

Goldilocks & the three sedation strategies

If you snooze do you really lose?

Nepean WTET summary 19/5/20

Background and Rationale

- Deep sedation is particularly indicated for management of specific disease conditions to include severe hypoxic respiratory failure with impaired compliance and ventilator dyssynchrony, hyperthermic emergencies (and shivering during TTM post OOHCA), super refractory status epilepticus, intracranial hypertension and medical management of intraabdominal hypertension. In other critically ill invasively patients the primary goals of sedation are usually to facilitate ongoing management (be that specific therapies or simply 'time') and/or minimising oxygen consumption/demands whilst ensuring patient comfort and minimising distress
- Early heavy sedation was found by the SPICE investigator group to be an independent risk factor for delayed extubation, higher hospital and 180d mortality. Beyond the well established complications of delayed extubation (delayed wakeup due to long infusions of context sensitive agents with a deeper strategy) and dose-related side effects of individual drugs (e.g. hypotension, myocardial depression +/- ?immune modulation) there may be other factors at play also
- Avoidance of over sedation can be achieved by a number of mechanisms to include – daily sedation holds/interruptions/holidays, careful titration to a conservative RASS or a no-sedation approach

Advantages and Disadvantages of each

- Daily sedation interruption (DSI) strategy;
 - Advantages
 - Daily reset of accumulated context sensitive drugs (even if long ICU stay), reduced VAP
 - Allows more detailed neurological examination, interaction with physio and assessment for extubation
 - Disadvantages
 - Potential for post-traumatic stress disorder (PTSD) for patient
 - Leads to more bolusing of sedation and associated fluctuations in CVS stability
 - Often only facilitates a once-daily assessment of suitability for extubation
 - Potential for self-extubation, accidental line removal, ventilator dyssynchrony
- Titration only strategy;
 - Advantages
 - Potentially less accidental line loss, reduced nursing workload
 - Disadvantages
 - RASS subjective, range difficult to adhere to with fluctuant nature of delirium leading to frequent over/under sedation cycles with bolusing and associated CVS instability
- No sedation strategy;
 - Advantages
 - Preserved neuromuscular function, less CVS instability from sedatives, less VTE
 - Disadvantages
 - Potential increased PTSD and use of physical restraints, more ventilator dyssynchrony
 - High risk self-extubation and accidental line loss; high nursing burden

Evidence

- Kress et al. NEJM 2000
 - Single center RCT, n=128, randomised to DSI versus sedation interruption at discretion of treating clinician and each subgroup further randomised to propofol (PPF) vs midazolam (midaz) primary sedative (all received analgesic also)
 - Duration of mechanical ventilation significantly less in the DSI group (4.9d vs 7.3d P=0.004) with associated reduction in ICU LOS (6.4 vs 9.9 P=0.02), no difference between PPF and midaz
 - 2003 Am J Resp & Crit Care Med published follow-up of n=32 (agreed to be interviewed of 105 survivors) 19 from control, 13 from intervention group (?enrollment bias) → no difference in anxiety and depression and significantly less PTSD in DSI group
- ABC Lancet 2008
 - MC RCT; 4 ICUs in USA, n=336. In absence of contraindications, spontaneous awakening trial SAT (which if successful followed by a spontaneous breathing trial SBT) versus SBT alone daily
 - Shorter duration of mechanical ventilation (14.7d vs 11.6d, P=0.02) with shorter ICU LOS (9.1d vs 12.9d, P=0.01) and hospital LOS in the SAT arm. Similarly statistically less mortality at 1y
 - More self extubation in SAT arm
- Strøm et al. Lancet 2010
 - Single center (Danish) n=140; No continuous sedation vs continuous sedation with DSI
 - 4.2 fewer days of invasive ventilation in no sedation group (P=0.019) and shorter ICU LOS
 - ?External validity (?no sedation units usual policy)
- SLEAP JAMA 2012
 - RCT, 16 ICUs (USA and Canada) n=430, protocolised sedation +/- DSI; benzodiazepine first line
 - No difference in median time to extubation or ICU LOS. No increase in accidental extubation
- Cochrane Review 2018
 - RCT, 9 ICUs, n=1282; DSI vs non-DSI for critically ill invasively ventilated
 - DSI did not reduce duration of mechanical ventilation though significant heterogeneity amongst studies. Fewer tracheostomies in DSI group
 - Studies that showed significant reduction in duration of mechanical ventilation with DSI also showed significant reduction in drug consumption
- Nonseda NEJM 2020
 - Scandinavian MC RCT 1:1, n=700 ITT; light sedation (RASS -2 to -3) with DSI vs non-sedation
 - Analgesia (morphine bolus) allowed in non-sedation group; 27% cross-over to get sedation
 - RASS in non-sedation -1.3 d1 to -0.8 d7 versus in sedation arm -2.3 d1 to -1.8 d7
 - No difference in 90d mortality or ventilator free days at day 28. But fewer major venothromboembolic events (0.3% vs 2.8%) in non-sedation group

Summary (my practice)

- There are certain conditions where deep sedation is indicated in the invasively ventilated critically ill. For those where this is not the case, I titrate sedation to RASS usually to -2 to 0 paying attention to total sedation requirements. Where high levels of sedation are needed I consider pain, delirium or withdrawal as other contributing factors that may need addressing separately. I try to maximise non-pharmacological approaches to managing agitation also
- DSI does not form part of my usual practice in my current institution, however in specific cases where certain interventions are required regularly (e.g. detailed neurological examination) it may appear so
- A no sedation approach does not form part of my usual practice either. However frequently tracheostomised patients and at times some intubated patients are incredibly ventilator and/or tube tolerant and a no sedation approach is safe and appropriate and is not associated with distress.