Penicillin Allergy Direct Oral Amoxicillin Challenge: Inpatients (Nursing Procedures)

Site Applicability

Providence Health Care (PHC):

- St. Paul's Hospital
- Mount Saint Joseph Hospital (Acute Care)

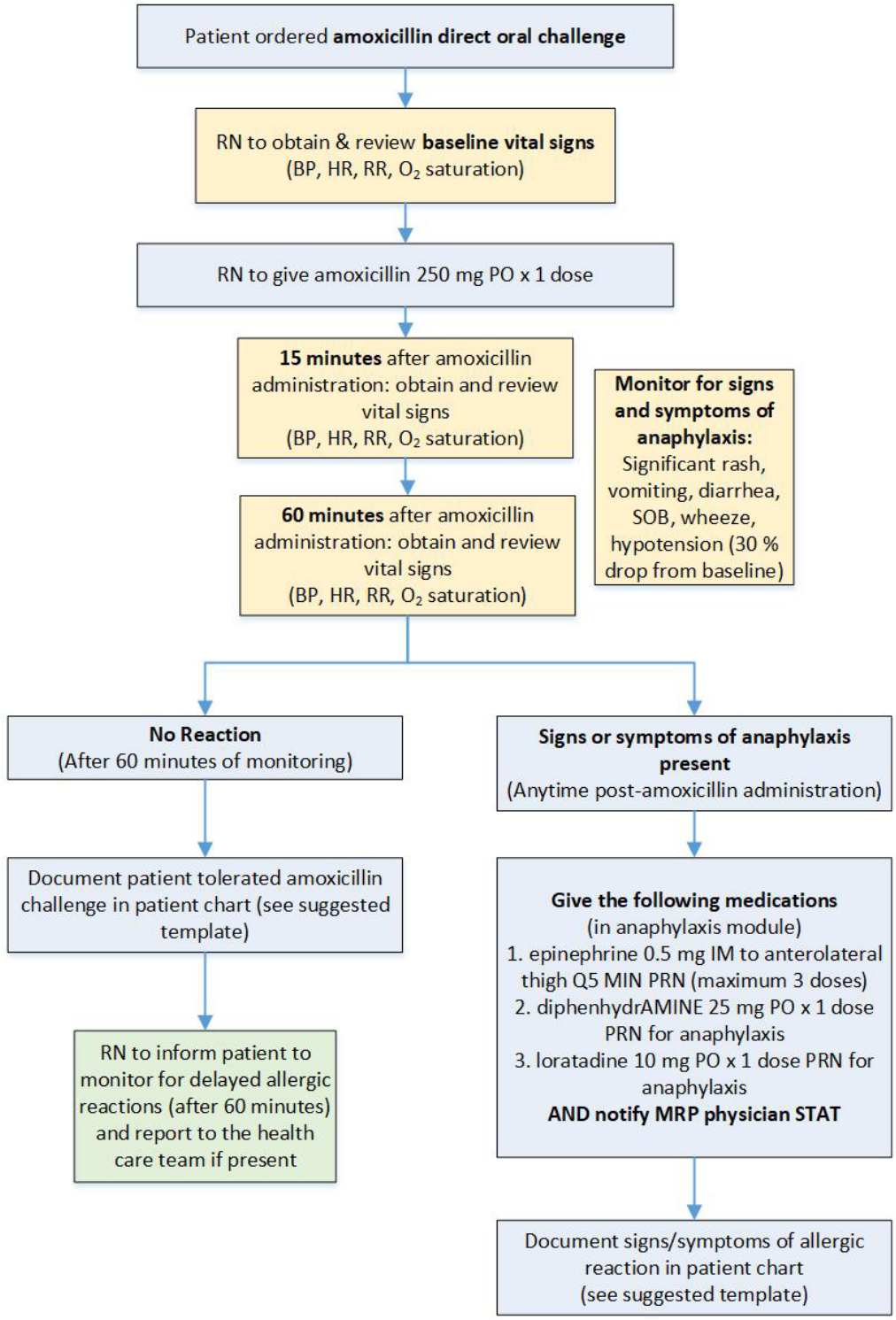
Practice Level

- Registered Nurses

Requirements

- Active order for direct oral amoxicillin challenge must be placed for patient on a weekday (Monday to Friday) for administration before 15:00 hr
  - Order must be approved by MRP (most responsible physician)
  - Patient should be clinically stable at baseline prior to administration of amoxicillin PO (if not, contact MRP to confirm if oral challenge is appropriate)
  - No direct oral amoxicillin challenges will be given after 15:00 hr on weekdays or on weekends
- RN must be readily available nearby patient or patient room during full 60-minute monitoring period following administration of amoxicillin dose
- RN must have completed the appropriate education and training for anaphylaxis management [refer to separate SHOP procedure: Anaphylaxis: Initial Emergency Management (Adult and Pediatric)]

Algorithm



Need to Know

Patient-reported penicillin allergies are frequently encountered and many patients labelled as allergic do not have a true allergy (less than 1% of the population is truly allergic to penicillin)[1]. Penicillin allergies are associated with antimicrobial resistance, poor patient outcomes, and significantly affect the judicious and appropriate use of antimicrobials[2-7]. Currently, patients at St. Paul's Hospital (SPH) identified with a history of a penicillin allergy undergo penicillin skin test followed by amoxicillin challenge administered by the Allergy and Immunology team only.

