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Policies & Procedures: The following policies & procedures have been approved and are being reformatted for posting on the C&W intranet:

High Alert Medications Policy

Safe Medication Order Writing Policy, including list of unacceptable abbreviations

These two policies are related to Accreditation Required Organizational Practices. More information will be coming via Accreditation communications and education over the next 2 months.

Standard Concentrations of IV opioids for continuous infusion

To meet the accreditation ROP on Standardizing Medication concentrations across the organization, a decision was made to proceed with standardizing Continuous Opioid Infusions at Children’s Hospital. More information and education will be coming with a planned go live date for the beginning of May 2012.

Pharmaceutical Manufacturer Representative Policy

Sample Medication Handling Policy

The policy for pharmaceutical manufacture representatives visiting clinicians at C&W and the policy for handling, storage and responsibilities around sample medications for clinicians with their only office located at C&W have been revised.

IV Phenytoin administration

• The policy & procedure for IV administration of phenytoin has been updated to address the routes of delivery issue (PICC line administration) of IV phenytoin. Based on a review of the evidence, practices at other centres and local PSLS reports, it has been determined that phenytoin seems to be preferred to be given via peripheral IV, but can be administered via PICC lines if required.

• It should be stressed that phenytoin is not compatible with dextrose containing solutions and that the issue of clogging usually arises when the PICC line is not flushed adequately.

• The main change to the procedure is to dilute phenytoin to a concentration of 5 -10mg/mL using normal saline (from 5mg/mL)

Continuous Epidural Analgesia

• Epidurals are now being managed on 3M. If thoracic, the child stays in PAC for 2 hours. The receiving and transferring nurse do an assessment when transferred to the ward (3R and 3M). Pre-printed orders match this policy.

Alprostadil Infusion on 3M Children’s Heart Unit:

The policy & procedure revised to permit changes in frequency of monitoring based on clinical status and dosage adjustments to permit weaning off or to minimum effective dosage in stable patients on 3M.

Additions to Formulary:

The following medications have been added to formulary at C&W:

Ciclesonide (inhaled corticosteroid in a metered dose inhaler):

PT&N has tentatively approved the addition of ciclesonide to formulary pending the availability of a 30 dose metered dose inhaler (100 micrograms per puff) and favorable cost comparison. This item will be clarified at a future meeting.

Medication Backorders:

We continue to be facing shortages of a substantial number of medications, anticipated to continue for the coming weeks and months (likely through the summer), due to Sandoz Canada manufacturing challenges. Most are injectable medications. The Pharmacy Department continues to monitor supplies and usage.

In cases where we anticipate supply issues with medications within a period of 4 weeks or less, pharmacy will coordinate alternate source or drugs or alternate therapeutic agents for patients. We are reviewing all affected medications in a systematic fashion in order to minimize the impact on direct patient care.

We appreciate all the assistance in reviewing options to mitigate the shortages (using oral/rectal routes, changing to alternative medications, changing to other brands and strengths, etc). Be aware that some of the changes can arise from acute, unanticipated shortage and staff should be mindful of the potential for medication errors as any changes are considered or implemented.

Many thanks to the pharmacy purchasing/buying staff: Susan Kemp, Zerlina Percival, Laurie Switzer, and Stephanie Ngai, for working hard to monitor and mitigate this situation and to Linda Morris (Director, Pharmacy Services) for her diligent work at the Health Authorities and local level.

Also, many thanks to the physicians and staff for their continued efforts to decrease wastage and optimize use of alternate routes of administration, as appropriate. Please continue to switch to enteral route for medications as soon as clinically feasible.

Updates are available on the C&W Intranet page “Sandoz” button and are provided on an as needed basis for stock issues that directly affect patients and prescribers at BC Children’s Hospital, BC Women’s Hospital, Sunny Hill and Children’s and Women’s Mental Health.
Why do we check drug levels for some medications?
Monitoring of drug levels is required for certain medications to ensure the safety and efficacy of medication therapy. When dosed according to standard dosing regimens, most medications reach predictable concentrations across various ages, weights, and liver and kidney function. However, the drug levels of some medications will vary from person to person and cannot be accurately predicted through standard dosing alone. For these medications, drug dosing must be individualized according to blood concentrations.

At BC Children’s Hospital (BCCH), drug levels for the following medications are commonly ordered:
- Antibiotics (Vancomycin, Gentamicin, Tobramycin)
- Cyclosporine
- Methotrexate
- Phenytoin
- Tacrolimus

Is there a procedure for drawing bloodwork for drug levels at BCCH?
Yes. Specific procedures are available on the BCCH Child and Youth Guidelines on drawing blood samples from central venous access catheters. There are also specific procedures to follow depending on the type of drug level requested. These procedures are available online on the BCCH eLab Handbook (1). http://www.elabhandbook.info/osh/Default.aspx

Why is it recommended to obtain drug levels from the opposite lumen of multi-lumen CVCs or to obtain peripheral samples?
Drug levels are sometimes obtained through central venous catheters (CVCs) in order to avoid repeated venipuncture in pediatric patients. However, several previous studies have demonstrated that drug levels drawn through CVCs may be falsely elevated and can subsequently lead to incorrect dosing recommendations.

