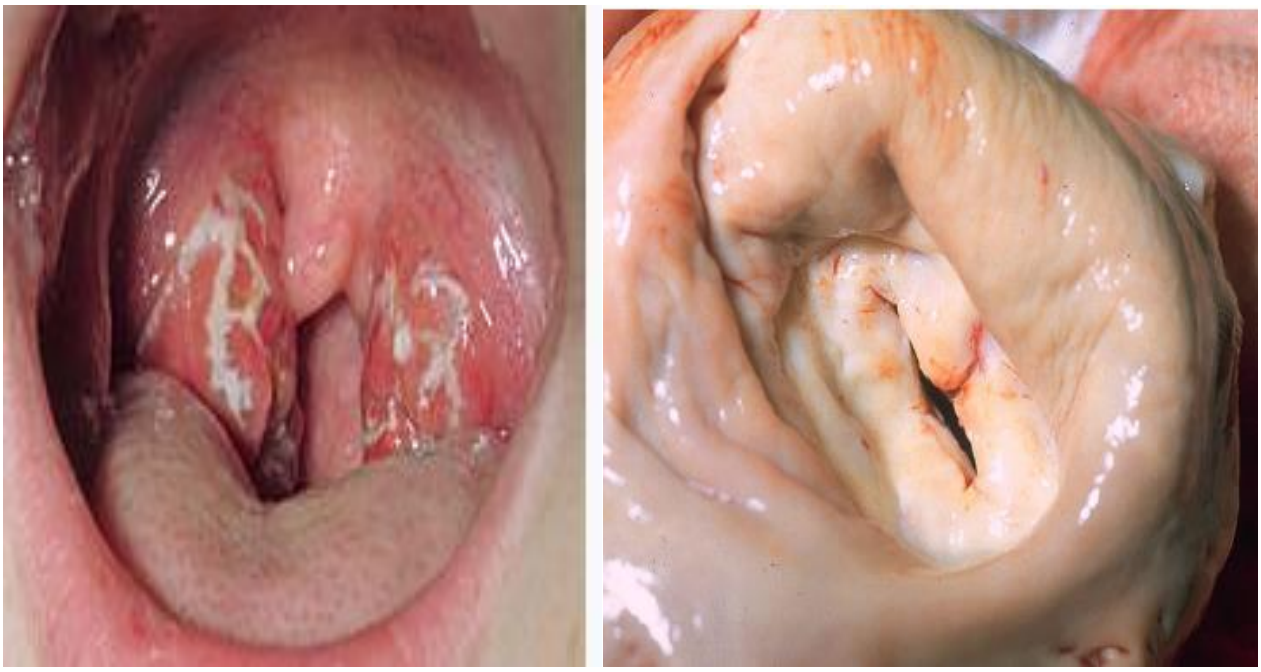
Federal Democratic Republic of Ethiopia



Guideline for Use of Benzathine Penicillin G for the Prevention of Rheumatic Heart Disease in Ethiopia

November 2024

Addis Ababa, Ethiopia

Acknowledgment

The Ministry of Health expresses its appreciation for the individuals and institutions who have participated in the development of this guideline on the use of Benzathine Penicillin. We would like to thank AAU RHD Center of Excellence project office for taking this initiative, organizing meetings and identifying experts for developing this guideline. The Ministry also acknowledges FDA drug safety advisory committee for their invaluable inputs.

The Ministry also recognizes the following experts for their contribution, either as guideline development or guideline review group.

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Abbreviations

AHA: American heart Association

BPG: Benzathine Penicillin G

CVD: Cardiovascular Diseases

FDA: Food and Drug Authority

GAS: Group A streptococcus

MOH: Ministry of Health

NCD: Non-communicable Disease

RHD: Rheumatic Heart Disease

WHO: World Health Organizations

Forward

Rheumatic heart disease remains the major cause of cardiovascular disorder in Ethiopia. Benzathine penicillin G (BPG) is the corner stone in the prevention of occurrence and progression of Rheumatic Heart Disease (RHD). Recent reports of sudden death particularly in severe valve lesions have challenged the use of BPG for prophylaxis. The aim of this guideline is to review the evidence available regarding the use of BPG and suggest local recommendations to increase the delivery of BPG.

