

RESEARCH NEWS

Lung recruitment and titrated PEEP in moderate to severe ARDS

J. Pillay

Department of Intensive Care, Academic Medical Center Amsterdam, the Netherlands

Correspondence

J. Pillay - j.pillay@amc.uva.nl

Keywords - ARDS, recruitment, PEEP**Article**

Effect of lung recruitment and titrated PEEP vs. low PEEP on mortality in patients with ARDS. Published in JAMA, in October 2017.^[1]

Why was this research done?

ARDS causes collapse, flooding and consolidations in large parts of the lung. This increases the risk of ventilator-induced lung injury due to over-distention of aerated lung and cyclic opening and closing of collapsed alveoli (atelectrauma).

To reduce ventilator-induced lung injury, the open lung concept has been advocated and is accepted practice in many ICUs. Recruiting collapsed lung regions using recruitment manoeuvres (RM) and applying PEEP to keep these regions open reduces atelectrauma and more evenly distributes the tidal volume, thus limiting over-distention of the aerated lung. The level of PEEP needed and how to determine this for the individual patient is, however, unknown.

Three large RCTs applying high PEEP and RM in patients with ARDS (P/F ratio <300) did not show an effect on mortality.^[2-4]

However, a meta-analysis of these trials suggested a reduction in mortality in patients with a P/F ratio <200.^[5]

This RCT was conducted to study the effect of RM and titrated PEEP on mortality in moderate to severe ARDS (P/F ratio < 200).

What was the research question?

Does a strategy of lung recruitment and titrated PEEP vs. no recruitment and low PEEP reduce 28-day mortality in patients with moderate to severe ARDS?

How was this investigated?

The authors performed a multicentre randomised controlled trial in 120 ICUs from 9 countries. Patients were included over a 6-year period.

A total of 1013 patients with moderate to severe ARDS were randomised after exclusion of 1064 patients. The main

reasons for exclusion were P/F ratio >200 after standard ventilation (296 patients), increasing dose of vasoconstrictor or mean arterial pressure <65 (273 patients), pneumothorax or pneumomediastinum (139 patients) and contraindications to hypercapnia (129 patients). The remaining patients were randomised to receive lung recruitment and PEEP titrated according to the best lung compliance (501 patients) or low PEEP without recruitment (512 patients).

In the RM and titrated PEEP group patients received neuromuscular blocking agents and fluid loading in preparation for the RM. RM consisted of incremental PEEP up to 45 cm H₂O followed by decremental PEEP titration to best lung compliance. PEEP was set at this level + 2 cm H₂O. In the low-PEEP group PEEP was set according to the ARDSnet table. In both groups, patients were ventilated with 6 ml/kg (or less) tidal volumes and plateau pressures were kept under 30 cm H₂O.

The primary endpoint was 28-day all-cause mortality. Secondary endpoints were length of ICU and hospital stay, ventilator-free days, pneumothorax requiring drainage or barotrauma within 7 days, and ICU, in hospital and 6-month mortality.

Main findings

Compared with the control group, RM and titrated PEEP increased 28-day all-cause mortality (55.3% vs 49.3%; hazard ratio [HR] 1.20; 95% CI 1.01 to 1.42; p=0.041). In addition, 6-month mortality was increased (65.3% vs 59.9%; HR 1.18; 95% CI 1.01 to 1.38; p=0.04) and ventilator-free days were decreased (5.3 vs 6.4; 95% CI -2.1 to -0.3; p=0.03). The RM and titrated PEEP group showed an increased risk of pneumothorax (3.2% vs 1.2%; 95% CI 0.0% to 4.0%; p=0.03) and barotrauma (5.6% vs 1.6%; 95% CI 1.1% to 6.5%; p=0.01).

PEEP in the intervention group was 3-4 cm H₂O higher over the first 7 days. The mean P/F ratios were higher in the RM and titrated PEEP group; however, the decrease in driving pressure in this group was less than 2cm H₂O compared with the control group.

Discussion, conclusion and consequences for daily practice

This large multicentre RCT studied two interventions (RM and high PEEP) to ‘open up the lung and keep it open’ and compared this with a strategy of low PEEP, set according to the ARDSnet table. It shows that RM and titrated PEEP increases mortality in patients with moderate to severe ARDS. It has previously been shown that high PEEP does not influence mortality in a study group consisting of mild, moderate and severe ARDS;^[2-4] however, no or milder recruitment manoeuvres were used in those studies. In this study, there was a relatively small difference in the PEEP levels between the experimental and control group (3-4 cm H₂O); in addition, the driving pressure was only 2 cm H₂O lower in the experimental group. This suggests only minimal recruitment after the RM. It is conceivable that individual patients with recruitable lungs might have benefited from an RM; however, this analysis was not performed. In addition, a major variable between the two groups was the fluid loading in preparation for an RM. Excessive administration of fluids could have increased detrimental outcome in the experimental group; however, the exact amount of fluids or fluid balances was not reported.

In conclusion, this study emphasises the risk of RM and questions the routine use of titrated PEEP in patients with moderate to severe ARDS.

Disclosures

The author declares no conflict of interest. No funding or financial support was received.

