Management of Hyperemesis Gravidarum Using Steroid Therapy

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Abstract

Background: To compare the efficacy of short course of steroid with dimenhydrinate (antihistamine) in the treatment of intractable hyperemesis gravidarum.

Methods: In this descriptive study fifty patients were assigned to receive intravenous hydrocortisone 100 mg eight hourly as a daily dose for three days. Subsequently, oral prednisolone 45 mg which was tapered off in 5 days. Fifty patients were given intravenous dimenhydrinate 50 mg three times daily for 3 days, followed by oral tablets of 50 mg three times a day for 5 days. Patients were followed up during the therapy course and for 2 wks following discharge.

Results: There was a significant reduction in vomiting episodes in the hydrocortisone group compared with the dimenhydrinate group (p < .0001). None of the patients from the hydrocortisone group but eight of the patients receiving dimenhydrinate were readmitted for intractable vomiting within 1 wk after discharge.

Conclusion: Short corticosteroids' course is an effective treatment for intractable hyperemesis gravidarum.

Key Words: Hyperemesis; Steroid; Dimenhydrinate

Introduction

Nausea and vomiting are the most common symptoms experienced in early pregnancy. Severe nausea and vomiting is associated with maternal morbidity although there is no evidence of fetal damage. Upto 3% of these women experience hyperemesis gravidarum, a severe form of vomiting due to pregnancy characterized by weight loss, electrolyte abnormalities, dehydration, and ketonuria. Complications associated with hyperemesis gravidarum include a tear in the mucosa at the junction of the esophagus and stomach (Mallory-Weiss tear) or an esophageal perforation and Wernicke encephalopathy, a neurological disorder characterized by confusion, disorientation, involuntary rolling of the eyeballs (nystagmus), double vision (diplopia), and coma, rhabdomyolysis, coagulopathy, and low birth weight infants. Severe dehydration can result in hypovolemia, leading to shock. Maternal failure to gain weight can cause intrauterine growth retardation.

Symptoms usually start between 4 and 7 weeks gestation and resolve by 16th week. Serious complications are possible if condition is left untreated. Women with hyperemesis gravidarum who gain less than 15.4 pounds (7 kg) throughout the pregnancy are more likely to give birth to low birth weight infants and are thought to have an increased risk for preterm birth.

The general care of women with severe hyperemesis extends beyond the use of steroid therapy. Mobilization must be gradual as physical movement exacerbates the underlying nausea. Discharge is not wise as soon as intravenous fluids are no longer necessary, as this may be associated with loss of control precipitated by the journey home.

Patients and Methods

From January 2010 to December 2011, 100 women presenting to Gynae out patient department of District Head Quarter hospital complaining of nausea and vomiting during the first half of pregnancy (less than 20 weeks' and more than 10 weeks gestation) were enrolled to compare the efficacy of steroids with dimenhydrinate group, both given intravenously for first 3 days and then orally for 5 days.

Women considered eligible for this study were those who previously had not responded to outpatient therapy and who demonstrated 3+ or 4+ dipstick urinary ketones as evidence of severe dehydration or weight loss of more than 5 percent of prepregnancy weight. Before enrollment into the study, an ultrasound was performed to exclude molar pregnancy, to confirm a live fetus, and to establish gestational age. All women underwent assessments of thyroid function, liver function, pancreas (amylase and lipase) and electrolytes.

All were provided intravenous hydration with crystalloid until ketonuria cleared. The first litre of crystalloid included thiamine 100 mg. Women were assigned to two groups. Group A was given...
Hydrocortisone 100 mg intravenously for 3 days followed by tapering regimen of oral prednisone (40 mg for day 4, 30 mg for day 5, 20 mg for day 6, and 10 mg for day 7). Group B was treated with dimenhydrinate 10 mg intravenously every 8 hours for 3 days followed by the same regimen administered orally for 5 days until discharge from the hospital. Both groups of women were allowed to have small meals on request and were advanced to a regular diet as tolerated, at which time discharge was permitted. Each woman was counselled about diet, and told to have frequent small meals. At discharge, all women were instructed to report back, if vomiting recurred. Women requiring readmission for hyperemesis gravidarum were given oral dimenhydrinate.

**Results**

Hundred women were recruited between January 2010 to December 2011. Three patients were lost from follow up, two from the dimenhydrinate group and one from the steroid group. There were 62 primigravidas. Gestational age was between 10 weeks to 20 weeks (Table 1). Adverse effects of drug were not found in any patient. Severity of hyperemesis gravidarum was assessed by number of vomits per day and weight loss in the current pregnancy as compared to prepregnancy weight, and it was almost similar between two groups (Table 1).

