Two major dilemmas about application of mechanical ventilation is when and how to start it (initiation) and when and how to start reducing the mechanical respiratory support (deescalation). Both of these dilemmas are not easy to resolve, especially if the physician who is facing with them is young and unexperienced. The basic concept of initiation of mechanical ventilation is simple and consists of adjusting the inspiratory oxygen concentration (FiO₂) and positive end-expiratory pressure (PEEP) in order to control oxygenation, as well as tidal volume (Vt) and respiratory rate in order to ensure adequate elimination of CO₂. Deescalation of mechanical ventilation is a process that should be initiated promptly as respiratory status and general condition of the patient begin to improve. There is a useful consensus that deescalation of mechanical ventilation should be considered practically from the moment of initiation. Deescalation involves adapting and adjusting of FiO₂, PEEP and the level of support. It can be performed by any model of mechanical ventilation which continues with PSV (“pressure support ventilation”) with a gradual reduction of FiO₂, PEEP and pressure support, depending on the process of the underlying disease.

Key words: mechanical ventilation, initiation, deescalation.

INITIATION AND DEESCALATION OF MECHANICAL VENTILATION

Mechanical ventilation (MV) is an integral part of intensive therapy and without its application we cannot imagine the modern approach in the treatment of critically ill patients. Although the MV saved millions of lives, its insufficient knowledge and inadequate application may be the reason for the occurrence of many complications, some of which directly threaten the patient’s life.

The development of science and technology has led to the emergence and the application of sophisticated and complex apparatus for MV. Their use requires continuous training and education of doctors, and other staff in the Intensive care units (ICU). This approach is important for the efficient and safe use of MV in critically ill patients.

There are many dilemmas in monitoring the MV. Among them two dilemmas stand out, such as when and how to start the application MV (the initiation) and at what point and how to start reducing the ventilatory support (deescalation of MV). The above-mentioned dilemmas are not easy to resolve, especially if the physician, who is faced with them, young and inexperienced. Therefore it is important to define protocols and introduce them into everyday clinical practice in the ICU, with specific guidelines for both the initiation and de-escalation of MV. Protocols for MV should be used only as a guideline and should be applied to each patient individually. Success in implementing of MV depends on time and adequate recognition of the clinical problem in each patient 1. But success depends on timely made plan of MV that adapts to each patient with respect to all the principles of MV strategy that protects the lungs from further secondary damage.

MV plan includes a clear definition of the goals that we want to achieve. The most important goals of the MV are: sufficient elimination of carbon dioxide (CO₂), sufficient oxygenation of arterial blood and a third, but not less important goal, is to help functioning of the respiratory muscles. Another equally important issue is that is the cause of respiratory failure primary lung disease or not. If the answer is yes, we need to clearly define whether the lung disease is obstructive, restrictive or mixed. The next element in the planning of MV refers to
an appropriate timing in the application of MV ie. when to start, how long to apply a particular model of MV-maintenance (escalation), at what time to start deescalation and, of course, when you separate the patient from MV. When planning MV we also must choose a general approach that can be aggressive, conservative or balanced. Aggressive approach is to achieve the normal gas exchange no matter how, and the conservative approach gives priority to the principles of the protective strategy to protect the lungs. It is best to have a balanced approach.

**INITIATION OF MECHANICAL VENTILATION**

The basic concept of initiation of MV is very simple. It means adjust the inspiratory oxygen concentration (FiO₂) and positive endexpiratory pressure (PEEP) in order to control oxygenation and tidal volume (VT) and respiratory frequency (RF) to achieve adequate elimination of CO₂². These are the two most important goals for the initiation MV.

**CONTROL OF OXYGENATION IN MECHANICAL VENTILATION**

In the treatment of impaired oxygenation normoxemia is the ideal situation we wish to achieve. Normoxemia is when blood gas analysis (BGA) achieve partial pressure of oxygen (PaO₂) of 100 mmHg or 13.5 kPa. This target value of PaO₂ declines with ages, but it also depends on the general condition of the patient, and should be individually determined. It can also be corrected and in relation to the possible undesirable effects of treatment which are used for improving oxygenation. Permissive hypoxemia is defined as the value of PaO₂ of 80 mmHg (11kPa) and represents the desired level to which we aspire by the implementation of measures for improvement the oxygenation of arterial blood, if it is not possible to achieve normoxemia³. It is generally accepted that this value can be 60 mmHg (8 kPa), or sometimes even lower, in case that the hypoxemia is refractory to treatment, or when the risk of unwanted effects of MV is too high⁴. The realization of this objective has top priority regardless of the nature of the underlying disease, which leads to respiratory failure.

