MEDICATION MANAGEMENT IN AGED CARE WHILE MITIGATING COVID-19

RESPIRATORY CONDITIONS

Infection with severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2, also known as COVID-19) may result in significant lung morbidity and death.

Infection with COVID-19 stimulates an inflammatory response that is responsible for some of the cardinal features of COVID-19 such as shortness of breath and cough (see **Figure 1**). In severe cases, this inflammatory response intensifies and an acute respiratory distress syndrome may result from the ensuing cytokine storm. A number of immune suppressive agents are being investigated for therapeutic use during this phase of the disease, and corticosteroids are currently recommended for adults with moderate to severe COVID-19.[1]

KEY POINTS

Patients with mild to moderate asthma do not appear to be at increased risk of worse outcomes from COVID-19.

Patients with COPD are at increased risk of worse outcomes, including mortality, from COVID-19.

Optimising lung function in patients with COPD will likely improve outcomes in the event of COVID-19.

Optimising and simplifying inhaler device usage leads to reduced frequency of COPD exacerbations.

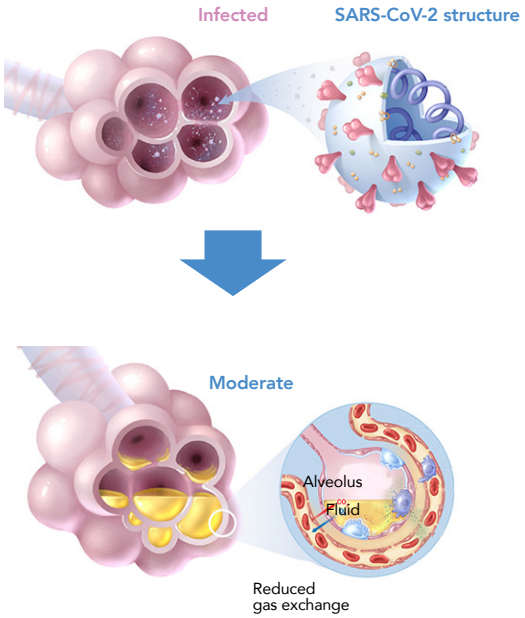
The presence of pre-existing lung pathology (asthma, chronic obstructive pulmonary disease and smoking) may impact on the likelihood of becoming infected with SARS-CoV-2 and may also impact on the clinical course and outcome of COVID-19. Optimising respiratory function pre-emptively is likely to improve COVID-19 outcomes.

Viral infection

The spike proteins covering the coronavirus bind ACE2 receptors primarily on type 2 alveolar cells, allowing the virus to inject its RNA. The RNA "hijacks" the cell, telling it to assemble many more copies of the virus and release them into the alveolus. The host cell is destroyed in this process and the new coronaviruses infect neighboring cells.

Immune response

1. After infection, type 2 cells release inflammatory signals that recruit macrophages (immune cells).
2. Macrophages release cytokines that cause vasodilation, which allows more immune cells to come to the site of injury and exit the capillary.
3. Fluid accumulates inside the alveolus.
4. The fluid dilutes the surfactant which triggers the onset of alveolar collapse, decreasing gas exchange and increasing the work of breathing.
5. Neutrophils are recruited to the site of infection and release Reactive Oxygen Species (ROS) to destroy infected cells.
6. Type 1 and 2 cells are destroyed, leading to the collapse of the alveolus and causing Acute Respiratory Distress Syndrome (ARDS).
7. If inflammation becomes severe, the protein-rich fluid can enter the bloodstream and travel elsewhere in the body, causing Systemic Inflammatory Response Syndrome (SIRS).
8. SIRS may lead to septic shock and multi-organ failure, which can have fatal consequences.



Impaired gas exchange

When the immune system attacks the area of infection it also kills healthy alveolar cells. This results in three things that hinder gas exchange:

1. Alveolar collapse due to loss of surfactant from type 2 cells
2. Less oxygen enters the bloodstream due to lack of type 1 cells
3. More fluid enters the alveolus

Figure 1: Inflammatory processes and their consequences in the alveolus after COVID-19 infection

RESPIRATORY CONDITIONS AND COVID-19 INCIDENCE/ PROGRESSION

Asthma

A meta-analysis of 57 studies examining asthma and COVID-19 infection and outcomes with an overall sample size of 587,280 was undertaken by an Australian group of authors.[2] The prevalence of asthma among those infected with COVID-19 was 7.46% (95% CI=6.25-8.67), similar to global estimates for asthma. Pooled analysis showed a 14% risk ratio reduction in acquiring COVID-19 (95% CI=0.80-0.94; p<0.0001) and 13% reduction in hospitalisation with COVID-19 (95% CI=0.77-0.99, p=0.03) for people with asthma compared with those without. There was no significant difference in the combined risk of requiring admission to ICU and/or receiving mechanical ventilation for people with asthma (RR=0.87 95% CI=0.94-1.37; p=0.19) and risk of death from COVID-19 (RR=0.87; 95% CI=0.68-1.10; p=0.25). The overall findings suggest that, reassuringly, people with asthma seem to have a lower risk than those without asthma for acquiring COVID-19 and if they do acquire it, have similar clinical outcomes to people without asthma.

Smoking

Smoking is already known to be a risk factor for many other respiratory infections, including colds, influenza, pneumonia and tuberculosis. Smoking is also associated with increased development of acute respiratory distress syndrome, a key complication for severe cases of COVID-19.

