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Practical Aspects of Artesunate Administration in Severe Malaria Treatment

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In management of severe malaria, aresunate is preferred antimalarial drug. It is better than quinine in reduction of mortality. Parenteral artesunate may be given either intravenous (IV) or intramuscular (IM) routes. However IV route is preferred route of administration since during severe falciparum malaria infection, capillary sequestration may delay drug absorption from muscle via IM administration to blood circulation. Artesunate can be activated by dissolving the powder of artesunic acid with sodium bicarbonate [1]. During mixing artesunic powder with sodium bicarbonate, the solution should be shaked strongly until dissolved, then the solution will be cloudy. The reconstituted solution will clear in about 1 min. If it is not clear, it should be discarded. Artesunate is poorly soluble in water and has poor stability in aqueous solutions at neutral or acid pH. Artesunic acid is sufficiently soluble in sodium bicarbonate injection (50 mg/ml) to prepare a clear solution [2]. The pH of the final solution is not greater than 8. After dissolving with sodium bicarbonate, artesunate solution in vial should be freshly used for each administration. Unused solution should be discarded and should not be stored in refrigerator for the next dose administration.

The recommended dose of artesunate for severe malaria is 2.4 mg/kg body weight at time 0, 12, and 24 h then daily once a day [3]. One vial contains artesunate 60 mg. Many clinicians do not calculate the exact body weight of the patients and give only 2 vials/dose of artesunate for adult severe malaria patients. If the patient weights 50 kg, 2 vials is enough. If the patient weights 60 kg, artesunate 144 mg/dose is needed; therefore 2 vials of artesunate (containing artesunate 120 mg) is not enough and 3 vials has to be used. Artesunate is not necessary given exact 144 mg/dose, but 150 mg/dose can be used. A bit higher dose of artesunate is acceptable and preferred rather than under dose since artesunate has wide therapeutic index, in contrast to quinine (which has narrow therapeutic index). For easy practice, number of vials for injectable artesunate for severe malaria can be used regarding to weight ranges, eg. 2 vials for 26-50 kg, 3 vials for 51-75 kg, and 76-100 kg body weight respectively [1].

Before injection, artesunate dissolved with sodium bicarbonate should be diluted in 0.9% sodium chloride or 5% dextrose or glucose solution [2]. Water for injection is not appropriate dilutant. For IV route artesunate solution should be made to concentration 10 mg/ml and rounded up to the next whole number, e.g. dose in ml needed for 60 kg patient is 2.4×60/10=14.4 ml which can be rounded up to 15 ml. For IM route artesunate solution should be made to concentration 20 mg/ml and rounded up to the next whole number, e.g. dose in ml needed for 60 kg patient is 2.4×60/20=7.2 ml which can be rounded up to 8 ml [1].

Parenteral 3 doses of artesunate should be given at least 24 h before switched to oral effective ACT, e.g. artesunate plus amodiaquine, artemether plus lumefantrine or dihydroartemisin plus piperaquine or artesunate plus clindamycin /or doxycycline. If the patient cannot take oral drug, parenteral artesunate should be given for a maximum of 7 days, until oral medication can be given [3,4]. World Health Organization (WHO) guideline mentioned mefloquine containing regimens should be avoided if the patient presented initially with impaired consciousness due to increased incidence of neuropsychiatric adverse effects associated with mefloquine following cerebral malaria [4]. In Thailand, parenteral/oral artesunate and mefloquine are available but non-mefloquine effective ACT or effective combination drug of ACT (artemether plus lumefantrine, dihydroartemisinin plus piperaquine, and amodiaquine) are not available. Artesunate plus doxycycline/ or clindamycin are not first-lined antimalarials for falciparum malaria in Thailand. Around 2 decades many clinicians in Thailand have had experience to use oral artesunate plus mefloquine after parenteral artesunate administration for management of severe malaria including cerebral malaria. A study of severe falciparum malaria in Thailand showed mefloquine (25 mg/kg in 2 divided doses) given on day 5 after parenteral artesunate administration to adult patients with severe falciparum malaria did not cause convulsions or psychosis or consciousness deterioration (as mefloquine neuropsychaitric adverse effects) in survived patients after mefloquine administration [5]. Therefore mefloquine may be safe as a combination drug of ACT after parenteral artesunate administration for severe falciparum malaria patients in Thailand where oral non-mefloquine effective ACT regimens are not available.

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