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PRESRIPTION COMPOUNDING FOR

GENERAL PRACTICE

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We customize individual prescriptions for the specific needs of our patients.
The following study suggests that a vancomycin dosage of 60 mg/kg/d was predicted to optimize achievement of the pharmacodynamic target of AUC(0-24)/MIC >400 for invasive MRSA infections in children. “Prediction of vancomycin pharmacodynamics in children with invasive methicillin-resistant Staphylococcus aureus infections: a Monte Carlo simulation” (Clin Ther. 2010 Mar;32(3):534-42).

**BACKGROUND:** Due to the emergence of community-associated strains, the prevalence of invasive methicillin-resistant Staphylococcus aureus (MRSA) infections has increased substantially in pediatric patients. A vancomycin AUC(0-24)/MIC index >400 best predicts treatment outcomes for invasive MRSA infection in adults. Data on whether recommended vancomycin doses in children achieve this break point are lacking.

**OBJECTIVE:** This study aimed to assess the likelihood that currently recommended vancomycin doses in children achieve AUC(0-24)/MIC >400.

**METHODS:** Vancomycin AUC(0-24)/MIC predictions were conducted across a range of dosages (40-70 mg/kg/d) using a Monte Carlo simulation (n = 5000). AUC(0-24) was calculated as daily dose divided by vancomycin clearance, and daily dose was fixed for a given simulation. Three literature-reported estimates in children were used to define vancomycin clearance and its variance. For the MIC distribution of MRSA isolates, susceptibility data were obtained from the University of California, San Francisco Children's Hospital, San Francisco, California (n = 180; 40% < or =0.5 mg/L; 59% = 1 mg/L; and 1% = 2 mg/L).

**RESULTS:** Using the recommended empiric dosage of 40 mg/kg/d, 58% to 66% of children were predicted to achieve AUC(0-24)/MIC >400. Increasing the vancomycin dosage to 60 mg/kg/d substantially increased the likelihood (88%-98%) of achieving this pharmacodynamic target. On sensitivity analysis, a dosage of 40 mg/kg/d was more strongly influenced by small changes in MIC compared with 60 mg/kg/d.

**CONCLUSIONS:** Recommended empiric vancomycin dosing in children (40 mg/kg/d) was not predicted to consistently achieve the pharmacodynamic target of AUC(0-24)/MIC >400 for invasive MRSA infections. A vancomycin dosage of 60 mg/kg/d was predicted to optimize achievement of this target in children. PMID: 20399990

This study states that a starting dose of 60 mg/kg/d should be used in settings where isolates with MIC of 1.0 are common - “Current recommended dosing of vancomycin for children with invasive methicillin-resistant Staphylococcus aureus infections is inadequate” (Pediatr Infect Dis J. 2009 May;28(5):398-402).

**BACKGROUND:** Vancomycin area-under-the-concentration-time-curve (AUC) for 24 hours divided by the minimum inhibitory concentration (MIC) (AUC24/MIC) >400 optimally treats invasive methicillin-resistant Staphylococcus aureus (MRSA) infections in adults. It is unknown whether recommended vancomycin dosing regimens for children achieve this value.

**METHODS:** AUC24/MIC was calculated in children using vancomycin doses of 40 and 60 mg/kg/d. AUC24 was calculated as daily dose/vancomycin clearance. Vancomycin clearance in children was estimated by 2 approaches: (1) previously literature-reported vancomycin clearance, and (2) calculated vancomycin clearance using previously derived predictor models and a hypothetical population of healthy children. Representative MIC of hospital MRSA isolates was used (0.5, 1.0, and 2.0 microg/mL).

**RESULTS:** The MIC50/90 for pediatric MRSA isolates in the previous year was 1.0 microg/mL. With a dose of 40 mg/kg/d, both approaches consistently predicted AUC24/MIC <400 when MIC was 1.0 microg/mL. At 60 mg/kg/d, AUC24/MIC >400 was more readily achieved when MIC was 1.0 microg/mL, however, an MIC of 2.0 microg/mL resulted in AUC24/MIC <400 for both dosing regimens.

