INTUBE study

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INternational observational study To Understand the impact and BEst practices of airway management of critically ill patients

Study acronym identifier: **INTUBE**

Rationale

Endotracheal intubation (ETI) in critically ill patients is a potentially life-threatening procedure and approximately one-third of ETIs is complicated by severe hypoxia, cardiovascular collapse and cardiac arrest [1,2]. Critically ill are prone to severe complications as the consequence of the underlying acute respiratory failure or hemodynamic instability, reduced oxygen stores and increased oxygen consumption [1,3]. Moreover, the rate of difficult airway management may be higher in the intensive care unit (ICU) and in the Emergency Department (ED), prolonging the apnea time and the risk of desaturation [4]. Finally, operator's skills, procedures, devices and drugs, among others, may influence airway management success and patient's outcome [5]. Despite the high risk of the procedure, different interventions lack high-quality evidence and we hypothesize that a heterogeneous practice among different centres and geographical areas may be found [6,7].

The primary aim of our study is to evaluate the incidence of intubation-related adverse events in critically ill patients. Secondary aim is to evaluate current clinical practices on airway management in the in-hospital critical care setting.

METHODS

Study design

Prospective observational multi–centre international cohort study.

Recruitment

We aim at creating a large database on in-hospital airway management practices of critically ill patients from a large and geographically heterogeneous population.

We launched a website: www.intubestudy.com where we will publish study information and documents (e.g. protocol, case report form, national coordinator list) which will be available for potentially interested investigators. From the website, it will be possible to complete a

form for center and principal investigator data collection. Social media (e.g. *twitter*) will be used to promote the study. Personal connections of steering committee members will be used for study promotion and call for centers. The project will be presented and a call for centres will be announced during international meetings of intensive care.

We will also apply for receiving the endorsement of the European Society of Intensive Care Medicine (ESICM), the Society of Critical Care Medice (Discovery program) and the Difficult Airway Society (DAS).

Inclusion criteria

We will include all adult (≥ 18 years old) critically ill patients undergoing intubation during the period of observation. We will consider all in-hospital intubations. We will define critically ill those patients with a life-threatening condition requiring intubation for either respiratory failure or airway protection.

Exclusion Criteria

- Intubation performed in the out-of-hospital setting
- Intubation during cardiac arrest
- Intubation performed for anaesthesia (during either diagnostic/endoscopic or surgical procedures)

Primary outcome

At least one of the following (composite outcome):
- Severe hypoxemia (SpO_2 < 80%) occurring within 30 minutes from intubation
- Cardiac arrest occurring within 30 minutes from intubation
- Cardiovascular collapse (at least one of the following), occurring within 30 minutes from intubation:
    - SAP < 65 mmHg recorded 1 time
    - SAP < 90 mmHg for > 30 minutes
    - New need of vasopressors/their increase and/or fluid load > 15 ml/kg to maintain the target blood pressure.

Secondary outcomes

- Difficult intubation (> 2 laryngoscopic attempts)
- Cardiac arrhythmia
- Emergent surgical airway
- Aspiration of gastric contents
- Oesophageal intubation
- Pneumothorax/pneumo-mediastinum
- Dental injury
- Airways injury

Long term outcome

- Mortality at ICU-discharge

Data collection

We will collect the following information:

- Demographic and clinical characteristics
- Monitoring applied during the procedure
- Reason for intubation/re-intubation
- Ongoing respiratory support before intubation (standard nasal cannula, high-flow nasal cannula, facemask O_2, Venturi system, CPAP, noninvasive positive pressure ventilation)
- Patient's parameters and gas exchange (within 30 minutes) before intubation
- Operator's training (years of experience, number of endotracheal intubations performed in a week) and duty hours before the procedure
- Characteristics of intubation (anticipated difficult airway management, degree of emergency)
- Intubation procedure (position during preoxygenation, rapid sequence induction applied)
- Preoxygenation method and use of apneic oxygenation
- SpO_2 at the end of preoxygenation
- Drugs used for induction (molecules and doses)
- Elective method for laryngoscopy
- Method used for the second (and following) attempt

- Method used for adequate tube placement confirmation
- Value of first $EtCO_2$ registered
- Duration of laryngoscopy
- Outcome of endotracheal intubation (total number of attempts, laryngoscopic view, minimum SpO_2 during laryngoscopy, need for LMA)
- Major intubation-related complications (severe cardiovascular collapse, severe hypoxemia, cardiac arrest within 30 minutes from intubation)
- Minor intubation–related complications (difficult intubation, supraventricular/ventricular arrhythmia, aspiration of gastric contents, esophageal intubation, dental injury, airway injury pneumothorax/pneumomediastinum, emergent tracheostomy)
- Status at ICU discharge (dead, alive, transferred).

Data will be collected on paper case report forms (CRFs). Local investigators are expected to transcribe all collected data into an interned-based electronic CRF (eCRF, Research Electronic Data Capture – RedCap). Each local investigator will be trained in how to use the eCRF and will receive a personalized username and password. Each patient will be coded through a patient identification number (PIN) generated by the eCRF and no patient names or initials will be present on the paper CRF. Data will be handled confidentially and the paper CRF will be stored behind a lock at each local site. Each centre should keep data stored for the length of the study and the time foreseen by local rules but at least 10 years from the date of study completion.

The paper CRF is attached at the end of this protocol.

Sample size

Our aim is to collect data from at least 1000 major adverse events from airway management.

The reported incidence of at least one major intubation-related complication (severe hypoxia, hemodynamic collapse, cardiac arrest) is approximately 28% [1]. Therefore, we plan to collect data from 3600 intubations.

Intubation rate may vary from 0.5 to 2 ETIs/day according to different centres (e.g. total hospital beds, number of ICUs and ICU beds) and local policies. Each center will be asked to collect data from 20 ETIs. A maximum time window of 8 weeks will be allowed for each

center (i.e. for centers with a slower recruitment rate, data collection will stop after 8 weeks irrespective of total number of ETIs collected data). Each center will select a start date for recruitment from 1 October to 31 March 2018. We plan to recruit at least 180 centers worldwide.

Statistical analysis

We will report mean and standard deviation of normally distributed variables and we will compare them using the student T-test. We will report non-normally distributed variables as median and interquartile range, comparing them using the Mann-Whitney U test. Categorical variables will be expressed as proportion and compared using the Chi-square or Fisher exact test as appropriate. We will perform a bivariate analysis to identify variables associated with the composite outcome of major ETI-related complication and significant variables will be then used to construct a multivariate logistic model in order to identify independent variables. A two-sided p-value < 0.05 will be considered statistically significant. Statistical analysis will be performed by the SPSS software package.

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