Medications and Travel

Petr Prochazka BSc. Pharm
Disclosure of Potential for Conflict of Interest

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Objectives

- How to adjust insulin when travelling across several time zones
- How to best take common travel medications
- Common medication interactions
Insulin Administration Across Multiple Time Zones

- Travelling through time zones may require insulin adjustment
- If travelling east the day is shortened
- If travelling west the day is lengthened
- Basal/bolus insulin regimen will be used
- Insulin adjustment is based on number of time zones crossed and duration of stay
- Timing of insulin injections and meals can be changed by up to 2 hours a day without adjusting insulin dose or meal plan
- Generally crossing 5+ time zones will require some insulin dose adjustment
Insulin Administration Across Multiple Time Zones

- Flying east (from Winnipeg to London, with 1.5 hour stop over in Toronto)
- Flight time is 9.5 hours (total travel time 11 hours)
- Crossing 6 time zones
- Flight leaves Winnipeg at 4:00 PM Saturday local time, arrives London at 9:00 AM Sunday local time
- Normal insulin dose is rapid insulin before meals and basal insulin (40 units) at 10:00 PM
- On day of departure basal insulin dose will need to be reduced to account for shortened day
Insulin Administration Across Multiple Time Zones

- Adjusted basal travel dose:
  \[
  \text{Adjusted dose} = \left( \frac{\text{Usual Basal Dose}}{} \right) \times 0.9 \times \frac{\# \text{ of time zones crossed}}{\text{hours between basal insulin doses}}
  \]

- Our traveller:
  \[
  \text{Adjusted dose} = (40) \times 0.9 \times \frac{6}{24}
  \]

- Adjusted dose: 26 units
Insulin Administration Across Multiple Time Zones

- On Friday night take usual 40 units basal insulin at 10:00 PM.

- On Saturday, board plane at 4:00 PM, keep watch on Winnipeg time.

- Take bolus insulin as needed for meals while on plane and after landing, check blood sugar often.

- At 10:00 PM Winnipeg time (traveller still on the plane), give reduced basal dose (26 units) and set time on watch to London time (i.e. 4:00 AM or 6 hours ahead).

- On arrival day, Sunday, give usual basal dose of 40 units at 10:00 PM London time.
Insulin Administration Across Multiple Time Zones

- Traveller flying west (from London to Minneapolis)
- Flight time is 9.25 hours
- Crossing 6 time zones
- Flight leaves London at 1:00 PM Friday local time, arrives Minneapolis at 4:15 PM Friday local time
- Normal insulin dose is rapid insulin before meals and basal insulin (40 units) at 10:00 PM
- On day of departure basal insulin dose will need to be adjusted to account for lengthened day
Insulin Administration Across Multiple Time Zones

• On Thursday night take usual 40 units basal insulin at 10:00 PM

• On Friday, board plane, keep watch on London time (1:00 PM) and take bolus insulin as needed for meals while on plane (check blood sugar often)

• At 10:00 PM London time (just before landing) give half the usual basal dose (20 units) and set time on watch to Minneapolis time (i.e. 4:00 PM or 6 hours earlier)

• At 10:00 PM Minneapolis time (on Friday) take the other half of usual basal dose (20 units)

• On Saturday, resume usual basal insulin dose at 10:00 PM Minneapolis time
Antimalarials

- Atovaquone-Proguanil (Malarone®)
- Chloroquine
- Mefloquine
- Doxycycline
Atovaquone-Proguanil

• Best administered with fatty meal or milk
• Fatty meal WILL increase rate and extent of GI absorption of atovaquone and is essential for improved chemoprophylaxis
• In travellers with swallowing issues, tablet can be crushed and mixed with yogurt, jam or other highly flavoured product
• Pediatric doses can be prepared ahead of time if needed
• Dose should be repeated if vomiting occurs within 1 hour of taking tablet
Atovaquone-Proguanil

• Adverse effects
  • Common
    • Abdominal pain/nausea/diarrhea
    • Headache
    • Fatigue
    • Increased liver enzymes
    • Decreased appetite
    • Myalgia
  • Less Common
    • Photosensitivity
    • Cough
  • Rare
    • Oral ulcers
    • Rash
Atovaquone-Proguanil

- **Interactions**
  - Atovaquone-proguanil increases effects of
    - Warfarin
    - Zidovudine
  - Atovaquone-proguanil decreases effects of
    - Indinavir
  - Drugs that decrease effect of Atovaquone-proguanil
    - Metoclopramide
    - Efavirenz
    - Rifampin
    - Ritonavir
    - Tetracycline
    - Antidepressants (fluoxetine, fluvoxamine, citalopram)
Atovaquone-Proguanil