Aminoglycosides and Vancomycin
Two studies evaluating aminoglycoside levels taken from CVCs have demonstrated falsely elevated levels, despite withdrawing and discarding 3 to 5 mL of blood from the CVC prior to obtaining the antibiotic level(2,3). Boodhan et al. (2) compared drug levels obtained from a CVC and a peripheral site in 45 pediatric patients treated with gentamicin. In this study, the levels obtained from the CVC differed from the peripheral level by -27.9% to +26% and would have led to clinically significant dosage adjustments in 42% of cases. In this study, 93% of patients had a single lumen vascular access device (VAD). In the study by Mogayzel et al. (3), mean tobramycin levels drawn from CVCs were false elevated when compared to peripheral levels. Similar results were obtained in a study evaluating vancomycin. In these studies limit direct comparisons. The hypothesized mechanism for these results is due to the lipophilic nature of cyclosporine which may bind to the surface of the catheter and leech off during the sampling procedure.

Intravenous Cyclosporine
The flushing strategy described above may not resolve CVC sampling issues with other medications. Studies evaluating CVC vs. peripheral sampling when patients are treated with intravenous cyclosporine have demonstrated marked discrepancies. Shulman et al.(4) found that drug levels of cyclosporine obtained centrally could overestimate peripheral values by +450 mg/mL (374 nmol/L). These observations are consistent with previous studies although limitations in accurate reporting of volume of blood discarded and drug administration in these studies limit direct comparisons.

Can we get away with one less poke?
No, drawing drug levels from the line through which the drug was infused can result in falsely elevated levels. This may lead to erroneous dose adjustments or may necessitate repeating levels. It is preferable to obtain drug levels from the opposite lumen of multi-lumen CVCs or to obtain peripheral samples. If this cannot be done, consultation with a pharmacist to determine the best sampling method is recommended.

References
2. Boodhan S, Maloney AM, and Dupuis LL. Extent of agreement in gentamicin concentration between serum that is drawn peripherally and from central venous catheters. Pediatrics. 2006;118:e1650-e1656.
Some women are asking about giving Innovite K2™ to their newborns for preventing hemorrhagic disease of the newborn.  

**What is Innovite K2™?**

Innovite K2™ is a product that contains vitamin K (menaquinone) and vitamin D3 in the form of a liquid for oral use.

**Does this product meet the Canadian Pediatric Society (CPS) recommendations for the prevention of hemorrhagic disease of the newborn?**

No. The recommended form of vitamin K is vitamin K1 (phytonadione). The CPS recommends vitamin K1 (phytonadione) intramuscular injection given once within 6 hours of birth [http://www.cps.ca/english/statements/fn/fn97-01.htm](http://www.cps.ca/english/statements/fn/fn97-01.htm) The intramuscular dose is 0.5 mg (birthweight 1500 grams or less) or 1 mg (birthweight greater than 1500 grams). For parents who refuse the intramuscular injection, vitamin K1 (phytonadione) injection may be given orally as an alternative. The oral dose is 2 mg at the time of first feeding and must be repeated at 2 to 4 weeks of age and again at 6 to 8 weeks of age. The CPS recommends advising parents that this oral regimen has been shown to carry a greater risk of hemorrhage, as compared to the intramuscular dose, particularly for exclusively breastfed infants.

**Is there a safety concern with Innovite K2?**

Yes. The product contains 100 mcg of vitamin K2 (menaquinone) and 500 international units of vitamin D3 per mL. In order to provide enough vitamin K, this would result in significant vitamin D exposure.

**What does BC Women’s Hospital (BCW) recommend?**

The BCW hospital policy, in accordance with the recommendation of the Canadian Pediatric Society, is for the routine use of Vitamin K1 (phytonadione) intramuscular injection given once within 6 hours of birth to prevent early and latent hemorrhagic disease of the newborn. Patient information is available from the Family Support and Resource Centre:

[Click here to get the Women’s Hospital Vitamin K pamphlet](#)

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**Take the Challenge – What’s the Difference?**

**Bupropion SR vs. XL**

Dean Elbe, PharmD, BCPP

Bupropion is an antidepressant that blocks norepinephrine and dopamine re-uptake. There is a small risk of seizures associated with the use of bupropion. At doses up to 300 mg/day (the manufacturer recommended maximum daily dosage), the incidence of seizures is low. At doses above 400 mg/day, the incidence of seizures increases to 0.4%. Neither formulation of bupropion should be crushed or chewed.