References

1. Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators, Effect of Lung Recruitment and Titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on Mortality in Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial. *JAMA*. 2017;318:1335-45.
2. Brower RG, Lankester PN, MacIntyre N, et al. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. *N Engl J Med*. 2004;351:327-36.
3. Mercat A, Richard JC, Vielle B, et al. Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. *JAMA*. 2008;299:646-55.
4. Meade MO, Cook DJ, Guyatt GH, et al. Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. *JAMA*. 2008;299:637-45.
5. Briel M, Meade M, Mercat A, et al. Higher vs lower positive end-expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and meta-analysis. *JAMA*. 2010;303:865-73.

When care is critical, balance is everything

dexdor®
dexmedetomidine

To achieve a calm, cooperative patient

See more of the person, treat more of the patient

By striking just the right balance in sedation, **dexdor®** optimises pain, agitation and delirium (PAD) management¹⁻⁴ in the ICU to achieve a calm and cooperative patient. With reduced times to extubation^{5,6} and shorter overall stays in the ICU⁷, **dexdor®** can help play a critical role in restoring your patient to the person that they really are.

For further information visit www.dexdor.eu

* vs propofol and vs midazolam ¹ vs propofol or midazolam in pooled analysis

PRESCRIBING INFORMATION
dexdor® 100 micrograms per ml concentrate for solution for infusion (dexmedetomidine) Prescribing Information. Indication: Sedation of adult ICU patients requiring sedation level not deeper than arousal in response to verbal stimulation (RASS 0 to -3). Dosage and administration: Hospital use only, by healthcare professionals skilled in management of patients requiring intensive care. Administer only as diluted intravenous infusion using controlled infusion device. Dexmedetomidine is very potent and the infusion rate is given per hour. Switch patients already intubated and sedated to dexmedetomidine with initial infusion rate of 0.7 micrograms/kg/h and adjust stepwise within range 0.2 to 1.4 micrograms/kg/h to achieve desired sedation level. Consider lower starting infusion rate for frail patients. After dose adjustment, new steady state sedation level may not be reached for up to one hour. Do not exceed maximum dose of 1.4 micrograms/kg/h. Switch patients failing to achieve an adequate level of sedation with maximum dose to an alternative sedative agent. Loading dose not recommended. Administer propofol or midazolam if needed until clinical effects of dexdor® established. No experience in use of dexdor® for more than 14 days. Use for longer than this period should be regularly reassessed. Elderly: No dosage adjustment required. Renal impairment: No dosage adjustment required. Hepatic impairment: Caution advised; consider reduced dose. Children aged 0-18 years: Safety and efficacy not established. Contraindications: Hypersensitivity. Advanced heart block (grade 2 or 3) unless paced. Uncontrolled hypertension. Acute cerebrovascular conditions. Warnings and precautions: Intended for use in intensive care setting, use in other environments not recommended. Continuous cardiac monitoring required. Monitor respiration in non-intubated patients due to the risk of respiratory depression and in some cases apnoe. Do not use as induction agent for intubation or to provide sedation during muscle relaxant use. dexdor® reduces heart rate and blood pressure but at higher concentrations causes peripheral vasoconstriction and hypertension. Not suitable in patients who will not tolerate lack of deep sedation and easy rousability. Users should be ready to use alternative sedative for acute control of agitation or during procedures, especially during the first few hours of treatment. Caution with: pre-existing bradycardia, high physical fitness and slow resting heart rate, pre-existing hypotension, hypovolaemia, chronic hypotension or reduced functional reserve; severe ventricular dysfunction; the elderly; impaired peripheral autonomic activity (e.g. due to spinal cord injury); ischaemic heart disease or severe cerebrovascular disease; severe hepatic impairment; severe neurological disorders such as head injury and after neurosurgery. Reduce dose or discontinue if signs of myocardial or cerebral ischaemia. Additive effects may occur with other substances with sedative or cardiovascular actions. Some patients receiving dexdor® have been observed to be arousable and alert when stimulated; this alone should not be considered as evidence of lack of efficacy. Do not use as sole treatment in status epilepticus. Consider possibility of withdrawal reaction if patient develops agitation and hypertension shortly after stopping dexmedetomidine. Not recommended in malignant hyperthermia-sensitive individuals. Discontinue treatment in event of sustained unexplained fever. Undesirable effects: Very common (≥1/10): Bradycardia, hypotension, hypertension. Common (1:100 to <1/10): Hyperglycaemia, hypoglycaemia, agitation, myocardial ischaemia or infarction, tachycardia, respiratory depression, nausea, vomiting, dry mouth, withdrawal syndrome, hyperthermia. Uncommon (1:1,000 to <1/100): Metabolic acidosis, hypoalbuminaemia, hallucination, atrioventricular block first degree, cardiac output decreased, dyspnoea, apnoea, abdominal distension, drug ineffective, thirst. See SPC for further details.

Market authorization numbers EU/1/11/1718/001-002, EU/1/11/718/004, EU/1/11/718/006-007. Date of first authorisation: 16 september 2011. Date of renewal of the authorization: 26th May 2016. Orion Pharma BVBA • Battelsteenenweg 455D • 2800 Mechelen Tel. +32 (0) 15 64 10 20 • Fax: +32 (0) 15 64 10 21 •

ORION PHARMA