To optimize delabeling of penicillin allergies, pharmacist and MRPs will use a validated penicillin allergy clinical decision support tool (PEN-FAST) to identify low-risk patients who may safely undergo direct oral amoxicillin challenge (without Allergy and Immunology consult). Patients with a PEN-FAST score of 0 have less than 1% risk of a positive penicillin allergy test and will be eligible for direct oral amoxicillin challenge ordered by the pharmacist and MRP (if no other exclusion criteria are met, see Appendices for details). Patients who do not consent to a direct oral challenge or have a PEN-FAST score of 1 or more will be referred to the Allergy and Immunology team for further assessment and possible penicillin skin testing.

Amoxicillin is the preferred agent for direct oral challenge (instead of penicillin VK (phenoxymethylpenicillin) or benzylpenicillin) as it includes a potentially antigenic side chain and accounts for the majority of penicillin-class antibiotic usage.[8] Tolerance of amoxicillin therefore excludes selective amoxicillin allergy due to side-chain reactivity and provides reassurance of tolerance to the wider penicillin family.[8]

Procedure

Assessment

The following vital signs are assessed and reviewed to establish patient's baseline:

1. Blood pressure (BP)
2. Heart rate (HR)
3. Respiratory rate (RR)
4. Oxygen saturation (O_2 saturation)

The above vital signs should be repeated at **15 minutes** and **60 minutes** after administration of the amoxicillin oral challenge. RN should be readily available throughout the 60-minute period after administration of amoxicillin (nearby patient or room).

Monitor for signs and symptoms of anaphylaxis:

- Significant rash
- Vomiting
- Diarrhea
- Shortness of breath
- Wheeze
- Hypotension (greater than or equal to 30% drop from baseline)

Interventions

Report the following findings to the MRP and clinical pharmacist:

- Signs and symptoms of anaphylaxis (as listed above)
    - Give pre-specified medications in the anaphylaxis powerplan module
    - Notify MRP STAT if suspected anaphylaxis
    - Document severity, timing/onset, and interventions regarding patient's anaphylactic reaction
- Signs and symptoms of any other noted allergic reaction (e.g. rash)
- Use of any medication used in the anaphylaxis module (see algorithm)

Steps

1. RN to give amoxicillin 250 mg PO x 1 dose
2. RN should be nearby patient/room during the full 60-minute monitoring period
3. Document three sets of vitals:
    a. At baseline (before amoxicillin administration)
    b. 15 minutes (after amoxicillin administration)
    c. 60 minutes (after amoxicillin administration)
4. Monitor for signs and symptoms of anaphylaxis (i.e. significant rash, vomiting, diarrhea, SOB, wheeze, hypotension [30% drop from baseline])
    a. If suspected anaphylaxis:
        - Administer Anaphylaxis Module medications including:
            - epinephrine 0.5 mg IM to anterolateral thigh Q5MIN PRN (maximum 3 doses)
            - diphenhydrAMINE 25 mg PO x 1 dose PRN for anaphylaxis
            - loratadine 10 mg PO x 1 dose PRN for anaphylaxis
        - Contact MRP STAT
5. RN to clearly document if any signs and symptoms of allergic reaction occur or if patient tolerated challenge after 60 minutes (see suggested template below)
    a. Patient to monitor for any delayed reactions after 60 minutes and inform RN if reactions occur
6. Inform CTU pharmacist of test results (who will update allergy on chart)

Documentation

Once the 60-minute monitoring period is completed, RN to complete brief interdisciplinary note summarizing direct oral challenge results in patient's chart.

Example RN interdisciplinary note templates:

Example 1 – **Successful direct oral challenge**

Patient did not have any allergic reaction to the amoxicillin oral challenge. Vitals were stable at all 3 monitoring points (baseline, 15 mins post-dose, and 60 mins post-dose), which are documented.