A Guideline committee was established by the Federal Ministry of health and Addis Ababa University Rheumatic Heart Disease Project office to develop draft a guideline. Which was subsequently reviewed by local and international experts before it was finally approved by Federal Ministry of health for implementation.

The guideline is a focused update on the use of BPG for prevention of Rheumatic heart disease in the 2021 national RHD treatment protocol and is believed to improve delivery of BPG with continuing recommendation for those patients who benefits the most and reduce the risk associated with its use in selected patients at risk of developing severe side effects.

The guideline focuses on BPG prophylaxis for prevention of acute rheumatic fever and rheumatic heart disease and readers are advised to refer to the 2021 national guideline for detailed discussion on diagnosis and other aspects of treatment of acute rheumatic fever and rheumatic heart disease.

I would like to thank all the experts and managers involved in the development of the guideline.

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Key words: Benzathine Pencillin G, Rheumatic heart disease, Ethiopia

Introduction

Rheumatic heart disease remains major cause of heart failure in Ethiopia with prevalence of 2/1000 and responsible for 40-60% of cause of heart failure in Ethiopia (1,2). Recurrence of rheumatic fever following Group A streptococcal infection contributes to the rapid progression of the disease in many developing countries like Ethiopia (3). Earlier and recent evidence demonstrated the benefits of long-acting penicillin, Benzathine Penicillin G (BPG), in reducing the recurrence of rheumatic fever and hence progression of RHD (4). Recent studies and reports of sudden deaths immediately after injection have however challenged the use of BPG for prophylaxis due to fear of administration by health professionals and adherence to long-term use by the patients has been severely compromised (5-7).

Ethiopia has adopted the WHO recommendation for control of rheumatic heart disease with integrated RHD control activities like training of health professionals, development of treatment guidelines, registry-based care at primary and tertiary levels and collaboration with partners to improve care (8,9). One such collaboration is the establishment of MOH-AAU RHD control programs since 2017 which has been working on training of health professionals on Echocardiography, development of treatment guidelines and establishment of RHD advisory committee. MOH has recently started implementing PEN plus project at two pilot sites where RHD is one of the disease priorities.

For safe use of BPG for secondary prophylaxis and reduce the fear of health professionals with recent incidents of deaths while taking BPG, revision of indications for prophylaxis is required. WHO has just released a new update on Prevention and treatment of Rheumatic Heart Disease which is more general, and recommended countries have their own national guidelines based on the general framework of the guideline (8). This guideline is believed to reduce the fear of health professionals with BPG administration and therefore they will continue to give BPG for those who will benefit most with minimal adverse events.

Methods

Guideline committee was established by MOH and AAU RHD Project office. The guideline committee held meetings, received reports of adverse events and reviewed the scientific papers regarding the benefits of BPG and other alternatives for secondary prophylaxis. The committee also looked at recommendations from other countries, mainly 2022 AHA recommendations (10) and the 2024 WHO RHD guidelines for preparing this guideline (9). This will be supplement to the national 2021 updated Sore throat, Acute Rheumatic Fever and Rheumatic heart disease guideline. The draft guideline has been reviewed by local and international experts before it was finally submitted to FMOH for approval. Inputs from Ethiopian food and drug authority and Ethiopian Society of Cardiac Professionals were also incorporated in this guideline.

Recommendations

Recommendation 1: Treatment of GAS pharyngitis

For primary prophylaxis of acute rheumatic fever (treatment of GAS pharyngitis), Intramuscular BPG is the first line treatment.

Alternatives include Amoxicillin 50mg/kg divided to three doses for 10 days or Erythromycin for ten days or azithromycin for 05 days

Recommendation 2: Acute Rheumatic Fever with/without non severe Valve lesions

For secondary prophylaxis after an episode of acute Rheumatic Fever and non-severe valve lesions monthly BPG should be given. For penicillin allergy Azithromycin (see doses below).

Recommendation 3: Asymptomatic Severe Valve lesions

For patients with severe Rheumatic heart disease (severe MS, Severe MR, severe AR, and Severe AS) with no heart failure, normal ejection fraction and not on diuretics, BPG should be given preferably at hospitals. Patient clinical status should be assessed before giving monthly BPG.