• No dose adjustment required in mild to moderate renal and hepatic impairment

• Not approved for malaria prophylaxis during pregnancy

• Can be used for malaria prophylaxis when breastfeeding infants >5 kg
Chloroquine

- Best administered with food
- Take dose weekly on same day, if missed take as soon as possible and continue weekly from that day
- Watch dosing guidelines (155 mg chloroquine base = 250mg chloroquine phosphate)
- Tablets may be crushed and mixed with food
- Caution; GI irritation with alcohol consumed
- Antacids decrease chloroquine absorption-avoid within 4 hours of taking chloroquine
Chloroquine

• Adverse effects
  • Common
    • Diarrhea/nausea
    • Headache
    • Skin issues (psoriasis)
  • Less Common
    • Vision issues
  • Rare
    • Myopathy
    • Skin pigmentation
    • Alopecia
    • CNS issues (agitation, psychosis, seizure)
    • Blood dyscrasias
    • Hearing loss
    • QT interval prolongation
Chloroquine

- **Interactions**
  - Chloroquine increases effects of
    - Metoprolol, propranolol
    - Paroxetine
    - Flecainide
    - Digoxin
    - Cyclosporine
  - Chloroquine decreases effects of
    - Ciprofloxacin
    - Methotrexate
  - Drugs that increase effect of Chloroquine
    - Trimethoprim (TMP-SMX)
    - Macrolides
    - Azole antifungals
  - Drugs that decrease effect of Chloroquine
    - Antacids, kaolin/pectin
    - Dexamethasone
Chloroquine

Increased risk of QT interval prolongation can occur when chloroquine taken with the following medications:

- Sotalol
- Amiodarone
- Azole antifungals
- Macrolides
- Metronidazole
- Antidepressants
- Antihistamines
- Domperidone
- Tricyclic antidepressants (TCA)
- Efavirenz
- Haloperidol
- Levofloxacin
- Paliperidone
- Propafenone
- Quetiapine
- Risperidone
- Solifenacin
- TMP-SMX
- Calcineurin Inhibitors
- Trazodone
- Citalopram, Escitalopram
Chloroquine

• Dosage adjustment not required in renal impairment
• Use with caution in hepatic impairment
• Acidification of urine increases chloroquine elimination
• Considered safe in all trimesters of pregnancy and for breastfeeding
Mefloquine

- Best taken with food and at least 1 cup fluid
- If vomiting occurs within 30 minutes of taking dose, repeat whole dose
- If vomiting occurs within 30-60 minutes of taking dose, take additional half dose
- Tablets may be crushed and mixed in water
- Avoid or minimize alcohol consumption
- Contraindicated if allergic to quinine or quinidine
- Avoid use in travellers with seizure history and psychiatric disorders (recent history of depression, generalized anxiety, schizophrenia, psychosis)
Mefloquine

• Adverse effects
  • Common
    • Dizziness
    • GI issues (nausea/vomiting/diarrhea/abdominal pain)
    • Headaches
    • Insomnia
    • Abnormal dreams
  • Less Common
    • Spatial acuity/coordination
    • Sensory and motor neuropathies
    • Confusion/forgetfulness
Mefloquine

- **Adverse Effects**
  - **Less Common (continued)**
    - Hallucinations
    - Anxiety/agitation/aggression
    - Mood changes (depression)
    - Restlessness
    - Psychotic/paranoid reactions
    - Panic attacks
    - Seizures
  - **Rare**
    - Suicidal ideation
Mefloquine

- Interactions
  - Mefloquine increases effects of
    - Calcineurin inhibitors (tacrolimus, cyclosporine)
    - mTOR inhibitor (sirolimus)
  - Mefloquine decreases effects of
    - Anticonvulsants (phenytoin, carbamazepine, valproic acid)
  - Drugs that increase effect of Mefloquine
    - Macrolides
    - Azole antifungals (ketoconazole, fluconazole, itraconazole)
    - Antiretrovirals (HIV meds)
  - Drugs that decrease effect of Mefloquine
    - Rifampin
    - St John’s Wort
    - Efavirenz
Mefloquine

Increased risk of QT interval prolongation can occur when chloroquine taken with the following medications:

- Sotalol
- Propranolol
- Amiodarone
- Flecainide
- Azole antifungals
- Macrolides
- Metronidazole
- Antidepressants
- Antihistamines
- Domperidone
- Tricyclic antidepressants (TCA)
- Efavirenz

- Haloperidol
- Levofloxacin
- Paliperidone
- Propafenone
- Quetiapine
- Risperidone
- Solifenacin
- TMP-SMX
- Calcineurin Inhibitors
- Trazodone
- Citalopram, Escitalopram
Mefloquine

