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PRESCRIPTION COMPounding FOR

OBSTETRICS & GYNECOLOGY

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**MIGRAINE HEADACHE**

The following study finds that a combination of indomethacin, prochlorperazine, and caffeine is effective in treating migraine headache - “Efficacy of dosing and re-dosing of two oral fixed combinations of indomethacin, prochlorperazine and caffeine compared with oral sumatriptan in the acute treatment of multiple migraine attacks: a double-blind, double-dummy, randomised, parallel group, multicentre study” *(Int J Clin Pract. 2007 Aug;61 (8):1256-69).*

**AIMS AND METHODS:** In this double-blind, double-dummy, randomised, parallel group, multicentre study, the efficacy of dosing and re-dosing of a fixed combination of indomethacin, prochlorperazine and caffeine (Indoprocaf) was compared with encapsulated sumatriptan in the acute treatment of two migraine attacks. Additionally, in the group taking Indoprocaf, two different oral formulations were tested: effervescent tablets and encapsulated coated tablets.

**RESULTS:** Of 297 patients randomised (150 assigned to Indoprocaf and 147 to sumatriptan), 281 were included in the intention-to-treat efficacy analysis. The initial dosing of Indoprocaf and sumatriptan was similarly effective with pain-free rates higher than 30% (95% CI of odds-ratio: 0.57-1.28) and headache relief rates of about 60% (95% CI of odds-ratio: 0.82-1.84) with both the drugs. The efficacy of re-dosing of Indoprocaf as rescue medication was more effective than that of sumatriptan with pain-free values of 47% vs. 27% in the total attacks with a statistically significant difference in the first migraine attack in favor of Indoprocaf. The efficacy of re-dosing to treat a recurrence/relapse was very high without differences between the drugs (pain-free: 60% with Indoprocaf and 50% with sumatriptan in the total attacks). Indoprocaf and sumatriptan were well-tolerated.

**CONCLUSION:** The study demonstrated that the efficacy of the initial dosing of Indoprocaf was not higher than that of sumatriptan, but that the strategy to use the lowest effective dose as soon as the headache occurred, followed by a second dose if the headache has not relieved or to treat a relapse, was very effective, especially with Indoprocaf. PMID: 17627707

This study suggests that IndoProCaf should be able to abort migraine attacks independently from the time of administration - “Indomethacin, alone and combined with prochlorperazine and caffeine, but not sumatriptan, abolishes peripheral and central sensitization in vivo models of migraine” *(J Pain. 2004 Oct;5 (8):413-9).*

**ABSTRACT:** “Recently it has been proposed that the throbbing pain of migraine is mediated by sensitization of peripheral trigemino-vascular neurons, and that cutaneous allodynia of migraine is mediated by sensitization of central trigeminovascular neurons, and, moreover, that the triptans are less effective in aborting a migraine attack if the central sensitization is already established. The combination of indomethacin, prochlorperazine, and caffeine (IndoProCaf) is a drug of well-established use in the acute treatment of migraine. The aim of this study was to investigate whether the 3 active principles of IndoProCaf, alone and combined, compared to sumatriptan, were able to abolish the peripheral sensitization induced by kainic acid and the central sensitization induced by N-methyl-D-aspartate (NMDA) in vivo models of hyperalgesia. The study showed that indomethacin or IndoProCaf is able to abolish both the kainic acid-induced and the NMDA-induced hyperalgesia. If administered at different times, IndoProCaf was always effective in reversing the kainic acid-induced hyperalgesia. Sumatriptan was not able to reverse either the kainic acid-induced or the NMDA-induced hyperalgesia. The efficacy of indomethacin, alone and combined with prochlorperazine and caffeine, in abolishing peripheral and central sensitization in vivo models of hyperalgesia is a further explanation of the clinical efficacy of IndoProCaf in the treatment of migraine.