<table>
<thead>
<tr>
<th>Bupropion SR (Wellbutrin® SR, Zyban®)</th>
<th>Bupropion XL (Wellbutrin® XL)</th>
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<tbody>
<tr>
<td>Formulation</td>
<td>Sustained release tablet</td>
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<tr>
<td>Dosing frequency</td>
<td>Twice daily</td>
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<tr>
<td>Maximum recommended dose</td>
<td>150 mg twice daily</td>
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<td></td>
<td>* Doses above 150 mg must be taken at least 8 hrs apart to minimize the risk of seizures</td>
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Research


Teng JFT, Mabasa VH, Ensom MHH. The Role of Therapeutic Drug Monitoring of Imatinib in Chronic Myeloid Leukemia (CML) and Metastatic or Unresectable Gastrointestinal Stromal Tumor (GIST) Patients. Ther Drug Monit. 2012;34:85-97.


Research Grant


Editor's Corner

We would like to thank Joanie Tulloch for her work as Editor in 2011 and welcome Sonia Jeffries to the editorial team! Please contact the Editor if you would like to be added to the distribution list. The Editorial team welcomes comments and ideas. We will be publishing select letters to the Editor in future editions.

Editorial Board

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Intranasal Midazolam for Prolonged Seizure Rescue

Reviewed by Jennifer Kendrick, BScPharm PharmD

Intranasal administration of midazolam was approved at the Pharmacy, Therapeutics and Nutrition Committee as a rescue medication for prolonged seizures in specific patients. Buccal administration of midazolam is still the preferred route in most patients requiring non-IV administration of a benzodiazepine.

Rationale for Addition to Formulary
Intranasal administration of midazolam was previously excluded from use and buccal was deemed the preferred route due to ease of administration, no special devices being required, and the avoidance of nasal irritation which may occur with the intranasal route.

Recently circumstances have occurred in which buccal of midazolam was felt not to be adequately absorbed in certain patients, requiring an alternative route. Specifically, in patients with excessive oral secretions, it was found that buccally administered midazolam was often expelled prior to adequate absorption. Often these patients were receiving midazolam via the intranasal route in community due to this reason.

Thus, intranasal midazolam has been approved for the following situations:

- As rescue medication for prolonged seizures (seizures lasting longer than 5 minutes or a cluster of seizures with no return to baseline) in patients meeting at least one of the following criteria:
  - Patients with excessive oral secretions in whom buccal midazolam may not be adequately absorbed
  - Patients who have been using this route in community prior to admission
  - Patients in whom the buccal route has been ineffective in the past

Efficacy
Evidence exists to support the efficacy of midazolam administered via the intranasal route for prolonged seizure rescue (1-6). A few of these studies have reported on the pre-hospital or home use (5,6) Two prospective randomized controlled studies report the use of intranasal midazolam as a medication for prolonged seizures in an institutional setting (1,2). Bhattacharya et al. reviewed 46 pediatric patients with a total of 188 prolonged seizure episodes. Intranasal midazolam (0.2 mg/kg) was compared to rectal diazepam (0.3 mg/kg). The mean time to seizure cessation was significantly shorter in the intranasal midazolam group (126.9 sec vs. 178.9 sec, p=0.005). It was also found to be equally effective as rectal diazepam in controlling seizure episodes within 10 minutes. (96.7% vs. 88.5%, p=0.06). No significant adverse reactions were noted (1) Lahat et al. reviewed 47 pediatric patients (age 6 mos to 5 yrs). Intranasal midazolam (0.2 mg/kg) was compared to intravenous diazepam (0.3 mg/kg). The mean time to control of seizure was faster with intravenous diazepam (2.5 sec vs. 3.1 sec), but the mean overall time to cease seizure was faster with intranasal midazolam (6.1 sec vs. 8.0 sec). No significant adverse reactions were noted (2)

One additional recent randomized controlled study reports the tolerability and efficacy of midazolam for sedation via different non-IV routes. Klein et al. reviewed 169 pediatric patients (age 0.5 to 7 yrs) requiring sedation for laceration repair. This study showed that although intranasal midazolam resulted in a slightly faster onset than buccal, it resulted in the most irritation and discomfort (cough, gag, and sore throat) during administration (3)

Unfortunately, no studies thus far have directly compared intranasal midazolam to buccal for prolonged seizures; therefore there is a lack of evidence to support the superiority of intranasal to the buccal route.

Adverse Reactions
Intranasal administration of midazolam will be expected to have similar possible systemic adverse reactions including drowsiness, sedation, confusion, respiratory depression, nausea and vomiting. In addition reactions that may be specific to the intranasal route of administration of this medication may include bitter taste and sore throat, nasal irritation and/or pain, headache and coughing (3)

Dosing and Administration
Midazolam 0.2 mg/kg intranasal (Maximum 10 mg/dose, 5 mg (1mL) per nostril) using the injectable 5 mg/mL injectable solution
Administer using a 1-3 mL syringe and atomizer device according to the Intranasal Medication via Atomizer Policy

References
5. Wilson MT, MacLeod S, O'Regan ME. Nasal/buccal midazolam use in the community. Arch Dis Child 2004; 89: 50-51