- No dosage adjustment needed in renal impairment
- No dosage guidelines provided by manufacturer in hepatic impairment, elimination may be prolonged
- Dosing in geriatrics same as younger adult dosing, issues may arise with adverse effects
- Recommended for use in pregnancy when travelling to areas where chloroquine resistance is present
- Small amount (3-4% of a 250 mg dose) is excreted into breast milk
- Use in breastfeeding considered safe
- Currently mefloquine recommended in Canada for prophylaxis in infants travelling to malaria endemic areas
Doxycycline

• Take capsule with full glass water, best to not open capsule as contents may irritate mouth and esophagus

• Advisable to take while sitting or standing, do not give at bedtime

• Doxycycline has least affinity for calcium of current tetracyclines

• Best taken with food to reduce risk of nausea

• Enteric coated doxycycline hyclate tablets cause less GI issues (nausea/vomiting) than capsules, but cost is higher

• Alcohol reduces effectiveness of doxycycline
Doxycycline

- Adverse effects
  - Common
    - GI issues - nausea, vomiting, diarrhea, dyspepsia
    - Vaginal candidiasis
    - Photosensitivity
  - Rare
    - Skin rash
    - Joint/back pain
    - Dry mouth
    - Esophageal issues
    - Blood dyscrasias
Doxycycline

- Interactions
  - Doxycycline increases effects of
    - Warfarin
    - Glimepiride
    - Methotrexate
  - Doxycycline decreases effects of
    - Oral Travellers’ diarrhea and Cholera vaccine
    - Oral Typhoid vaccine
Doxycycline

- Interactions
  - Drugs that decrease effect of Doxycycline
    - Phenytoin, carbamazepine
    - Rifampin
    - Bismuth subsalicylate (Pepto-Bismol®)
    - Antacids (containing calcium, magnesium, aluminum)
    - Multivitamins/minerals/iron
    - Quinapril
    - Alcohol
  - Isotretinoin concurrent use can increase risk of pseudotumor cerebri
Doxycycline

• No dose adjustment required in renal impairment

• No dosage guidelines provided by manufacturer in hepatic impairment

• If currently taking minocycline for acne, should be switched to doxycycline, finish entire therapy then resume minocycline
Doxycycline

- Geriatric dosing same as adult dosing
- Use in pregnancy contraindicated
- Doxycycline is excreted in breast milk in small amounts
- Use in breastfeeding is not contraindicated
- Can be used in children 8 years and older
Travellers’ Diarrhea

• For Self Treatment
  • Fluoroquinolones (ciprofloxacin, levofloxacin)
    • Traditionally first line in non-pregnant
    • Falling out of favour due to side effects and resistance
    • Levofloxacin/ciprofloxacin can increase INR
    • Avoid supplements containing iron, magnesium, calcium, aluminum, zinc
    • Diabetics and blood glucose monitoring
    • Ciprofloxacin reduces clearance of caffeine
    • NSAIDS/ciprofloxacin interaction in patients with seizure history
    • Sildenafil should be avoided while on ciprofloxacin
Travellers’ Diarrhea

- Recent articles highlighting acquisition and spread of extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBL-E) by international travellers

- Greater frequency of acquisition occurs in travellers to South Asia (especially Indian subcontinent)

- Predictors for acquisition include:
  - Antibiotic use during travel
  - Occurrence of diarrhea during travel and especially if persisting after return
  - Pre-existing chronic bowel disease
Travellers’ Diarrhea

• For Self Treatment
  • Azithromycin
    • First line In pregnancy and breastfeeding
    • Falling out of favour due to resistance
    • Can increase INR during treatment or after completion
    • HIV meds (lopinavir, efavirenz) can cause QT interval prolongation
  • 3rd generation cephalosporins (cefixime)
    • Second line agents during pregnancy
Travellers’ Diarrhea

- **Dukoral®**
  - Generally not recommended by CATMAT due to poor efficacy against by Enterotoxigenic E coli (ETEC)
  - To help protect against diarrhea caused by Enterotoxigenic E coli (ETEC)
    - Adults and children 2 years and older require 2 doses
    - Doses should be spaced at least 1 apart (maximum 6 weeks apart)
    - Protection starts about 1 week after 2\textsuperscript{nd} dose and lasts 3 months - finish last dose at least 1 week before departure
  - **Booster dose**
    - 1 dose required if last dose taken between 3 months to 5 years before
Travellers’ Diarrhea