**FiO₂ ADJUSTMENT TO CONTROL OXYGENATION**

One of the first measures in the control of oxygenation is increase of FiO₂. This measure is especially effective in dealing with hypoxemia due to ventilation-perfusion (V/Q) disorders. When we increase FiO₂ to correct hypoxemia, it is important to take care of the possible toxicity of O₂, and it is best to stick to the rules which recommend to implement FiO₂ of the lowest value that will ensure satisfactory oxygenation. FiO₂ of 0.6 is a safe level even for a longer period of time²⁴⁵. Despite the fact that higher values of FiO₂ can be toxic to the lungs, sometimes we have to use them, even for a long time in clinical situations when it is necessary to avoid severe hypoxemia. We must not forget the fact that the application of MV with high values of FiO₂ inhibits hypoxic pulmonary vasoconstriction (HPV). HPV is a compensatory mechanism that increases pulmonary vascular resistance (PVR) in the parts of the worse ventilated lung, which leads to a redirection of blood in better ventilated areas.

**SETTINGS OF PEEP IN ORDER TO CONTROL OXYGENATION**

Control of oxygenation can be achieved by the application of appropriate levels of positive endexpiratory pressure (PEEP). PEEP is defined as an increase in transpulmonary pressure at the end of expiratory flow that keeps the alveoli open, thereby increasing the functional residual capacity (FRC), reducing intrapulmonary shunt, improves compliance of lung (C), which results in an improvement in oxygenation³⁶⁷. The role of PEEP in MV is protective, as PEEP prevents atelectotrauma that occurs due to cyclic collapse and reopening of unstable alveoli. Unfortunately, the application of PEEP in MV can be helpful as much as harmful. Using an adequate level of PEEP is complex and still require consideration of the benefits and harms. In the case of initiation of MV recommended value of PEEP is 5 cmH₂O, which has minimal side effects and can be administered without the consequence in the most of patients⁵. In patients with diagnosis of ARDS/ALI and cardiogenic pulmonary edema, oxygenation will be significantly improved by applying adequate, sometimes significantly higher PEEP values. For the most patients with ARDS / ALI is necessary to apply PEEP between 10-15 cmH₂O⁶. Severe forms of ARDS require the application of PEEP even greater than 15 cmH₂O. It is known that the application of PEEP, particularly high values, are limited with numerous pulmonary and extrapulmonary side effects. Generally speaking, PEEP may reduce cardiac output (CO), cause excessive distension of the alveoli and deteriorates oxygenation at unilateral lung diseases and at existence of a cardiac shunt⁷. Application of inadequate PEEP values can lead to excessive distension of other parts of the lungs causing barotrauma (pneumothorax or pneumomediastinum), but also biotrauma- diffuse damage of lung and other organs due to release of inflammatory mediators⁸. Intrathoracic pressure variations in the MV which occur with the use of special high values of PEEP may also affect the function of the cardiovascular system, and thus the distribution of perfusion. This is due to the fact that increased intrathoracic pressure can reduce the filling of the right ventricle of the heart with a consequent reduction in CO, which will result in an undesirable deterioration of oxygenation of arterial blood. When setting a value of PEEP it is recommended to use invasive hemodynamic monitoring to assess the volume status of the patient and to minimize the side effects on the perfusion⁹. It should not be forgotten that the brain injury with increased intracranial pressure (ICP) is the most important relative contraindication for using of these
high values of PEEP. Titration of optimal level of PEEP is still a question of debate and numerous studies. For determining of adequate levels of PEEP there are numerous methods. One method is to set the PEEP to the desired level of oxygenation. The desired level of oxygenation is defined as achieving the target value of PaO2 and SaO2 in BGA by applying the appropriate level of PEEP that allows the reduction of FiO2 to 0.6 without hemodynamic disturbances. Another method is the one that the desired level of PEEP is determined by a typical curve pressure / volume. A typical individual curve pressure / volume is obtained when the lungs are inflated with defined volume of air and then noted a certain airway pressure. By following the curve of the pressure / volume, parameters of MV can be adjusted as to benefit the region with the highest compliance (C). Target PEEP value is determined to be 2-3 cmH2O higher than the value of the crossing points of zone I to the zone II on the observed curve (LIP - lower inflection point). Next method that is generally reserved for patients with a diagnosis of ARDS/ALI is esophageal pressure measuring. This pressure measurements determines transpulmonary pressure which then serves as a guide in choosing an adequate level of PEEP.

In order to achieve adequate oxygenation we can also use application of recruitment, increasing of the I: E ratio, maintaining spontaneous respiratory activity and patient positioning.

