



Letter to Editor

Fatal outcome of intravenous injection of benzathine penicillin G in a neonate – A case report

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Sir

Benzathine Penicillin G is a commonly prescribed antibiotic in neonates born from mothers who are diagnosed sexually transmitted diseases during prenatal screening. It is given intramuscularly after the dermal test dose is done. Yet reports of overdose or death with this drug are not uncommon. We report two cases in which the neonates developed complications following intravenous injection of Benzathine Penicillin. One developed cardiac arrest within an hour of intravenous injection and died shortly, and the other survived several episodes of convulsions (fits) and a prolonged stay in the neonatal Intensive care unit.

Benzathine Penicillin G is a medicine, which should be given strictly intramuscularly and in both these cases it was given intravenously by ignorance or by negligence by a midwife.

Two pregnant mothers were admitted to the prenatal ward of Victoria Hospital. Both were diagnosed with TPHA positive during antenatal care and treatments were given to both mothers. Both babies were born by normal deliveries which were uneventful. The treating paediatrician had started Penicillin G with both babies after the test dose. The next Benzathine penicillin G injections were given to the two babies by intramuscular route by competent nurses. However, on the termination of the treatment, the last dose of Benzathine Penicillin G was given intravenously to both babies by a new midwife. The immediate loss of consciousness by one of the babies was noticed by the nurse and the mother, and the baby was taken immediately to the neonatal ICU. Resuscitation started but was in vain. The baby was declared dead. The other baby started getting convulsions and was also transferred to the Neonatal ICU, and treatment started immediately and the baby survived.

Penicillin G benzathine and penicillin G procaine injectable suspension contains equal amounts of the benzathine and procaine salts of penicillin G¹. It is available for deep intramuscular injection. Penicillin G benzathine is prepared by the reaction of dibenzylethylene diamine with two molecules of penicillin G. It is chemically designated as (2S, 5R, 6R)-3,3-Dimethyl-7-oxo-6-(2-phenylacetamido)-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid compound with N,N'dibenzylethylenediamine (2:1), tetrahydrate (**Figure 1**). It occurs as a white, crystalline powder and is very slightly soluble in water and sparingly soluble in alcohol.

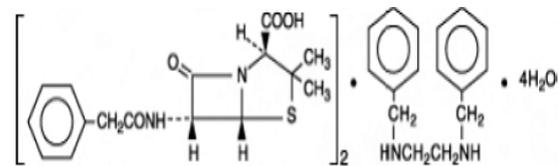


Figure 1: Penicillin G benzathine

Penicillin G procaine, (2S,5R,6R)-3,3-Dimethyl-7-oxo-6-(2-phenylacetamido)-4-thia-1-azabicyclo [3.2.0]heptane-2-carboxylic acid compound with 2-(diethylamino) ethyl paminobenzoate (1:1) monohydrate, is an equimolar salt of procaine and penicillin G (**Figure 2**). It occurs as white crystals or as a white, microcrystalline powder and is slightly soluble in water.

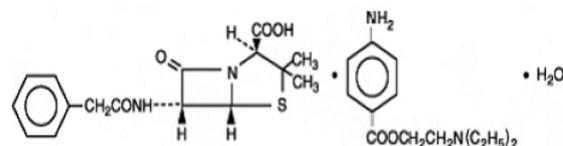


Figure 2: penicillin G procaine

Each disposable syringe (2 mL size) contains the equivalent of 1,200,000 units of penicillin G comprising the equivalent of 600,000 units of penicillin G as the benzathine salt and the equivalent of 600,000 units of penicillin G as the procaine salt in a stabilized aqueous suspension with sodium citrate.

An autopsy was carried on the unfortunate baby. The autopsy did not reveal much, except congestion of all organs and no congenital malformation. The cause of death was acute pulmonary edema. Blood samples were sent to the FSL for toxicological analysis and organs were sent for histopathology. No significant pathology was noted on microscopic examination. The toxicological analysis of the blood revealed the presence of Benzathine Penicillin, and the same was also confirmed from the suspected vial, which was used by the midwife.

Crystalline penicillin is usually preferred in neonates when penicillin is indicated. Procaine penicillin is recommended as an alternative to crystalline penicillin especially for infections like congenital syphilis and neonatal sepsis. Procaine penicillin may be more practical for the community management of neonatal sepsis because of the once daily dosing schedule, cost, availability, and ease of administration². However, there is paucity of data on the efficacy and safety in such settings. This drug has been in use for several decades and there are very few reports on adverse events in the neonate.

Most WHO guidelines recommend crystalline penicillin as the first choice in neonates, when penicillin is indicated. Reports on adverse events in neonates are few, especially when the correct dose and the proper route of administration are used. In neonates, infants, and small children, injection into the midlateral muscles of the thigh is preferred³.

Penicillin G benzathine must be administered by the intramuscular (IM) route only and should never be administered via the intravenous route. Special precautions should be taken to avoid intravascular injection. Avoid intramuscular injection of these suspensions near major nerves or blood vessels because this could cause neurovascular damage. There have been reports of inadvertent intravenous administration of penicillin G benzathine, which has been associated with cardiorespiratory arrest and death.

The most likely pathophysiologic explanation for these fatalities is that the Benzathine Penicillin G compound is a crystalline powder that may cause direct damage when injected into a blood vessel, possibly eliciting vascular spasm and subsequent occlusion by the large crystals of the penicillin

salt⁴. Penicillin in over dosage has the potential to cause neuromuscular hyperirritability or convulsive seizures.

Although the exact cause of her cardiac arrest was not known, the most likely cause was probably due to intravenous bolus injection of Benzathine Penicillin, as inferred from the presence of Benzyl Penicillin in the deceased child's blood. Moreover, both the neonates were given intravenous injections by the same nurse and prepared from same vial and both developed complications immediately. No other medication was given at that time. Fatal non-allergic reactions to Benzathine Penicillin G may occur as quickly as a few minutes following administration.

This report should encourage healthcare professionals to administer Benzathine Penicillin G only when clearly indicated and to be prepared for life-threatening situations. This medication must not be injected into a vein or mixed with solutions that will be injected into a vein. Before using it, check the product visually for particles or discoloration. If either is present, do not use the liquid. Learn how to store and discard medical supplies safely. Do not share this medication with others. Properly discard the product when it is expired or no longer needed. In case of emergency, contact a poison control center or emergency room immediately.

REFERENCES

1. Goodman LS, Gilman A. The Pharmacological Basis of Therapeutics, 4th, Edition, Macmillan Co, New York. 1970:1215.
2. WHO, Explore simplified antimicrobial regimens for the treatment of neonatal sepsis - meeting (2002) report. 2003.
3. Cocoman A, Murray J. Recognising the evidence and changing practice on injection sites. *Br J Nurs.* 2010;19(18):1170-4.
4. Levetan BN, Conradie EA, Linton DM. Inadvertent intravenous administration of a long-acting depot penicillin preparation. *South Afr Med J.* 1988;74:42-28.

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