in risk so small for the relevant period of exposure that it would not materially affect an individual decision (from

1.0 in 400 to 1.3 in 400)[9]. As an association has been demonstrated between any stressful event in pregnancy and cleft lip or palate by the same authors, it must be considered that the stress of any underlying illness for which steroid may be recommended might have more effect than treatment[10]. Given that the palate fuses before eight weeks gestation, this extremely small and possibly absent risk has to be put into perspective for each individual. Successful control of hyperemesis using prednisolone allows the achievement of absolutely normal growth for baby, and this is a major aim of the steroid therapy – to restore normal foetal nutrition[1].

The potential side-effects of steroids on the mother are identical to those seen out of pregnancy, with the exception of precipitation of diabetes. No steroid-associated diabetes has been observed in our Centre over nearly twenty years, and approximately 200 steroid-treated women with hyperemesis. This is likely to relate to two important features. Firstly, the individual has experienced a period of starvation and weight loss, and liver fat levels will have been sharply decreased removing the main underlying factor permitting emergence of diabetes[11]. Secondly, hyperemesis is seen and managed considerably before the onset of pregnancy-associated glucose intolerance (24 weeks onwards). Around 20% of women will experience a recurrence of their teenage acne, and this will persist for a month or two after the steroid therapy is withdrawn. If steroid therapy is required throughout pregnancy, there is a possibility that bone density may be reduced. The skeleton is in a state of major calcium flux by the end of pregnancy and the clinical effect of steroid therapy is not clear. However, bone scans carried out around three months after pregnancy in our Centre have not revealed any consistent tendency to persistent low bone mineral density. All of these factors should be explained to the individual woman so that she can make a well-informed decision on whether or not to accept steroid therapy. For most women with severe hyperemesis, the likelihood of complete control of symptoms and prevention of the disruption and upset of future hospital admissions is a major factor in determining acceptance.

The recent illness of Kate Middleton has drawn media attention to this poorly-understood, debilitating condition. If managed properly, with provision of sound advice and multifaceted therapy as described above, the health of mother and baby can be dramatically improved. From the perspective of the cash-strapped NHS, many bed days of unnecessary admissions are avoided. All physicians should be aware of this important therapeutic possibility.

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