Recommendation 4: Symptomatic or multiple Severe Valve lesions

For patients having two or more asymptomatic severe valve lesions, single valve severe lesions with heart failure or LV or RV dysfunction and or on diuretics alternative oral antibiotics preferably penicillin V twice daily should be prescribed. Since this drug is not currently available in Ethiopia, registration and availing the drug should be done as soon as possible. Until penicillin V is available and in those with penicillin allergy azithromycin (6mg/kg/d; maximum dose of 250mg/day) will be given (14,15). Azithromycin may cause QT prolongation and is better avoided in patients who have prolonged QT interval on ECG.

Recommendation 5: BPG for Post Valve interventions

Secondary prophylaxis should not be discontinued for patients with RHD for surgery or percutaneous intervention was done.

Recommendation 6: Patients on Anticoagulation

BPG injections should be continued in patients with RHD receiving anticoagulation unless there is evidence of uncontrolled bleeding or the international normalized ratio (INR) is greater than 4.5.

Recommendation 7: Echocardiographic Study not available

In areas where echocardiography cannot be done, any patient presenting with heart failure likely due to rheumatic heart disease should receive oral prophylaxis. These patients should be referred to the next level of health care for confirmation of the diagnosis and registration.

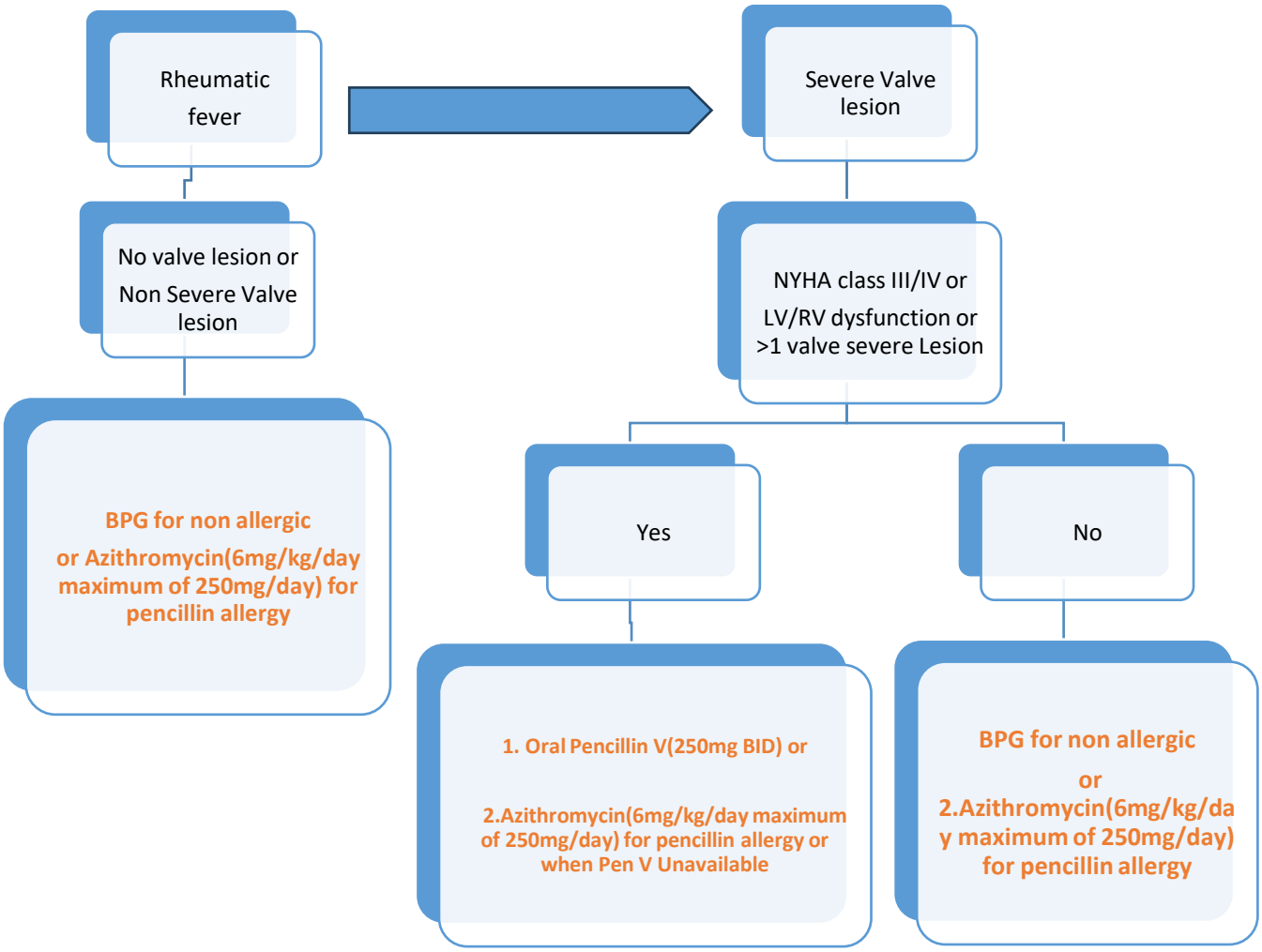


Figure 1: Secondary Prophylaxis for Rheumatic Heart Disease, November 2024

Recommendation 8: Periodic Assessment

- At each visit and administration of BPG proper assessment of clinical status should be done
- Echocardiography should be done every 2 years for moderate valve lesions or development of symptoms. For mild cases echocardiography should be done every three years.
- For severe valve lesions echocardiography should be done every 6-12 months, or anytime on suspicion of complications, for surgical evaluation when available or deterioration in clinical status.

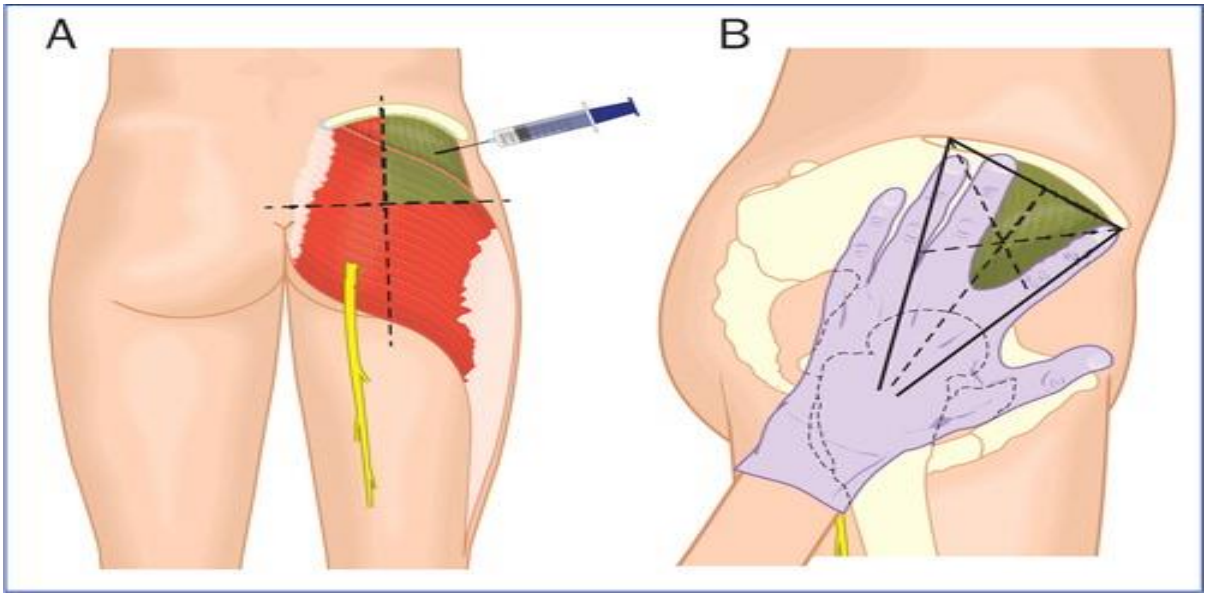
DORSOGLUTEAL SITE

CAUTION - Injections into the dorsogluteal muscle have been associated with sciatic nerve injury.