HOW TO ACHIEVE ADEQUATE VENTILATION CONTROL IN MECHANICAL VENTILATION?

Adequate, sufficient ventilation, i.e. CO2 elimination is achieved by adjusting the tidal volume (Vt) and respiratory frequency (RF). Today it is widely accepted that in prevention of secondary damage of the lungs ("VILLI") it is necessary to apply as lower Vt as possible and it should be in a range of 6-10 ml/kg of ideal body weight (IBW). Thus, in patients with a diagnosis of ARDS/ALI it is recommended that Vt should be limited to 6 ml / kg IBW, in patients with COPD is recommended Vt 6-8 ml / kg IBW, and for postoperative MV as well as in patients with neuromuscular diseases Vt should be in the range of 8-10 ml / kg IBW. In settings of Vt for each patient we should keep the rule according to which the measured plateau pressure should be in the range of 25-30 cm H2O, which is safe for most of patients. If the measured plateau pressure exceeds 30 cmH2O it is necessary to reduce the Vt value because this pressure can be potentially harmful, and can cause barotrauma. We must not forget that besides Vt, this pressure is also affected by the value of PEEP, the auto-PEEP and C.

Adequate ventilation i.e. elimination of CO2 can also be achieved by adjusting the respiratory frequency (RF). RF and Vt determine minute ventilation. RF should be set in the range of 15-25 /min. in order to achieve the minute ventilation of 100 ml/kg/min. Settings of RF adapts to each patient individually. Thus, in patients with a diagnosis of ARDS it is recommended to use lower Vt and larger RF with compensatory shorter expirium, because in ARDS there is lower value of C and near normal airway resistance (R). In patients with COPD will apply lower Vt with lower RF and a longer duration of expirium in order to prevent air trapping and dynamic hyperinflation. The basic algorithm of MV settings in order to control PaCO2 and pH values, must be adjusted to respect the criteria of mechanical safety in the application of MV. The criteria used to obtain mechanical safety are: Vt limited to 6 ml / kg IBW, maximum plateau pressure 28-30 cmH2O, limited peak airway pressure and avoiding the appearance of internal PEEP. In satisfying these criteria of mechanical safety, we should take care that the value of the static end-inspiratory pressure, peak airway pressure and internal PEEP depend also on passive mechanics of the respiratory system which consists of C, airway resistance (R) and the time constant that represents the product of R and C. In adults reasonable starting value of the minute ventilation is 100 ml / kg / min and relates to the IBW. However minute ventilation required to achieve good control of PaCO2 and pH is often much higher due to the large production of CO2 and impaired lung function. In that case also you must choose between an aggressive approach that applies as long as patients do not show side effects and permissive approach that allows permissive hypercapny i.e. exceeding the target value of PaCO2 and pH.

CHOICE BETWEEN NONINVASIVE AND INVASIVE MECHANICAL VENTILATION

At the initiation of MV it is important to make a good choice between the noninvasive (NIMV) and invasive (IMV) mechanical ventilation. It is also important to maintain spontaneous respiratory activity and to use a ventilator to assist spontaneous breathing of the patient and not to use it to provide complete controlled ventilation. During the initiation of MV, and later in its course, we have to adjust model of MV to a nature of the underlying disease with optimization of alveolar recruitment. Of course, we should not forget the principles of “lung protection strategy.” Right choice between noninvasive and invasive MV is often difficult to make. Firstly, we should try NIMV if there are indications for it, but we should not be late with IMV because the lost time irreparably, especially in critically ill patients.

Candidates for NIMV are patients with mild forms of R1 and this form of MV can be successfully applied in some patients who can quickly recover from the underlying disease. NIMV is indicated in patients wit: acute exacerbation of COPD, cardiogenic pulmonary edema, immunocompromised patients, after resection lung parenchyma, after separation from the ventilator and exubation.

NIMV can be applied by the oronasal or nasal masks, mostly with Pressure support ventilation (PSV), continuously or intermittently. NIMV can be also used by biphasic positive airway pressure (BIPAP). PS model achieves assisted spontaneous breathing. In applying of this model, ventilator generates an increased positive airway pressure synchronized with the action of the respira-
tory muscles and thus to act as an external mechanical assistance to the inspiratory muscles \(^5\). Physiological response to this is increased Vt, followed by a decrease in respiratory activity which will reduce RF and amplitude of contractions of the respiratory muscles.