**CONCLUSIONS:** A vancomycin dose of 40 mg/kg/d in children is unlikely to achieve the recommended pharmacodynamic target of AUC24/MIC >400 for invasive MRSA infections even when MIC is 1.0 microg/mL. A starting dose of 60 mg/kg/d should be used in settings where isolates with MIC of 1.0 are common. Alternatives to vancomycin should strongly be considered for patients with MIC > or =2.0 microg/mL. PMID: 19295465

An example of how you might prescribe follows:

**COMPONDED MEDICATION**

**Vancomycin 125mg/5ml**
**Flavored Oral Solution**
Quantity 280ml
Directions: 5ml po QID x 14 days

With our state of the art compounding lab and pharmaceutical knowledge and experience, we can compound vancomycin into a flavored oral solution; at doses that meet the unique needs of each one of your patients.
Fever

Ibuprofen is one of the standard treatments for children with fever—“Efficacy of ibuprofen in pediatric patients with fever” (Int J Clin Pharmacol Ther Toxicol. 1992 Mar;30(3):94-6).

ABSTRACT: “We studied the efficacy of ibuprofen in 56 infants and children (age 0.5-12 years) with rectal temperature greater than or equal to 38.3 degrees C, using a double-blind randomized placebo-controlled design. Ibuprofen liquid was given as a single dose, 5 mg/kg to 18 patients (group I) and 10 mg/kg to 18 patients (group II); placebo was administered to 20 patients (group III). Temperature and vital signs were measured every 0.5-1.0 hours for 8 hours. Multiple blood samples were also collected over this period; ibuprofen plasma concentrations were measured by HPLC. The mean temperature was 38.3 degrees C in group I, 38.1 degrees C in group II, and 38.9 degrees C in group III during 8 hours after drug or placebo administration. The temperature was significantly lower in group I vs III (ibuprofen 5 mg/kg vs placebo) (p less than 0.0005), and group II vs III (ibuprofen 10 mg/kg vs placebo) (p less than 0.0001). The temperature was also markedly different for patients in group I vs II (ibuprofen 5 mg/kg vs ibuprofen 10 mg/kg) between 4 and 8 hours after the dose (p less than 0.01). The duration of action was longer for ibuprofen 10 mg/kg than 5 mg/kg. The mean maximum decrease from baseline temperature was 1.3 degrees C, 1.8 degrees C and 0.8 degrees C for group I, II and III, respectively. The maximum reduction in temperature occurred at 3-4 hours in the ibuprofen groups, and at 7 hours in the placebo group.” PMID: 1506123

With our state of the art compounding lab and pharmaceutical experience, we have the ability to compound and custom dose ibuprofen, based on body weight, into a suppository or transdermal gel for those patients who may have difficulties swallowing medicine.

Examples of how you might prescribe follow:

Compounded Medication

Ibuprofen 200mg
Suppository
#24
Insert one suppository rectally Q6-8H PRN

or

Ibuprofen 200mg/ml
Transdermal Gel
30ml
Apply 1ml to neck or inner wrist Q6-8H PRN
**GERD**

Omeprazole is an effective treatment for GERD in children, however as the following study notes, dosings on a milligram-per-kilogram basis are recommended: "Pharmacokinetics of omeprazole in healthy adults and in children with gastroesophageal reflux disease" (Ther Drug Monit. 2004 Feb;26(1):3-8).

"Studies of the pharmacokinetics of omeprazole in children with gastroesophageal reflux disease (GERD) remain scarce despite the vast number of reports on its efficacy. The objectives of this study were to assess the pharmacokinetics of omeprazole in healthy adults and in children with GERD. Omeprazole (Losec, delayed-release capsules) was administered orally to 18 healthy adults (mean age 36.8 years) and 12 children with GERD (mean age 6.1 years). Blood samples were collected over 5 hours, and plasma concentrations were assessed using liquid chromatography. Population pharmacokinetic parameters were calculated using NONMEM. A 1-compartment model with zero-order absorption and a lag time was used. The population approach was well suited to the limited number of samples available, and residual variability was low. Oral clearance (CL/F) and apparent volume of distribution (V(ss)/F) in healthy adults (Mean +/- SD: 0.62 +/- 0.27 L/h/kg and 0.76 +/- 0.26 L/kg, respectively) were not significantly different than those in children with GERD (0.51 +/- 0.34 L/h/kg and 0.66 +/- 0.25 L/kg, respectively). Healthy adults displayed a statistically significantly longer delay in drug absorption (Lag time: 0.62 +/- 0.15 hours) as compared with that observed in children with GERD (0.12 +/- 0.03 hours, P < 0.05). On the basis of these findings, omeprazole dosings on a milligram-per-kilogram basis are recommended with no further adjustments for the treatment of GERD in children." PMID: 14749542