Example 2 – **Failed direct oral challenge**

Patient did not tolerate the amoxicillin oral challenge and had an allergic reaction. The patient developed _____(signs/symptoms) that occurred _____ minutes after taking amoxicillin. _____ (medications) were administered and _____ (signs/symptoms) resolved after _____ minutes. The MRP was contacted and informed of the allergic reaction. The patients vitals during the amoxicillin oral challenge were: Baseline = 15 minutes post-dose = 60 minutes post-does =

Patient and Family Education

- Inform patient to monitor for any delayed allergic reactions (i.e. occur after 60-minutes) and report to the healthcare team if present
- Patient penicillin allergy handout (VCH Aspires) – given by clinical pharmacist
- Negative penicillin allergy card – given by clinical pharmacist

Related Documents

1. PHC Antimicrobial Stewardship website – PEN-FAST score
2. Firstline App: Guidelines (Penicillin Allergy) PEN-FAST Assessment Tool

References

1. Joint Task Force on Practice Parameters representing the American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology (2010). Drug allergy: an updated practice parameter. Ann Allergy Asthma Immunol. 105(4):259-273.
2. Trubiano J, Vogrin A, Chua K, et al. (2020). Development and Validation of a Penicillin Allergy Clinical Decision Rule. JAMA Intern Med. 180(5):745-752
3. Trubiano J, Chen C, Cheng A, et al. (2016). National Antimicrobial Prescribing Survey (NAPS). Antimicrobial allergy “labels” drive inappropriate antimicrobial prescribing: lessons for stewardship. J Antimicrob Chemother. 71(6):1715-1722.

4. Blumenthal KG, Peter JG, Trubiano JA, Phillips EJ. (2019). Antibiotic allergy. Lancet. 393(10167):183-198.
5. MacFadden DR, LaDelfa A, Leen J, et al. (2016). Impact of reported beta-lactam allergy on inpatient outcomes: a multicenter prospective cohort study. Clin Infect Dis. 63(7):904-910.
6. Trubiano J, Leung V, Chu M, et al. (2015). The impact of antimicrobial allergy labels on antimicrobial usage in cancer patients. Antimicrob Resist Infect Control. 4:23.
7. Macy E & Contreras R. (2014). Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: a cohort study. J Allergy Clin Immunol. 133(3):790-796.
8. Krishna MT & Misbah SA. (2019). Is direct oral amoxicillin challenge a viable approach for "low-risk" patients labelled with penicillin allergy? J Antimicrob Chemother. 74(9):2475-2479.

Definitions

- MRP: most responsible physician
- RN: registered nurse
- RPh: registered pharmacist
- PEN-FAST: validated penicillin allergy clinical decision support tool used to identify low-risk patients who may safely undergo direct oral amoxicillin challenge

Appendices

- Appendix A: PEN-FAST Tool
- Appendix B: Patients Excluded from Direct Oral Amoxicillin Challenge by MRP/RPh

Appendix A: PEN-FAST Tool

Figure 1. PEN-FAST tool and associated risk of positive penicillin skin test [2]

PEN	*Penicillin allergy reported by patient*	☐ *If yes, proceed with assessment*
F	*Five years or less since reaction*[a]	☐ **2 points**
A	*Anaphylaxis or angioedema*	
	OR	☐ **2 points**
S	Severe cutaneous adverse reaction[b]	
T	*Treatment required for reaction*[a]	☐ **1 point**
		☐ **Total points**

Interpretation

Points	
0	**Very low risk** of positive penicillin allergy test <1% (<1 in 100 patients reporting penicillin allergy)
1-2	**Low risk** of positive penicillin allergy test 5% (1 in 20 patients)
3	**Moderate risk** of positive penicillin allergy test 20% (1 in 5 patients)
4-5	**High risk** of positive penicillin allergy test 50% (1 in 2 patients)

a = includes unknown; b = Forms of severe delayed reactions include potential Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, and acute generalized exanthematous pustulosis. Patients with a severe delayed rash with mucosal involvement should be considered to have a severe cutaneous adverse reaction. Acute interstitial nephritis, drug induced liver injury, serum sickness and isolated drug fever were excluded.

Appendix B: Patients Excluded from Direct Oral Amoxicillin Challenge by MRP/RPh

Patients **Excluded** from Direct Oral Amoxicillin Challenge by MRP/RPh:

(not appropriate for direct oral amoxicillin challenge without consultation from an Allergist)

- No penicillin-allergy documented or reported by patient
- PEN-FAST score 1 or more
- Reported allergic or adverse reaction included:
  - Acute interstitial nephritis or renal dysfunction
  - Hepatitis or hepatotoxicity
  - Drug fever
  - Seizures
  - Hemolytic anemia
  - Thrombocytopenia, leukopenia, or neutropenia
  - Joint pain or rheumatologic manifestations
- Critically ill patients or hemodynamic instability (labile BP, HR)
- Requiring supplemental oxygen greater than baseline requirements
- Pregnancy
- Cognitive impairment or altered level of consciousness (GCS less than 15, not oriented x 3)
- Unable to provide reliable history or consent
- Psychiatry documentation deeming lack of capacity
- Already received and tolerated a penicillin-class antibiotic previously
- Patients admitted to services outside of CTU

Persons/Groups Consulted:
Allergy and Immunology Providers
Antimicrobial Stewardship Team
Clinical pharmacist, Medicine
Nurse Educators
PHC Pharmacy & Therapeutics Committee

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