**PERSPECTIVE:** This study suggests that, although triptans were shown to be able to abort migraine attacks only if given before the establishment of cutaneous allodynia and central sensitization, IndoProCaf should be able to abort migraine attacks independently from the time of administration, because it is able to abolish an already established peripheral and central sensitization.” PMID: 15501422

An example of how you might prescribe follows:

**COMPOUNDED MEDICATION**

**Indomethacin 25mg/Prochlorperazine 4mg/Caffeine 75mg Suppository**

#30

Insert 1 suppository rectally Q6-8H PRN

With our state of the art compounding lab and pharmaceutical knowledge and experience, we can compound indomethacin, prochlorperazine, and caffeine into a suppository.

With our state of the art compounding lab and pharmaceutical knowledge and experience, we can compound indomethacin, prochlorperazine, and caffeine into a suppository.
In this clinical trial the intravaginal application was as effective as the oral administration of metronidazole in treating BV. However, significantly less adverse events were reported after short-term intravaginal use as compared to oral application, and probably led to a better patient compliance - “Intravaginally applied metronidazole is as effective as orally applied in the treatment of bacterial vaginosis, but exhibits significantly less side effects” (Eur J Obstet Gynecol Reprod Biol. 2008 Sep 3).

OBJECTIVE: Metronidazole is the drug of choice for the treatment of bacterial vaginosis (BV). However, so far the oral administration has not been clinically compared to the intravaginal application regarding efficacy, side effects and patient satisfaction in a scientific sound fashion.

STUDY DESIGN: Therefore, this randomized, double-blind, placebo-controlled clinical trial was designed to demonstrate non-inferiority of short-term intravaginal (i.vag.) application of metronidazole (2x 1000mg pessaries 24h apart) vs. a single oral dose (p.o.) of metronidazole (1x2000mg tablets) in 263 patients with BV (double-dummy design). The follow-up period was 12 weeks. In addition, the number and the type of adverse events induced by the two regimens were compared, assuming better tolerability of the intravaginal application.

RESULTS: Following the diagnosis of BV a total of 129 women (mean age 36.2 years) was orally treated with a single dose of 2g metronidazole whereas a total of 134 patients (mean age 35.5 years) was treated intravaginally with 1g metronidazole each day on two consecutive days and included in the per-protocol analysis. Non-inferiority of i.vag. application compared to p.o. administration was statistically significant regarding efficacy: Following intravaginal application the cure rate, assessed on day 8 after starting of the treatment, was 92.5% as compared to 89.9% after oral administration. Nausea was the most common adverse event reported in 10.2% i.vag. vs. 30.4% p.o. of all cases (p<0.001), abdominal pain in 16.8% i.vag. vs. 31.9% p.o. (p<0.01), a "metallic taste" in 8.8% i.vag. vs. 17.9% p.o. (p<0.05). Women treated i.vag. were highly satisfied with the treatment and more content compared to the women treated p.o. with metronidazole (p<0.05, intent-to-treat analysis).

CONCLUSION: In this clinical trial the intravaginal application was as effective as the oral administration of metronidazole in treating BV. However, significantly less adverse events were reported after short-term intravaginal as compared to oral application (p=0.023) and probably led to a better patient compliance. PMID: 18775597

The following study found that metronidazole/nystatin intravaginal combination was significantly more effective than metronidazole alone - “Intravaginal metronidazole gel versus metronidazole plus nystatin ovules for bacterial vaginosis: a randomized controlled trial” (Am J Obstet Gynecol. 2004 Dec;191(6):1898-906).

OBJECTIVE: We compared metronidazole 0.75% gel (containing 37.5 mg metronidazole per dose) with ovules containing metronidazole 500 mg and nystatin 100,000 U, for intravaginal treatment of bacterial vaginosis (BV).

STUDY DESIGN: In a single-blinded trial, symptomatic women with BV by both Amsel and Nugent criteria were randomly assigned to gel or ovules, once nightly for 5 nights, and asked to return 3 times after treatment. Analyses were intent-to-treat.

