

DOI: [10.4081/monaldi.2020.1176](https://doi.org/10.4081/monaldi.2020.1176)

**Use of inhaled devices during a hospital exacerbation of COPD: a summary of an interdisciplinary audit held at ICS Maugeri Pavia, Italy (March- June 2019)**

**Michele Vitacca<sup>1</sup>, Cinzia Lastoria<sup>2</sup>, Monica Delmastro<sup>2</sup>, Domenico Fiorenza<sup>1</sup>, Pasquale De Cata<sup>2</sup>, Barbara Fusar Poli<sup>2</sup>, Sonia Gilè<sup>3</sup>, Paola Prometti<sup>1</sup>, Mara Paneroni<sup>1</sup>, Cristina Bianchi<sup>2</sup>, Elena Mandora<sup>1</sup>, Roberta Porri<sup>2</sup>, Claudio Fracchia<sup>1</sup>**

Department of Respiratory Rehabilitation, ICS Maugeri IRCCS

<sup>1</sup>Institute of Lumezzane (BS); <sup>2</sup>Institute of Pavia; <sup>3</sup>Institute of Montescano (PV), Italy

**Correspondence:** Michele Vitacca, Istituti Clinici Scientifici Maugeri IRCCS, Department of Respiratory Rehabilitation, Via Salvatore Maugeri 4, 27100 Pavia, Italy. E-mail: [michele.vitacca@icsmaugeri.it](mailto:michele.vitacca@icsmaugeri.it)

**Key words:** Relapse; inhaled therapy; devices; COPD.

---

**Supplementary Table 1. Literature review.**

Author	Drug used	Observations
<b>Ref 17</b>		<p><b>Level I:</b> outpatient treatment: Short-acting <math>\beta</math>2-agonist and/or ipratropium MDI with spacer or hand-held nebuliser as needed. Consider adding long-acting bronchodilator if patient is not using one.</p> <p><b>Level II:</b> treatment for hospitalised patient; Short-acting <math>\beta</math>2-agonist and/or Ipratropium MDI with spacer or hand-held nebuliser as needed.</p> <p><b>Level III:</b> treatment in patients requiring special or intensive care unit Short-acting <math>\beta</math>2-agonist (salbutamol [albuterol] and ipratropium MDI with spacer, two puffs every 2-4 h. If the patient is on the ventilator, consider MDI administration. Consider long-acting <math>\beta</math>-agonist.</p>
<b>Ref 18</b>	<p>Albuterol, 5 mg nebulizer/ 800 mg MDI  Salbutamol, 2.5/5 mg nebulizer/  Metaproterenol, terbutaline 200x10/400x7/600mg x2</p>	<p>20 studies (507 pts); all studies (with the exception of 2) used the spacer device with MDI.  MDI and nebulizer were equivalent.  The method may depend by necessity, staff availability, costs.</p>
<b>Ref 19</b>	<p>It is recommended to use inhaled short-acting bronchodilators (<math>\beta</math>-2 agonists with or without anticholinergics) in case of AECOPD managed on an inpatient basis.  Evidence is lacking in the literature to propose the use of long-acting bronchodilators in case of AECOPD managed on an inpatient basis. In case of severe exacerbation, it is recommended to use a nebulized drug administration.</p>	<p>Evidence is lacking in the literature to propose the use of inhaled corticosteroids in case of AECOPD managed on an inpatient basis. Using inhaled magnesium is not recommended in the treatment of AECOPD.</p>
<b>Ref 20</b>	<p>Short-acting anti-muscarinic agent (SAMA) can be used as rescue medication to relieve patient symptoms.</p>	