IMV is indicated in patients with severe acute respiratory failure (ARF) with the criteria for orotracheal or nasotracheal intubation. This type of MV can be also applied by tracheostomocannula, usually in cases of prolonged MV. It is of great importance, especially for the young and inexperienced doctors in ICU, to define exact criteria for endotracheal intubation. These are: respiratory distress with dyspnea and using of auxiliary respiratory muscles and paradoxical abdominal breathing, RF more than 25 / min and the pH value of less than 7.35, with a PaCO\(_2\) greater than 45 mmHg \(^9\). IMV strategy depends on the severity of lung disease, associated diseases, the need for sedation and condition of the respiratory muscles. IMV can be volume or pressure controlled (VCV or PCV). According to a contemporary attitudes meaningful is to choose the modalities of MV which are pressure-controlled to protect the lungs from secondary damage \(^1\).

If oxygenation was significantly undermined, the rule is to start MV with FiO\(_2\) 1.0, while PEEP should be gradually increased. Initiation of IMV can be applied with fully controlled ventilation in more serious forms of ARF by application of volume controlled ventilation (VCV), pressure controlled ventilation (PCV), biphasic positive airway pressure (BIPAP), synchronized intermittent mandatory ventilation (SIMV) or PC-SIMV and that with a large number of mandatory ventilation. Milder forms of RI can allow a greater degree of respirator-patient interplay and application of PSV, BIPAP, SIMV / PC-SIMV with a small number of mandatory ventilation. Selection of an optimal model of MV is important, but more important is to set the parameters of ventilation \(^2\).

In VCV duration of inspiratory is determined by flow, Vt and the form of flow curve (flow pattern), while the in PCV inspiratory duration is set directly. It is normal that the expiration lasts longer than inspiration in the following ratio I: E - 1: 2. In severe forms of COPD, it is necessary to extend the duration of expiration ie. it is necessary to apply a lower I: E ratio, also less RF and lower Vt with higher inspiratory flow rate \(^2\). For severe forms of restrictive lung disease, parameters will be set as follows: smaller Vt, more RF with prolonged inspiratory duration and greater I: E ratio that will lead to an increase in mean airway pressure (MAP) and improve oxygenation (greater PaO\(_2\) in BGA) \(^2\). In both of these cases hemodynamic parameters and auto-PEEP must be carefully monitored. In very serious diseases as obstructive and restrictive sure to consider the acceptance of controlled hypoventilation and permissive hypercapnia to prevent even greater damage of the lungs caused by using the MV with the parameters that we want to achieve the ideal gas exchange.

**HELPING FUNCTION OF RESPIRATORY MUSCLES IN MECHANICAL VENTILATION**

Although applying MV always gives priority to the adequate oxygenation and ventilation, the third, but no less important goal of MV is helping respiratory muscles in overcoming muscle work \(^5\). Maintenance of spontaneous respiratory activity is important because of: recruitment of dependent parts of the lungs, prevention of respiratory muscle atrophy, reduce the need for sedatives, improve hemodynamic parameters \(^2\). In the application of certain modalities of MV, ventilator can generate an increase in positive airway pressure synchronously with action of respiratory muscles and thus to act as an external mechanical assistance inspiratory muscles. Physiological response to this will be accompanied by an increase in Vt, reduction of spontaneous respiratory activity leading to a reduction in RF and reducing the amplitude of respiratory muscle contraction. Various forms of assisted MV can be used in support of respiratory function that is performed with the effort at particular patient. PSV is a model of assisted MV which delivers the required level of support independent of patient effort to breathe. In Proportional assisted ventilation (PAV) and NAVA-assisted breathing set neuraly, level of support is adjusted from time to time to reduce the effort of breathing \(^5\).

The greater the effort, the greater work of breathing requires a higher level of assistance, support.

Targets MV is based on the basic principles of MV, which means always to avoid pronounced respiratory distress and fatigue, as well as total suppression of spontaneous breathing \(^1\). Some spontaneous respiratory activity we must maintain. Therefore, the ventilator should be used to assist spontaneous breathing of the patient, and not to provide absolute control of ventilation. What should be avoided is asynchrony, ie. the struggle between the patient and the ventilator \(^3\). It occurs mainly due to inefficient triggers. The combination of MV controlled by pressure and spontaneous breathing (PCV, BIPAP, or PC-SIMV) fits into the concept of MV that protects the lungs from secondary lesions, because it improves the oxygenation and hemodynamics, improves ventilation, prevents asynchronous ie. fight a patient with a ventilator, and of course saves sedatives and analgetics. Importantly, remember that at the initiation of MV requires sedation, or total suppression of spontaneous breathing and the application of muscle relaxants should be avoided wherever is possible \(^2\). But, in relatively recently published study by Papazian et al., they showed that, in case of severe ARDS short period MV fully controlled with the using of muscle relaxants, reduce mortality \(^2\). This basic strategy must be adjusted to the clinical condition of the patient with a shift to more or less spontaneous breathing, depending on the phase of MV, or whether it comes in escalation or deescalation phase. One of the dilemmas we face with is which model of MV to apply in certain groups of critically ill patients. Usually, there are more then one model of MV which we can use in every clinical problem. Which model of MV will be used for the initiation depends on the available equipment ie. the
type of ventilator that we use, as well as the experience of staff in the ICU.

