

Administration of Amphotericin B (AMB)

| | Conventional Amphotericin B (Amphotericin B deoxycholate) ABD | Liposomal Amphotericin B LAMB |
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| Dose | <p>0.5 to 1mg/kg body weight/day (Maximum 50 mg per infusion) Infuse over 4-6 hours (rapid infusion result in earlier onset of infusion related adverse effects)</p> <p>Higher dose can lead to cardiac toxicity – do not confuse with LAMB dosage</p> <p>After giving 1mg/kg/d for 2 weeks, 1.5mg/kg can be given 48 hourly or 72 hourly^{1,2}</p> | <p>3-5mg/kg body weight /day (Dose cap for obese patients with weight >100kg, fixed dose 500mg)</p> <p>May give up to 10mg/kg with CNS involvement</p> <p>Infuse over 4-6 hours. If tolerated infusion time can be reduced to 60minutes. (To minimize dose dependent side effects, since AMB is the only drug available to treat mucormycosis in Sri Lanka)</p> |
| Baseline Investigations | <p>Blood urea, Serum creatinine Serum potassium, Serum calcium, Serum magnesium FBC LFT</p> | |
| Pre-hydration | <p>With normal saline 500ml over 1hour -if it is not contraindicated with the patient’s cardio-renal status</p> | |
| | <p>Flush the cannula with 5% dextrose prior to start infusion</p> | |
| Other drugs | <p>Avoid other renal toxic drugs, radiocontrast, etc. if possible</p> | |
| Reconstitution of AMB | <p>Add 10ml water for injection to 50 mg vial to achieve 5mg/ml concentration</p> | <p>Add 12 ml of water for injection to 50 mg vial to achieve 4 mg/ml concentration</p> |
| | <p>Shake the vial vigorously for at least 30 seconds to disperse completely & solution is translucent / clear. Do not use if there is precipitate or particles</p> | |
| Storage | <p>Reconstituted drug can be stored in the refrigerator (2-8°C) for up to 24 hours before dilution with 5% dextrose</p> | |
| Not with SALINE | <p>AMB is not compatible with saline & it must not be reconstituted or diluted with saline. Other preparations for injection should not be added to the infusion.</p> | |
| Dilution | <p>Dilute in 490 ml of 5% dextrose to make final concentration 0.1 mg/ml (pH ≥4.2)</p> | <p>Dilute the dose in 500ml 5% dextrose to make final concentration between 1-2 mg/ml</p> |

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| | [final concentration should not exceed 0.1 mg/ml for peripheral infusion or 0.25 mg/ml for central infusion] | Use the 5 µm syringe filter supplied to add the dose to 5% dextrose bottle |
| Test dose (NOT essential in severe infection) | <p>1 mg in 50 ml of 5% dextrose over 1-2 hours (children <30kg 0.5 mg) Monitor temperature, pulse rate, respiratory rate & blood pressure every 30 minutes for 2 hours.</p> <p>Due to the risk of acute anaphylactoid reaction, or idiosyncratic reaction of severe hypotension & the unavailability of effective alternative antifungal drug in Sri Lanka to treat mucormycosis.</p> <p>If reaction occurs: stop the test dose, supportive treatment (IV hydrocortisone 200 mg and IV chlorpheniramine 10 mg stat).</p> <p>Continue the procedure (test dose and infusion) in a setting with resuscitation facilities eg: ICU, ETU</p> | No documented evidence on administration of a test dose. |
| Infusion | <p>If no reaction, give the rest of the dose in 500 ml of 5% dextrose infusion over 6 hours.</p> <p>No need to protect the infusion bottle from light</p> | If no reaction, give the rest of the dose in 500 ml of 5% dextrose infusion over 4-6 hours. |
| Post infusion | Flush the cannula with 5% dextrose after the infusion. | |
| Post hydration | With normal saline 500 ml over 1 hour if it is not contraindicated with the patient's cardio-renal status | |
| Infusion-related reactions | <p>Common (70% pts)</p> <p>fever, chills, rigors, myalgia, arthralgia & hypotension - differ from patient to patient</p> <p>Usually begin 1–3 hours after starting the infusion & last for about an hour.</p> | <p>Less common (20%)</p> <p>Triad of symptoms² -chest pain, dyspnoea & hypoxia -severe abdominal, flank or leg pain -vasodilation & urticaria -develop within a few minutes of the start of the infusion & can be severe.</p> |

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| | <p>Common during 1st week of treatment & often diminish thereafter.</p> <p>When reactions occur, stop the infusion, give IV hydrocortisone 200 mg & IV Chlorpheniramine 10 mg stat Slowing the rate of infusion may reduce these adverse effects.</p> <p>Can be prevented/ minimize by premedication with IV hydrocortisone 200 mg (30 minutes before starting ABD infusion), Chlorpheniramine 10mg, paracetamol 1g</p> <p>Pre-medicate with anti-emetics if the patient has nausea & vomiting</p> | <p>Can be prevented by pre-medication with Chlorpheniramine 10mg 30 minutes before the first infusion</p> |
| Nephrotoxicity | <p>Frequent, may be severe/ irreversible</p> <p>Hypokalemia, reduction of serum bicarbonate resulting in renal tubular acidosis, erythropoietin reduction causing anemia, hypomagnesemia</p> <p>To reduce nephrotoxicity; good hydration (pre & post infusion if not contraindicated)</p> <p>Avoid concomitant use of other nephrotoxic drugs (aminoglycosides, vancomycin, cyclosporine, tacrolimus, cidofovir, foscarnet, pentamidine, cisplatin)</p> <p>Concomitant furosemide & corticosteroids may induce hypokalaemia. If given together, serum potassium level should be monitored daily</p> | <p>Less frequent than in ABD</p> <p>Hypokalemia, reduction of serum bicarbonate resulting in renal tubular acidosis, erythropoietin reduction causing anemia, hypomagnesemia</p> <p>To reduce nephrotoxicity; good hydration (pre & post infusion if not contraindicated)</p> <p>Increased risk of nephrotoxicity if used concurrently with other nephrotoxic drugs eg: aminoglycosides, vancomycin, cyclosporine, tacrolimus, cidofovir, foscarnet, pentamidine, cisplatin</p> |

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| | <p>ABD can be continued till serum creatinine rises up to 3mg/dl^{2,3}</p> <p>May consider half the dose or alternate day dosing in drug related nephrotoxicity⁴</p> | |
| Other adverse effects | <p>Mild anaemia when treatment continued more than 2 weeks</p> <p>Local phlebitis: if the drug is given through a peripheral vein. Infusion site should be changed for each dose.</p> | less frequent &/or less intense compared to ABD abnormalities of LFTs |
| Monitoring | <p>Daily – Blood urea, S. creatinine until the levels stabilize</p> <p>Every 3rd day - Serum K⁺ (if detected hypokalaemia need to replace)</p> <p>Weekly - Serum Calcium, Serum Magnesium, LFT, FBC</p> | |

References

- 1 Fungal infection, diagnosis and management, 4th edition, Richardson M.D., Warnock D.W. 2012
- 2 Bennett, J.E., Dolin, R., Blaser, M.J. (Eds.), 2015. Mandell, Douglas, and Bennett's principles and practice of infectious diseases, Eighth edition. ed. Elsevier/Saunders, Philadelphia, PA. pg 482
- 3 Arunaloke Chakrabarti, personal communication, April 2022
- 4 CID, Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America

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