CHAPTER 1

INTRODUCTION

The cinchona alkaloids, quinine and quinidine have been successful antimalarial drugs for centuries. Quinine , usually combined with tetracycline, remains the oral treatment of choice in much of this region (1). Intravenous quinine dihydrochloride is currently a treatment of choice for severe malaria (e.g. cerebral malaria) caused by chloroquin-susceptible or chloroquin-resistant Plasmodium falciparum (2-4). Treatment of severe malaria, especially cerebral malaria, must be initiated as soon as possible (2-5). Rapid intravenous administration of quinine has resulted in severe hypotension, arrhythmias, and acute circulatory failure. Whenever quinine dihydrochloride is given IV, the drug should be administered by slow IV infusion and blood pressure and pulse should be monitored frequently (2). Most clinicians currently recommended that adult receive a 600 mg dose of quinine dihydrochloride administered by slow IV infusion over 2-4 hours; the dose is repeated every 8 hours until oral therapy can be initiated (1-4). In Thailand, some clinicians reported that patients with cerebral malaria caused by Plasmodium falciparum may required a loading dose of 20 mg/kg infused over 4 hours to attain therapeutic plasma concentration (5). Recently, Consecutive-infusion regimen for rapid quinine loading in severe falciparum Malaria was reported (7 mg of quinine dihydrochloride/Kg of body weight over 30 minutes followed by 10 mg of quinine dihydrochloride/Kg over 4 hours at 8-hour intervals) (6). The maximum IV dosage of quinine dihydrochloride is 1.8 Gm daily (2).

For administration by slow IV infusion, it is recommended that quinine dihydrochloride be dissolved in 0.9% normal saline solution (2,3), 5% dextrose in water and 5% dextrose in normal saline solution (1). There are two reports that deal with quinine's chemical interaction with excipients in suspension (7-8) but no stability data of quinine dihydrochloride in commonly used IV solutions has been reported (9). Furthermore, in some clinics, 3 doses (1.8 Gm) of quinine dihydrochloride are mixed in IV fluid at one time for the ease of preparation and the one-thirds of admixture is administered to the patient every 8 hours. The admixture may have stability problems because it must be kept at least 16 hours before the last portion will be used. Hence, this study was carried out to determine stability of this drug in commonly used IV fluids.

OBJECTIVES

1. To investigate the stability of quinine dihydrochloride in 4 commonly used intravenous solutions (5% dextrose in water, 5% dextrose in normal saline solution, 5% dextrose in half strength saline solution and normal saline solution.
2. To determine the condition for storing admixture of quinine that can maintain the stability for at least 24 hour.

SIGNIFICANCE OF THE STUDY

The stability data of quinine dihydrochloride in commonly used IV fluid from this study will have important applications in the selection of IV fluid which gives maximum stability of quinine dihydrochloride. The results of this study will also be used to establish guidelines for proper storage conditions of quinine dihydrochloride admixtures.