

**A COMPARISON BETWEEN METOCLOPRAMIDE AND  
PROMETHAZINE PLUS PYRIDOXINE IN THE  
MANAGEMENT OF HYPEREMESIS GRAVIDARUM: A  
RANDOMIZED CONTROLLED TRIAL**

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# ABBREVIATIONS

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ANCOVA	Analysis of covariance
BMI	Body mass index
BUSE	Blood Urea Serum Electrolyte
CI	Confidence interval
EDTA	ethylenediaminetetraacetic acid
<i>et al.</i>	and others
FEME	Full microscopic examination
FDA	Food and Drug Administration
GTT	Gestational transient thyrotoxicosis
HG	Hyperemesis gravidarum
HUSM	Hospital Universiti Sains Malaysia
hCG	Human chorionic gonadotrophin
i.e.	id est
IV	intravenous
M group	metoclopramide
MSU	mid stream urine
mg	miligram
NVP	Nausea and vomiting in pregnancy
OR	Odd ratio
PUQE	Pregnancy-Unique Quantification of Emesis and Nausea
POG	Period of gestation
PP group	Promethazine/Pyridoxine
RCT	Randomized controlled trial
SD	Standard deviation

<b>SPSS</b>	<b>Statistical package for the social sciences</b>
<b>TPN</b>	<b>Total parenteral nutrition</b>
<b>TSH</b>	<b>Thyroid stimulating hormone</b>
<b>US FDA</b>	<b>United States Food and Drug Administration</b>
<b>VAS</b>	<b>Visual analogue score</b>
<b>vs</b>	<b>versus</b>



# ABSTRACT (ENGLISH VERSION)

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**Introduction:** Hyperemesis gravidarum is a debilitating condition, involving the general health and psychological aspects of the patients, as well as creating financial burden to the family. An effective treatment will be very much beneficial in reducing these stressful conditions. The mainstay treatment for hyperemesis gravidarum is to stop the bouts of vomiting, rehydration as well as correcting the starvation state of the patients. A lot of antiemetics have been widely used as the first-line treatment. However, their efficacy has never been compared, thus the aim of this study.

**Objective:** This study was performed to compare the efficacy of metoclopramide with the combination of promethazine and pyridoxine as antiemetics in patients with hyperemesis gravidarum. The efficacy of either regime was measured by the mean PUQE score achieved after treatment, the duration taken to clear the ketones in the urine, duration of hospital stay as well as the side-effects encountered.

**Methodology:** Patients admitted to Ward 1 Utara of Hospital Universiti Sains Malaysia with hyperemesis gravidarum were randomized to receive either metoclopramide 10mg three times a day or combination of promethazine 25mg three times a day with pyridoxine 20mg three times a day. The degree of vomiting was assessed by using the PUQE score, performed at 12, 24, 36, 48, 60 and 72 hours after administration of each regime. Ketone in the urine was quantified daily. The duration of hospital stay as well as the side-effects encountered were compared.

**RESULTS:** A total of 60 patients were recruited with 30 patients in each regime. There was no difference in the PUQE score of patients receiving metoclopramide with those receiving combination of promethazine and pyridoxine after 72 hours of drug administration ( $5.4 \pm 1.4$  versus  $5.3 \pm 1.6$  respectively,  $p > 0.05$ ). The duration taken for urine ketone clearance did not significantly differ either ( $2.03 \pm 0.61$  days for metoclopramide group versus  $2.26 \pm 0.63$  days for the combination of promethazine and pyridoxine group;  $p$  value= 0.15). Both groups of patients have mean hospital stay of about three days. More than half of the patients in the combination of promethazine with pyridoxine group were sedated after the drug administration.

**Conclusion:** Both regimes have similar efficacy as antiemetic in patients with hyperemesis gravidarum, and may be used as the first-line antiemetic in such cases.

# ABSTRAK (VERSI BAHASA MALAYSIA)

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**Pendahuluan:** Hyperemesis gravidarum merupakan salah satu masalah kesihatan yang bukan sahaja mempunyai pelbagai komplikasi, malahan ia juga melibatkan masalah psikososial dan kewangan pesakit. Perawatan yang berkesan boleh membantu mengurangkan masalah- masalah tersebut. Perawatan pesakit hyperemesis gravidarum melibatkan pengambilan ubat penahan muntah, pemulihan hidrasi pesakit serta pemulihan keadaan 'kelaparan'. Pelbagai ubat digunakan secara meluas sebagai ubat penahan muntah. Walau bagaimanapun, keberkesanan ubat- ubat tersebut sebagai ubat penahan muntah tahap pertama tidak dibandingkan.

**Objektif:** Kajian ini dijalankan untuk membandingkan keberkesanan metoclopramide dan kombinasi promethazine dan pyridoxine sebagai ubat penahan muntah bagi pesakit- pesakit hyperemesis gravidarum. Keberkesanan ubat- ubat tersebut dibandingkan dari segi hitungan skor PUQE, masa yang diambil untuk membersihkan ketone di dalam air kencing, masa berada di dalam wad serta kesan sampingan yang dialami pesakit.

**Kaedah kajian:** Semua pesakit yang mengalami masalah hyperemesis gravidarum yang dimasukkan ke Wad 1 Utara Hospital Universiti Sains Malaysia dipilih secara rawak untuk menerima rawatan menggunakan metoclopramide 10mg, diberi tiga kali sehari atau kombinasi ubat promethazine 25mg tiga kali sehari dan pyridoxine 20mg tiga kali sehari. Skor PUQE pesakit dinilai pada 12, 24, 36, 48, 60 dan 72 jam selepas rawatan. Air kencing

pesakit diperiksa untuk kehadiran ketone pada setiap hari. Jangkamasa pesakit berada di dalam wad dan kesan sampingan bagi setiap cara perawatan dibandingkan bagi kedua- dua kaedah perawatan.

**Keputusan:** Seramai 60 pesakit telah menyertai kajian ini, di mana seramai 30 orang pesakit telah menerima setiap kaedah perawatan. Tiada perbezaan nyata didapati di dalam skor PUQE pesakit- pesakit setelah 72 jam menerima rawatan, di mana skor PUQE bagi kumpulan metoclopramide ialah  $5.4 \pm 1.4$  dan skor PUQE kumpulan kombinasi promethazine dan pyridoxine ialah  $5.3 \pm 1.6$ . Perbezaan nyata juga tidak terdapat di dalam masa yang diambil untuk penyahan ketone di dalam air kencing ( $2.03 \pm 0.61$  hari untuk kumpulan metoclopramide berbanding  $2.26 \pm 0.63$  hari untuk kumpulan kombinasi promethazine dan pyridoxine group,  $p \text{ value} > 0.05$ ). Pesakit- pesakit telah dirawat di hospital selama lebih kurang tiga hari bagi kedua- dua kumpulan. Lebih daripada separuh pesakit di dalam kumpulan kombinasi promethazine dan pyridoxine mengalami masalah mengantuk semasa di dalam perawatan.

**Kesimpulan:** Keberkesanan metoclopramide dan kombinasi promethazine dan metoclopramide sebagai ubat penahan muntah untuk pesakit- pesakit hyperemesis gravidarum adalah sama. Kedua- dua regim ubat boleh digunakan sebagai ubat penahan muntah tahap pertama untuk pesakit- pesakit tersebut.