	<p>Long term SAMA monotherapy on regular basis is not recommended.</p> <p>Short-acting <math>\beta</math>-agonist (SABA) can be used to relieve symptoms of dyspnoea as and when needed.</p>	
	<p>Inhaled SABAs should be used as the first-line agent because of quicker onset of action.</p> <p>SAMAs are however, in no way inferior to SABAs. Inhaled route is the preferred route of administering bronchodilators.</p> <p>Nebulizer or MDIs with spacer are equally effective. Nebulization should not be driven by oxygen; patients should receive oxygen separately through nasal cannula, with monitoring of oxygen saturation.</p> <p>Nebulized salbutamol at a dose of 2.5 mg every 20 min (or salbutamol pressurized metered dose inhaler (MDI) 100 <math>\mu</math>g 2-4 puffs every 20 min) for 1 h can be given initially.</p> <p>Further dosing would depend on the clinical response, generally every 4-6 h.</p> <p>If additional bronchodilation is desired, a combination of ipratropium (500 <math>\mu</math>g nebulized or 20 <math>\mu</math>g 2-4 puffs with MDI) and salbutamol (2.5 mg nebulized or salbutamol MDI 100 <math>\mu</math>g 2-4 puffs) every 4-6 h can be used.</p>	<p>Intravenous methylxanthines should not be routinely used.</p> <p>The use of intravenous or subcutaneous route of administering bronchodilators should be reserved in the most seriously ill mechanically ventilated patient demonstrating inadequate response to inhaled therapy.</p>
<b>Ref 21</b>	<p>Nebulized, short-acting bronchodilator 4 to 6 times daily as needed while hospitalized.</p> <p>Inhaled glucocorticoids twice daily combined with inhaled 2-agonist twice daily plus tiotropium 18 mg once daily.</p>	<p>To investigate whether a short-term (5 days) systemic glucocorticoid treatment in patients with COPD exacerbation is not inferior to conventional (14 days) treatment in clinical outcome.</p>
<b>Ref 22</b>	<p>Milder exacerbations may respond to an increase in the dose and/or frequency of existing bronchodilator therapy.</p>	

	Increasing the dose and frequency of short-acting bronchodilators is a necessary first step in the treatment of acute exacerbations, with the addition of oral corticosteroids for individuals unresponsive to the first intervention.	
<b>Ref 23</b>	Pharmacological treatment included bronchodilators, corticosteroids and antibiotics. Bronchodilator use ( $\beta$ -agonists and anticholinergics) ranged from 91% to 100%. In most cases, corticosteroids were administered in 80–88% of patients. Nebulizer use ranged from 32% to approximately 100%, metered dose inhaler use, which ranged from 44% to 60%.	Adherence to bronchodilator therapy was high, ranging from 90% to 100%. Bronchodilators were delivered by nebulizer in 80–98% of cases. Both ERS and GOLD guidelines advice against the use of nebulizers and recommend use of metered dose inhalers and dry powder inhalers if possible. Literature indicates that use of wet nebulizers is more expensive, require appropriate maintenance, and have many adverse effects ( <i>i.e.</i> highly variance in performance, less adherence to therapy).
<b>Ref 24</b>	SABA SABA + Ipratropium MDI/NEBULIZER	LOS as outcome
<b>Ref 25</b>	- Salbumatol - Ipratropium - ICS + LABA (Fluticasone/salmeterol o Budesonide/formoterol) -Tiotropium	In comparison to internists, pulmonologists prescribe triple therapy more frequently. Minor LOS in internal units vs respiratory units. Equal mortality.
<b>Ref 26</b>	SABA + SAMA Aerosol vs MDI	MDI devices present better efficacy compared to aerosol. MDI devices caused less costs.
<b>Ref 27</b>	Inhaled short-acting $\beta$ 2-agonists, such as albuterol, and anticholinergic bronchodilators, such as ipratropium are equally efficacious in the care	Patients receiving a short-acting $\beta$ 2-agonist plus an anticholinergic bronchodilator had marginally shorter lengths of stay and proportionally larger increases in FEV1, but hospital admission rates were similar. Because anticholinergic bronchodilators are associated with fewer and milder side effects, it is advisable to start with them and then add a short-acting $\beta$ 2-agonist.