**DEESCALATION OF MECHANICAL VENTILATION**

By definition, deescalation means a timely reduction of ventilatory support. When the condition of critically ill patients improves and as soon as the first signs of recovery shows, it is necessary to begin reducing of ventilatory support timely and step by step. Now, it is generally accepted consensus that it is useful to think about deescalation from the moment of initiation of MV. Deescalation of MV is based on good clinical practice and constant, focussed attention on the patient and his general condition. Practically, it consists of application of partial ventilatory support which provides a certain part of minute ventilation and the rest of minute ventilation is provided by inspiratory effort the patient. At this stage, interaction patient-ventilator is very important. Advantages of this approach of the MV are: prevention of respiratory muscles atrophy, keeps the respiratory strength and way of breathing, the less needs for sedatives and relaxants and better hemodynamic response to positive pressure ventilation, and a better ventilation in the dependent parts of the lungs. A disadvantages are harder reaching the desired gas usually great work of breathing.

Deescalation of MV requires an adjustment of the value of FiO₂, PEEP and the level of support. It can start with any model of MV with a gradual reduction of ventilatory support, and continues to PSV with the gradual reduction of FiO₂, PEEP and pressure support (PS). Depending on the development of primary disease, deescalation may take a short time (a few hours) or a longer period of time (several days or even weeks). If there is no progress in the reduction of the ventilatory support or if the patient’s condition deteriorates, deescalation may be interrupted. In patients with severe lung failure and with left ventricular insufficiency, deescalation of the positive pressure and PEEP should be done with special care and slowly.

Deescalation of PEEP should not be based only on the frequent monitoring of BGA, but also on the evaluation of lung mechanics and lung CT findings.

If deescalation of PEEP is done too fast, oxygenation dramatically worsens and the patient’s recovery is slowing significantly.

**CONCLUSION**

In everyday clinical practice, when we make a decision about intubation and initiation of mechanical ventilation, instead of the list of indications, it is better to follow next simple rules: indication for intubation and mechanical ventilation is already when you just thinking about them, the decision for intubation is not a reflection of personal weaknesses of physician who indicated it and the initiation of mechanical ventilation in a critical ill patient is not a kiss of death, but rather to say a chance for healing.

It is important to start initiation and deescalation of mechanical ventilation in a right time and implement them to each patient individually.

Today, it is generally accepted consensus that it is useful to think about deescalation from the moment of initiation of mechanical ventilation.

Ventilator for mechanical ventilation should be used for supporting of spontaneous breathing of the patient, not to provide absolute control of ventilation.

Lung protective strategy is very important as well during the initiation and deescalation of mechanical ventilatio, as during all phases of the implementation of mechanical ventilation.

**SUMMARY**

**INICIJACIJA I DEESKALACIJA MEHANIČKE VENTILACIJE**

Dve velike dileme vezane za primenu mehaničke ventilacije su kada i kako je započeti (inicijacija) i u kom trenutku i kako započeti smanjenje mehaničke respiratorne potpore (deeskalacija). Obe ove dileme nije lako razrešiti pogotovo ako je lekar koji se sa njima suočava mlad i neiskus. Osnovni koncept inicijacije mehaničke ventilacije je jednostavan i podrazumeva podešavanje inspiratorne koncentracije kiseonika (FiO₂) i pozitivnog end-ekspiratornog pritiska (PEEP) u cilju kontrole oksigenacije, kao i disajnog volumen (VT) i frekvence disanja u cilju adekvatne eliminacije CO₂. Deeskalacija mehaničke ventilacije je proces koji treba započeti blagovremeno čim respiratorni status i opšte stanje bolesnika počnu da se popravljaju. Postoji koristan konsensus da deeskalaciju mehaničke ventilacije treba razmatrati praktično od trenutka inicijacije. Deeskalacija podrazumeva prilagođavanje i podešavanje FiO₂, PEEP-a i nivoa potpore. Izvodimo je bilo kojim modelom mehaničke ventilacije koji se nastavlja sa PSV ("pressure support ventilation") uz postepeno smanjivanje FiO₂, PEEP-a i pritiska podrške, zavisno od toka osnovne bolesti.

Ključne reči: mehanička ventilacija, inicijacija, deeskalacija.

**REFERENCE:**