The following study found that omeprazole 1 mg/kg per day is an effective therapy for the majority of children with severe erosive oesophagitis due to abnormal isolated bile reflux or combined acid and bile reflux. "Treatment of oesophageal bile reflux in children: the results of a prospective study with omeprazole" (J Pediatr Gastroenterol Nutr. 2006 Apr;42(4):376-83).

**OBJECTIVES:** Reflux of duodenal juice into the oesophagus has a role in the pathogenesis of both oesophageal and laryngopharyngeal inflammatory and neoplastic lesions. As little is known about effective therapy, we studied the effect of proton pump inhibitor therapy on oesophageal bile reflux in children.

**METHODS:** Twenty-nine children with moderate to severe erosive oesophagitis and abnormal oesophageal bile reflux were studied before and after treatment with omeprazole 1 mg/kg per day. Outcomes included a clinical symptom score, oesophageal acid and bile reflux (simultaneous 24-hour pH and Bilitec 2000 monitoring), and mucosal healing.

**RESULTS:** After 8 weeks of therapy, 17 (59%) of the patients were symptom-free, and 5 (17%) had minimal symptoms. Mucosal healing or reduction to low-grade oesophagitis was achieved in 25 children (86%; P < 0.0005). Mean percentages of total, upright, and supine time with oesophageal pH less than 4 were reduced from 17.0%, 16.8%, and 19.2% before treatment, to 2.83%, 3.17%, and 2.07%, respectively, after treatment (all P < 0.00001). Similarly, mean percentages of total, upright, and supine time with bile reflux were reduced from 16.96%, 12.67%, and 22.0%, to 2.27%, 1.91%, and 2.23%, respectively (P < 0.000001, P < 0.00001, and P < 0.000001, respectively).

**CONCLUSIONS:** Omeprazole 1 mg/kg per day is an effective therapy for the majority of children with severe erosive oesophagitis due to abnormal isolated bile reflux or combined acid and bile reflux. It remains unclear how patients with treatment-resistant bile reflux should be managed. PMID: 16641575

An example of how you might prescribe follows:

<table>
<thead>
<tr>
<th>COMPOUNDED MEDICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole 2mg/ml</td>
</tr>
<tr>
<td>Oral Liquid</td>
</tr>
<tr>
<td>Quantity 150ml</td>
</tr>
<tr>
<td>As directed po daily</td>
</tr>
</tbody>
</table>

With our state of the art compounding lab and pharmaceutical knowledge and experience, we can compound omeprazole as an oral liquid that will allow for easy, accurate dosing.
**Prescriber Name**

**Prescriber Address**

City ______________________________ State __________ Zip _________________

Phone __________________________ Fax ___________________________

**Date _________________ Patient Name _______________________________ DOB _________________**

**Address ______________________________ City/State/Zip _______________________________ Phone ___________________________

☐ Patient will pick up at pharmacy ☐ Please ship to patient

**Insurance Plan: ___________________________ ID# ___________________________**

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**Methicillin-Resistant Staphylococcus**

- [ ] Vancomycin 125mg / 5ml Flavored Oral Solution Quantity 280ml Directions: 5ml po QID x 14 days

**Fever**

- [ ] Ibuprofen 200mg Suppository Quantity #24 Directions: Insert 1 suppository rectally Q6-8H PRN
- [ ] Ibuprofen 200mg/ml Transdermal Gel Quantity 30ml Directions: Apply 1ml to neck or inner wrist Q6-8H PRN

**Gerd**

- [ ] Omeprazole 2mg/ml Oral Liquid Quantity 150ml Directions: As directed po daily

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**All topical compound %’s are per 1 ml or 1 gm unless otherwise noted**

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**Directions**

________________________________________

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

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