		The efficacies of wet nebulization and dry aerosol delivery systems (metered-dose inhaler plus a spacer) are clinically equivalent.
<b>Ref 28</b>	SABAs, with or without short-acting anticholinergics inhaled and nebulized	Only 79% of patients in hospitals receive this treatment for exacerbations
<b>Ref 29</b>	<p>Albuterol Metered-dose inhaler 100–200 µg 4 times daily</p> <p>Albuterol Nebulizer 0.5–2.0 mg 4 times daily</p> <p>Albuterol Pill 4mg Twice daily</p> <p>Fenoterol Metered-dose inhaler 12–24 µg Twice daily</p> <p>Metaproterenol Nebulizer 0.1–0.2 mg 4 times daily</p> <p>Metaproterenol Pill 10–20 mg 3 to 4 times daily</p> <p>Terbutaline Metered-dose inhaler 400 µg 4 times daily</p> <p>Ipratropium Metered-dose inhaler 18–36 µg 4 times daily</p> <p>Ipratropium Nebulizer 0.5 mg 4 times daily</p>	<p>For both inpatients and outpatients, combined bronchodilator therapy should be used, with ipratropium bromide and albuterol administered every four to six hours initially.</p> <p>Nebulizers are recommended whenever the patient’s distress level raises doubt about the effective use of a metered-dose inhaler. As the condition improves and the distress level is reduced, metered-dose inhalers can be used in place of nebulizers.</p> <p>Inhaled beta-adrenergic agonists and anticholinergic agents can improve airflow during acute exacerbations.</p> <p>β-adrenergic agonists have not been shown to be superior to anticholinergic agents.</p> <p>Factors such as the time to peak effect (which is slightly more rapid with beta-adrenergic agonists) and the frequency of adverse effects (which are generally fewer and milder with ipratropium. Equivalent bronchodilation appears to be achieved with the use of metered-dose inhalers or nebulizers.</p> <p>Metered-dose inhalers cost less than nebulizers, but are frequently ineffective during respiratory distress, it is reasonable to initiate therapy with nebulizers and then switch to metered-dose inhalers when clinically feasible.</p>
<b>Ref 30</b>	<p>Short-acting β<sub>2</sub>-agonists with or without short-acting anticholinergics.</p> <p>Inhaled (metered dose inhalers (with or without a spacer device) or nebulizers.</p>	<p>There are no significant differences in FEV<sub>1</sub> when using metered dose inhalers (with or without a spacer device) or nebulizers to deliver the agent, although the latter may be an easier delivery method for sicker patients.</p> <p>Mild exacerbations treated with short-acting bronchodilators only.</p> <p>Moderate exacerbations treated with short-acting bronchodilators plus antibiotics and/or oral corticosteroids.</p>

<b>Ref 31</b>	SABA and SAMA	Methylxanthine is dangerous. FEV <sub>1</sub> % improved. Low side effects with ipratropium. Albuterol: urine retention, tremor, headache, nausea, palpitations No evidences that MDI are better than aerosol.
<b>Ref 32</b>	SABA + LAMA	There is no difference in the objective outcomes between the use of nebulized bronchodilators or bronchodilators given through an MDI with a spacer. Due to the lower cost of using MDIs with a spacer, this route is preferred in most situations. There is no role for the initiation of therapy with methylxanthines during an AECOPD. For patients who are already on an oral methylxanthine product, it is reasonable to continue the medication during an AECOPD.
<b>Ref 33</b>	DPIs (dry powder inhalers) DPI MDI salbutamol +/- spacer	Flow obstruction is a negative predictor for inhalation (mandatory minimum Inspiratory Flow >30 l/min)
<b>Ref 34</b>	Budesonide 4 mg - 8 mg Prednisone 40 mg every 6/12 h for >7 days Budesonide + formoterol or Budesonide + ipratropium	No inferiority study for ICS vs systemic steroid. PaO <sub>2</sub> was better (2 mmHg) with systemic steroid, but glycemia and arterial pressure worsened. Budesonide better in diabetics and CHF patients.
<b>Ref 35</b>	LABA + ICS + LAMA	No optimal treatment if conducted by internists
<b>Ref 36</b>	O <sub>2</sub> therapy (79%) Steroids per o.s. (82%) Antibiotics (87%) Shift from aerosol to inhaled devices (46%)	In rural hospitals new admissions were higher (27%) vs urban hospitals (7%).
<b>Ref 37</b>	All patients received inhaled bronchodilators: 65% patients received short-acting $\beta$ agonists (SABA), 78% received short-acting muscarinic agonists (SAMA), 24% received long-acting muscarinic agonists (LAMA),	Overall adherence to guidelines was moderately good. All patients received antibiotics, and most patients received oxygen, which are both recommended for all patients.

	2% received long-acting beta-agonists (LABA), and 40% received both SABA and SAMA	More patients received SAMA than SABA, although SABA is more effective and therefore the first-line treatment for COPD exacerbation.
<b>Ref 38</b>	Comparison between Switzerland and other European countries in hospital COPD relapse treatment	In comparison to other European countries, antibiotics were prescribed 14% less often in Switzerland. Only 79% of the patients in the Swiss cohort received treatment with a short-acting bronchodilator at admission.
<b>Ref 39</b>	Ipratropium bromide 83% Salbutamol 94% None documented 3% Nebulized 31% Through spacers 43%	Definition of exacerbations: i) increased dyspnoea; ii) increased sputum production; iii) increased sputum purulence; and iv) social issues. Most patients (65%) had documented input by respiratory physiotherapists.
<b>Ref 40</b>	ED treatment included inhaled short-acting $\beta$ agonists for 91% of patients, inhaled anticholinergics for 77%, methylxanthines for 0.3%, systemic corticosteroids for 62%, and antibiotics for 28%.	Important differences exist between guideline recommendations and actual Emergency Department management of COPD exacerbations in older adults.