Critical Care Services

Guidelines for the intravenous use of methylene blue in critical care

Indication

Patients with severe sepsis/SIRS who remain hypotensive despite conventional treatment (fluid resuscitation, vasopressor and inotropic support). Its administration may allow for a reduction in vasopressor/inotrope use. There is no evidence for an improvement in oxygen delivery or survival.

Animal studies have shown a benefit in haemodynamic state and acute lung injury in septic shock.

There is limited evidence in humans. There are two small randomised controlled trials (total 50 patients) and several case series using different dosing regimens and examining different end points.

Dose

- Load: 2mg/kg via a central line over 15 minutes
- Maintenance: Wait two hours following load, and then start infusion as follows:
    - 0.5mg/kg/hour for one hour
    - Increase to 1mg/kg/hour for one hour
    - Increase to 2mg/kg/hour for one hour or until **cumulative** dose of 6mg/kg has been reached
    - Maximum six hours of infusion
- Most efficient response will be seen above 0.5mg/kg

Weight (kg)	Loading Dose (2mg/kg) (***ml of 5mg/1ml solution***) over 15 minutes	0.5mg/kg/ hour (***ml/hour***)	1mg/kg/hour (***ml/hour***)	2mg/kg/hour (***ml/hour***)	Maximum Cumulative Dose (6mg/kg) ***in ml***
50	20ml	5ml/hour	10ml/hour	20ml/hour	60ml
60	24ml	6ml/hour	12ml/hour	24ml/hour	72ml
70	28ml	7ml/hour	14ml/hour	28ml/hour	84ml
80	32ml	8ml/hour	16ml/hour	32ml/hour	96ml
90	36ml	9ml/hour	18ml/hour	36ml/hour	108ml
100	40ml	10ml/hour	20ml/hour	40ml/hour	120ml

Administration

- There is an administration monograph for methylene blue on Medusa, the Injectable Medicines guide.
- Methylene blue (methylthioninium blue) is available as a 1% (10mg/1ml) solution.
- Dilute to 250mg/50ml with sodium chloride 0.9%, glucose 5% or sodium chloride 0.18% + glucose 4%.

▪ Although, a 0.45 micron filter is recommended for administration, anecdotal evidence suggests that this is not required, although it is recommended that the solution is drawn up using a filter needle.

Pharmacokinetics
▪ Half Life: 100 minutes
▪ Excretion: 75% of dose is excreted in the urine

Mechanism of Action
Methylene blue is a chemical dye that has been shown to inhibit nitric oxide mediated vasodilatation in sepsis. It increases systemic vascular resistance and increases MAP.

Cautions
▪ Renal impairment

Side Effects
▪ Formation of methaemoglobin
▪ Use of methylene blue causes increased pulmonary vascular resistance and will worsen pulmonary hypertension. Using an infusion rather than a bolus may lessen this effect.
▪ Mild thrombocytopenia
▪ With prolonged use, skin and bodily fluids can turn blue.
▪ Methylene blue has been continuously infused for up to 45 hours without toxic effects

References
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Written by: Dr Ian Nesbitt 2004
Updated by: Dr Lorna Barton & Nicola Rudall