- **Dukoral®**
  - To help protect against Cholera
    - Adults and children 6 years and older require 2 doses
    - Children 2-6 years of age require 3 doses
    - Doses should be spaced at least 1 week apart (maximum 6 weeks apart)
    - Protection starts about 1 week after last dose—finish last dose at least 1 week before departure
    - Adults and children 6 years and older protection lasts 2 years
    - Children 2-6 years of age protection lasts 6 months

- **Booster dose**
  - Adults and children 6 years and older, 1 dose required if last dose taken between 2 to 5 years before
  - Children 2-6 years of age, 1 dose required if last dose taken between 6 months to 5 years before
Travellers’ Diarrhea

- Dukoral not recommended during pregnancy, fever or acute GI illness
- Most common adverse effects of Dukoral® include nausea, vomiting diarrhea, abdominal pain
- Rarely can cause dehydration
- Best to complete Dukoral® vaccination course at least 3 days before starting antimalarial prophylaxis
- High dose PPI’s can increase risk of acquiring Travellers’ Diarrhea
- Bismuth subsalicylate can help reduce frequency of bowel movements (avoid in pregnancy, kaolin-pectin preferred)
- Motility modifier (loperamide) can help reduce diarrhea but, slows ability of body to rid itself of toxin
- Motility modifier diphenoxylate/atropine (Lomotil®) no longer recommended by CATMAT due to increased risk of toxic megacolon
Typhoid Vaccine

- Available as injection (Typherix®, Typhim Vi®) and oral (Vivotif®) formulations

- Injection formulations only requires 1 dose given at least 2 weeks before exposure, booster dose required every 2 years if still at risk

- Oral formulation requires 1 capsule every other day x 4 doses (on empty stomach), last dose must be at least 1 week before exposure, booster dose required every 5 years if still at risk

- Do not open capsule or crush/chew, no alcohol 1 hour before or 2 hours after taking, drink with cold or room temperature drink

- Capsules require fridge storage, if left at room temperature for more than 12 hours a replacement dose should be obtained

- Oral formulation can often cause GI issues (diarrhea, abdominal pain, nausea, vomiting), headache, skin rash

- Either formulation can be given at same time as other vaccinations
Typhoid Vaccine

- Generally not recommended by CATMAT for most destinations unless travelling to South Asia (Indian subcontinent)
- No data has been reported on use of any of the vaccines in pregnancy or breastfeeding
- Oral formulation should not be used in pregnancy
- Injection formulations unlikely to cause problems in pregnancy, should only be used in pregnancy if clearly needed
- Injectable formulation preferred in breastfeeding
- Oral formulation vaccination should be completed at least 3 days before starting doxycycline or other antibiotics
- Mefloquine, chloroquine at prophylactic doses can be given concomitantly with oral formulation
Jet Lag

- Short acting benzodiazepines commonly used
- Often taken when boarding flight
- Duration of action typically 6-8 hours, but effects can be prolonged especially in first time users
- Effects of drug may be felt even 20 hours after taking often leading to issues on arrival
- Melatonin is another product that is often used
- Melatonin less likely to cause prolonged drowsiness
- Melatonin may be started before departure and continued for few days after arrival or started after arrival only
Common Travel Meds

- Antidiarrheals
  - Loperamide
    - Considered safe in pregnancy and breastfeeding
    - Dose and frequency in children is reduced
  - Diphenoxylate/atropine (Lomotil®)
    - No longer recommended by CATMAT due to increased risk of toxic megacolon
    - Not recommended in pregnancy and breastfeeding
    - Can have significant anticholinergic effects

- Dimenhydrinate
  - Considered safe in pregnancy and breastfeeding
  - Has anticholinergic side effects
Common Travel Meds

- **Antihistamines**
  - **Diphenhydramine**
    - Considered compatible with pregnancy and breastfeeding although 2nd generation antihistamine preferred (cetirizine, loratadine)
    - In elderly best to start at 25 mg BID to TID
    - Pediatric liquid is alcohol free (adult liquid contains alcohol)
  - **Chlorpheniramine**
    - Similar pregnancy and breastfeeding considerations to diphenhydramine
    - In elderly best to start at 4 mg daily or BID
Common Travel Meds

- Antidiarrheals
  - Bismuth subsalicylate (Pepto-Bismol®)
    - Best to avoid in pregnancy and breastfeeding
    - Caution in renal impairment
    - May elevate INR if taking warfarin
    - Avoid in cases of bloody diarrhea
  - Attapulgite (Kaopectate®)
    - Insufficient data for use in pregnancy but unlikely to cause problem as not absorbed
    - Considered safe in breastfeeding
    - Separate from other medication by at least 2-3 hours
Thank-you and happy travels