After one week of treatment, eight women in steroid group and twenty women in dimenhydrinate group were still vomiting, of whom three in steroid group and sixteen in dimenhydrinate group were vomiting five or more than five times daily (Table 2). Patients who were vomiting more than five times a day were continued on intravenous therapy for three more days.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group A (steroid n=49)</th>
<th>Group B (dimenhydrinate n=48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primigravidas</td>
<td>28(56%)</td>
<td>34(68%)</td>
</tr>
<tr>
<td>Multigravidas (gestation&gt;3)</td>
<td>12(24%)</td>
<td>26(52%)</td>
</tr>
<tr>
<td>Gestation (weeks); mean(SD)</td>
<td>13.2SD(2.5)</td>
<td>11.5SD(2.1)</td>
</tr>
<tr>
<td>Weight (kg); mean(SD)</td>
<td>61.8(10.2)</td>
<td>58.3(12.5)</td>
</tr>
<tr>
<td>No of vomits &gt; 5 times per day</td>
<td>32(64%)</td>
<td>37(74%)</td>
</tr>
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Twenty five women, on steroids, achieved suppression of vomiting within 48 hours, while 16 felt better after one week of therapy. 8 patients were still vomiting at the end of one week therapy and 1 patient was lost to follow up. As for Dimenhydrinate group 11 patients achieved suppression of vomiting within 48 hours while 17 patients felt better after one week of treatment, 20 patients were still vomiting and 2 were lost to follow up. Control of vomiting was much better with steroids because number of patients still requiring intravenous infusions at the end of first week therapy was only 3 in steroid group as compared to 16 in dimenhydrinate group.

Number of patients requiring antiemetics at the end of first week of treatment was 8 in steroid group as compared to 20 in dimenhydrinate group. Seven patients from the dimenhydrinate group were readmitted within one week after discharge but no patient from the steroid group was readmitted (Table 3). There was a significantly greater improvement in the well being rate in the steroid group. Majority (67.32%) patients in the steroid group were tolerating oral food well at two weeks follow up, compared to 39.58% in dimenhydrinate group.

**Table 2. Primary outcome measures**

<table>
<thead>
<tr>
<th></th>
<th>Steroid (n=49)</th>
<th>Dimenhydrinate (n=48)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patients with vomiting after 1 week</td>
<td>8</td>
<td>20</td>
<td>0.00&lt;.05</td>
</tr>
<tr>
<td>No of patients on intravenous infusion</td>
<td>3</td>
<td>16</td>
<td>0.00&lt;.05</td>
</tr>
</tbody>
</table>

**Table 3. Secondary outcome measures**

<table>
<thead>
<tr>
<th></th>
<th>Steroid group</th>
<th>Dimenhydrinate group</th>
<th>RR(95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Readmission of patients</td>
<td>0</td>
<td>7</td>
<td>1.8791</td>
<td>0.00</td>
</tr>
<tr>
<td>Patients on antiemetics</td>
<td>8</td>
<td>20</td>
<td>1.6305</td>
<td>0.00</td>
</tr>
<tr>
<td>Well being rate after 2 weeks</td>
<td>33</td>
<td>19</td>
<td>1.3804</td>
<td>0.00</td>
</tr>
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Data are expressed as median (range). Relative risk (RR) and (95% confidence interval) are given for proportions RR (95% CI).

**Discussion**

Severe hyperemesis gravidarum causes profound maternal morbidity. Indications for the use of steroids in hyperemesis gravidarum are delineated. Most protocols suggest using steroids after the 10th week of pregnancy and limiting their use to one
month. The initial dose is typically high, then weaned down slowly after a few days. Present study registered cessation of vomiting was observed in most of the patients after initial dose of intravenous hydrocortisone. Maintenance prednisolone therapy permitted discharge from hospital within days, resumption of normal eating, reversal of muscle wasting and regain of lost weight, mean loss from prepregnant weight. Steroid use is typically saved for women who do not respond to other medications by the end of the first trimester, and are losing weight rapidly due to more severe nausea and vomiting. Use of steroids for hyperemesis gravidarum revealed benefits with respect of patients’ well being, food intake and weight gain. Studies have found adverse effects on the baby since the treatment duration is typically a month or less. Transplacental passage of prednisolone is low, which predicts minimal effect on fetus. There has been much anxiety in the past, concerning a possible association between steroid use in first trimester and oral facial clefts, the study of Rodriguez-Pinilla and Martinez-Frias is often quoted as demonstrating a significant effect of first trimester steroid use and cleft lip and palate, but three of the five identified cases appear unlikely to be relevant. One of the three received only two doses of prednisolone after eight weeks gestation when lip fusion would have already occurred, another was associated with multiple abnormalities and a third was receiving replacement doses of hydrocortisone. A larger study found oral cleft rates to be similar between controls and those taking steroids in the first trimester and failed to show any association between steroid use in the first trimester and oral facial clefts.

Although the severity of vomiting necessary for admission to the trial was specified, vomiting in pregnancy can have a variety of causes. Thus some women may have vomiting purely because of the hormonal effects of pregnancy but in others, emotional factors may have been dominant.

Conclusion
Steroid therapy, for hyperemesis gravidarum, after tenth week of gestation, will circumvent maternal and fetal deleterious implications.

References
11. Fraser FC, Sajoo A. Teratogenic potential of corticosteroids in humans. Teratology 1995;51:45–46