Daily Sedative Interruption versus Intermittent Sedation in Mechanically Ventilated Critically Ill Patients: a Randomized Trial.

BACKGROUND:

- The effect on time on mechanical ventilation of different protocols for sedation in ICU patients, such as daily sedative interruption and intermittent sedation needs to be established.
- All the sedation trials that showed efficacy and decreased ICU ventilator days, including trials of daily interruption (most studied), nursing implemented protocols or no sedation have been done in developed, not developing, countries. Developed countries have higher nursing staff than developing countries, and lower nursing staff in the ICU may expose patients on mechanical ventilation to care-associated risks.

OBJECTIVE:

- To compare sedative interruption and intermittent sedation in critically ill, mechanically ventilated patients in a low nursing staff ICU.

METHODS:

- Design: Randomized, parallel, non-blinded controlled experimental design
    - Patients in the daily sedative interruption group stayed on continuous sedation with midazolam and fentanyl and received daily interruption of sedation for a neurological evaluation until they reached a sedation agitation score (SAS) of 4 or more, then continuous sedation was restarted at half the previous dose.
    - Intermittent sedation patients stayed without any continuous sedation from the time of intubation and/or admission but received analgesics, usually fentanyl, as needed and sedatives (midazolam or propofol) when agitated with a SAS of 5 or more
- Inclusion Criteria:
    - Patients who required mechanical ventilation within the last 24 hours and were expected to need mechanical ventilation for more than 24 hours
- Exclusion Criteria:
    - Younger than 18 years-old
    - Pregnant
    - In need of deep levels of sedation
        - Examples--intracranial hypertension, status epilepticus, hypothermia after cardiac arrest, severe asthma exacerbations, and severe hypoxemic respiratory failure (PaO_2/FiO_2 ratio < 50)
    - Not expected to survive for more than six months
        - For example, metastatic cancer, NY functional class IV heart failure, Child C hepatic cirrhosis, oxygen-dependent, COPD
    - Previously cognitive impaired, e.g., advanced dementia
    - Readmitted to the ICU after participating in the trial
- Primary outcome measures: Ventilator-free days in 28 days
- Secondary outcome measure:
    - ICU and hospital mortality
    - ICU and hospital length-of–stay
    - Incidence of delirium
    - Delirium and coma-free days in sever days
    - Nurse workload
    - Self-intubation and re-intubation
    - Psychological distress six months after ICU discharge
    - Percentage of time on target sedation monitored by SAS
    - Accidental removal of catheters

    - Tracheostomy rates
    - Total sedative doses per patient
    - Differences in hemodynamic and ventilator variables
    - Total sequential organ failure assessment (SOFA) score
- Enrolled:
    - Total of 60 patients in a closed multidisciplinary six bed ICU that admits patients from the ED, surgical room and ward in a tertiary hospital from Jan. 2009 to Dec. 2011
    - More patients were planned to be enrolled to have sufficient power but due to the slow recruitment rate trial enrollment was stopped early.
- Data handling method: Intention- to- treat

RESULTS:

- 231 patients were assessed for eligibility, 60 were included in the trial
- Primary outcomes:
    - Ventilator-free days in 28 days:
        - No differences, not statistically significant (p=0.160)
- Secondary outcomes:
    - ICU and hospital mortality
        - No differences; not statistically significant (ICU, p=0.165, mortality, p=0.284)
    - Incidence of delirium
        - No differences; not statistically significant (p=0.0.472)
    - Nurse workload
        - Not different between groups but significantly reduced ($p < 0.001$) in both groups on day 5 compared to day 1
    - Self ex-tubation
        - No differences; not statistically significant (p=0.0.514)
    - Psychological distress six months after ICU discharge
        - Median scores were higher in daily interruptions sedation group; however, not statistically significant (p=0.750)
- Total doses of fentanyl and midazolam per patient were higher in daily interruption group
- Tidal volume was higher in the intermittent sedation group during the first five days of ICU stay

LIMITATIONS:

- Not able to recruit enough people in the trial to obtain at least 80% power
- Trial was conducted with patients from a single ICU; likely not representative of the population at large.
- Treatment options were very similar. Depending on the patient's SAS score it was difficult to determine what the difference actually was between the two intervention groups.
- Determination of sedation "at the discretion of attending physician" could be open to interpretation depending on different physicians or the resident attending. Could even be different depending on the time of day for the same attending physician.

CONCLUSIONS:

- There was no difference in the number of ventilator-free days in 28 days between intervention groups
- Intermediate sedation was associated with lower sedative and opioid doses although the two groups appeared very similar in design.

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