RESULTS: Of 151 women with BV by both criteria at enrollment, 138 (91%) returned at least once. Product limit estimates for persistence or recurrence of BV at 14, 42, and 104 days were 20% (95% CI 10%-29%), 38% (95% CI 25%-48%), and 52% (95% CI 37%-63%) after gel treatment, and 4% (95% CI 0%-9%), 17% (95% CI 7%-26%), and 33% (95% CI 21%-46%) after ovule treatment (P = .01). Among women without BV at first follow-up, subsequent intercourse without condoms independently predicted subsequent recurrence (P </= .01).

CONCLUSION: Metronidazole/nystatin ovules were significantly more effective than metronidazole gel. Unprotected sex predicted recurrence after initial improvement. PMID: 15592270

With our state of the art compounding lab and pharmaceutical knowledge and experience, we can compound metronidazole and nystatin into one intravaginal cream.

An example of how you might prescribe follows:

**COMPOUNDED MEDICATION**

**Metronidazole 125mg/ml + Nystatin 25,000u/ml Intravaginal Cream**

5ml

Insert 1ml intravaginally HS x 5 nights
HYPEREMESIS GRAVIDARUM


OBJECTIVES: Hyperemesis gravidarum (HG) is the second most common reason for hospitalization during pregnancy. Since 2002, a new HG treatment protocol consisting of metoclopramide plus diphenhydramine was put in place at CHU Sainte-Justine, affiliated to University of Montreal, Quebec, Canada. The objectives of this study were to evaluate the effectiveness of this new HG protocol regarding length of hospitalization for HG, rate of rehospitalization, evolution of nausea and vomiting symptoms, and rate of adverse events.

STUDY DESIGN: A retrospective cohort study was conducted from 2002 to 2006 on the population of pregnant women diagnosed with HG, and treated at CHU Sainte-Justine with the new protocol consisting of intravenous metoclopramide 1.2-1.8 mg/h plus diphenhydramine 50 mg every 6 h. These women were compared to a historical control group consisting of women diagnosed with HG, and treated in the same institution with intravenous droperidol 0.5-1 mg/h plus diphenhydramine 25-50 mg every 6h between 1998 and 2001.

RESULTS: During the study period, a total of 130 pregnant women were exposed to the new HG protocol versus 99 that were exposed to the droperidol and diphenhydramine combination between 1998 and 2001. Our study showed that the new HG protocol was associated with a greater improvement of vomiting symptoms (36% vs. 21%; p=0.0397), and with fewer adverse events. The new HG protocol was equivalent to the droperidol and diphenhydramine combination to reduce nausea symptoms, length of hospitalization (3.7 days vs. 3.1 days), and rate of rehospitalization for HG (19.23% vs. 24.44%).

CONCLUSIONS: The new protocol consisting of the combination of metoclopramide and diphenhydramine appears to be a good option in the management of hyperemesis gravidarum. PMID: 19135291

We have the ability to compound metoclopramide and diphenhydramine into a suppository, in doses that meet the unique needs of each of your patients.

An example of how you might prescribe follows:

<table>
<thead>
<tr>
<th>COMPOUNDED MEDICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metoclopramide 5mg / Diphenhydramine 12.5mg Suppository</strong> #30</td>
</tr>
<tr>
<td>Insert 1 suppository rectally Q6H PRN</td>
</tr>
</tbody>
</table>
Migraine Headache

[ ] Indomethacin 25mg/Prochlorperazine 4mg/Caffeine 75mg  Suppository
Quantity #30  Directions: Insert 1 suppository rectally Q6-8H PRN

Bacterial Vaginosis

[ ] Metronidazole 125mg/ml + Nystatin 25,000 u/ml  Intravaginal Cream
Quantity 5ml  Directions: Insert 1ml intravaginally HS x 5 nights

Hyperemesis Gravidarum

[ ] Metoclopramide 5mg/Diphenhydramine 12.5mg  Suppository
Quantity #30  Directions: Insert 1 suppository rectally Q6H PRN

Directions

________________________________________________________________________

Prescriber’s Signature____________________________________   Refills:  1    2    3    4    5    6    7    8    9    10   11   12    NR