1. Place the patient in a prone (face down) position, or lying on the side. Some patients may prefer standing up. Patients with valve disease at risk of cardiac decompensation must lie down (See *Non-allergic penicillin reactions*).
2. The site for injection can be identified by either:
   a) dividing the buttock into four quadrants, selecting the upper outer quadrant;
   b) drawing an imaginary diagonal line from the posterior superior iliac spine to the greater trochanter. From the middle of the line move up and out.

VENTROGLUTEAL SITE

1. Place the patient in a side-lying position.
2. Using your right hand on the patient's left hip; or left hand on the patient's right hip:
   a) With the palm of your hand, locate the greater trochanter of the femur.
   b) Place your index finger towards the front or anterior superior iliac spine, and fan the middle finger as far along the iliac crest as you can reach. (The thumb should always be pointed toward the front of the leg.)
3. The injection site is in the middle of the triangle between the middle and index fingers.
4. Remove your fingers prior to inserting the needle.



(https://images.app.goo.gl/t4scaCF6KBDqRH8D6) Figure 2: Sites for BPG administration

Recommendation 9: Risk Reductions

The following measures should be taken to reduce the intensity of pain and hence the risk of vasovagal reaction with the use of BPG.

1. Reduce patients' fear of injection with reassurance.
2. Give the injection at supine position over dorsogluteal region as this is more commonly used site by most health professionals in Ethiopia. Experienced nurses can also use the ventrolgluteal site for injection as this is safer with less nerve injury and better absorption.
3. Tell the patient to have a small meal before the injection.
4. Look for signs of dehydration or signs of cardiac compromise like low BP/low pulse volume, tachycardia, severe congestion or other acute clinical condition in which case the injection should be postponed or deferred based on the above indication.
5. For repeated doses, rotate the site of injection.
6. Non-pharmaceutical pain reducing techniques:
    - Firm pressure to the site for at least 10 seconds immediately before injecting.
    - Ice pack applied to the site before injecting
    - Refrigerating the needle prior to injection delivery.
7. Pharmaceutical strategies for managing injection pain include:
    - Oral paracetamol before injection and at appropriate time intervals afterwards as required.
    - Anesthetic spray before injections.
    - Lidocaine (lignocaine) injected with BPG.

How to prepare BPG with lidocaine:

1. Attach a drawing-up needle to a 3 mL syringe.

2. Draw the required contents of BPG from the pre-filled syringe into the 3mL syringe (2.3 mL for 1,200,000-unit dose and 1.17 mL for 600,000-unit dose).
3. Using a new needle, draw up 0.5 mL of 1% lidocaine or 0.25 mL of 2% lidocaine into the tip of the 3mL syringe.
4. Avoid mixing to keep the lidocaine in the tip of the syringe.
5. Push plunger up carefully to remove any air in the syringe.
6. Remove the drawing-up needle.
7. Attach IM needle (e.g. 21 gauge) to the syringe to administer injection.

Recommendation 10: Implementation and Monitoring

1. Safe injection techniques should be followed during administration of BPG.
2. BPG should be given preferably by nurses or other health professionals who have experience in giving injections or have received training on BPG injections
3. BPG should be given at health centers or higher levels which have facilities for resuscitation (Ambu bag, IV fluid, airway, oxygen, atropine, hydrocortisone, adrenaline). For those with severe asymptomatic valve lesions the injection should preferably be given at hospitals.
4. Every health institution giving BPG should generate quarterly injection reports using standard format (Attached).
5. Any serious side effect should be reported to the Federal Food and Drug Authority with standard format prepared by the authority (see attachment)
6. Every patient who comes with the right prescription and proper indications mentioned in this guideline shouldn't be denied BPG for fear of side effects.
7. Constant supply of both Penicillin V and BPG should be assured, and each institution should check their stock and request supply regularly for uninterrupted delivery of prophylaxis

8. National RHD task force should regularly review the reports of secondary prophylaxis and initiate discussions with appropriate stake holders to overcome challenges related to administration of BPG.

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