A systematic review and meta-analysis of 34 studies, pre-published in January 2021, showed that being a smoker or former smoker was a risk factor for worse progression of COVID-19 infection (OR 1.96, 95% CI, 1.36 - 2.83) and a greater probability of severe COVID-19, including ICU admission, intubation and death (OR 1.79, 95% CI, 1.19 - 2.70).[3]

Chronic obstructive pulmonary disease

A systematic review (November 2020) and meta-analysis reviewed 72 studies that examined associations between various lung conditions and mortality in 69,762 COVID-19 positive people (predominantly from China, Europe, the United Kingdom and the United States).[4] They included 46 studies that examined chronic obstructive pulmonary disease (COPD) or other chronic lung disease (not cancer or asthma) and found that the pooled odds ratio for death was 2.54 (95% CI 1.87 – 3.44) for COPD (28 studies) and 3.12 (95% CI 2.17 – 4.49) for chronic lung disease (18 studies).

CORTICOSTEROID USE

Systemic corticosteroids

The National COVID-19 Clinical Evidence Taskforce has made a consensus recommendation concerning the use of steroids for people with asthma or COPD who have COVID-19.[5] They suggest that oral corticosteroids are not recommended for symptoms of COVID-19 alone, however patients who are having an exacerbation of COPD should start a course of oral corticosteroids and/or antibiotics if they are clinically indicated.

If people are receiving oral corticosteroids as maintenance therapy for airways disease, stopping them may lead to exacerbation of symptoms of asthma or COPD and the risk of relative adrenal insufficiency. It should be noted that if people are receiving systemic corticosteroids for other indication, inhaled corticosteroids may no longer be required.

Inhaled corticosteroids

The use of inhaled corticosteroids for patients with COPD is recommended only in some situations. Use of high doses of inhaled corticosteroids (see **Table 1** for what constitutes high dose) has been associated with an increase in bacterial pneumonia events, while in appropriate circumstances, the use of inhaled corticosteroids can reduce the number of exacerbations of COPD. A number of factors are now considered relevant in determining when the use of inhaled corticosteroids may be beneficial. These factors are summarised below.[6]

Strong support for the use of inhaled corticosteroids:

- history of severe COPD exacerbation requiring hospitalisation
- two or more exacerbation in 12 months
- blood eosinophil count over 300 per microlitre
- history of concomitant asthma.

Factors arguing against the use of inhaled corticosteroids:

- repeated pneumonia events
- blood eosinophil counts <100 per microlitre
- history of mycobacterial infection.

Inhaled corticosteroid	Daily dose (micrograms)		
	Low	Medium	High
Beclometasone dipropionate (QVAR, Fostair)	100–200	250–400	>400
Budesonide (Pulmicort, Symbicort, DuoResp, Breztri)	200–400	500–800	>800
Ciclesonide (Alvesco)	80–160	240–320	>320
Fluticasone furoate (Arnuity, Breo, Trelegy)	—	100	200
Fluticasone propionate (Flixotide, Seretide, Cipla, Flutiform)	100–200	250–500	>500

Table 1: Dose ranges for inhaled corticosteroids available in Australia

INHALER DEVICES

There are a number of devices to assist delivery of respiratory medication to the alveolar/bronchial area. Dry powder inhaler devices often require reasonable inspiratory force and many patients obtain sub-optimal therapy due to either poor technique or insufficient inspiratory force to obtain maximum benefit. There is a variation in the resistance that different dry powder inhalers offer to delivery. A list of the relative resistance for different devices is shown in **Figure 2**.[7]

The Therapeutic Goods Administration (TGA) has recently approved the use of a triple therapy pressurised metered dose inhaler, Breztri (containing budesonide, glycopyrronium and eformoterol).[8]

Reviewing the technique and efficacy of inhaler device use with a view to optimising delivery of medication can improve respiratory outcomes, providing an improved baseline respiratory function should there be a COVID-19 outbreak.

Increasing resistance

Type of device	Examples
Pressurised metered dose inhaler	Ventolin Inhaler Seretide MDI Cipla Inhaler
Soft mist inhaler	Spiriva Respimat Spiolto Respimat
Breezhaler dry powder inhaler	Seebri Breezhaler Ultibro Breezhaler
Accuhaler dry powder inhaler	Seretide Accuhaler Serevent Accuhaler Flixotide Accuhaler
Ellipta dry powder inhaler	Anoro Ellipta Arnuity Ellipta Breo Ellipta Incruse Ellipta Trelegy Ellipta
Genuair dry powder inhaler	Bretaris Genuair Brimica Genuair
Breath actuated pressurised metered dose inhaler	Airomir Autohaler QVAR Autohaler Duoresp Spiromax
Turbuhaler dry powder inhaler	Bricanyl Turbuhaler Pulmicort Turbuhaler Symbicort Turbuhaler
Handihaler dry powder inhaler	Spiriva Handihaler

Figure 2: Relative inspiratory force required for different inhaler devices

MANAGEMENT OF LUNG DISEASE WHILE MITIGATING COVID-19

Information regarding COVID-19 and the management of lung conditions is available from the United Kingdom[9], Australia[10] and globally[11]. Fundamentally, these resources all focus on optimising management of the underlying respiratory condition and managing conditions as normal, with caveats around the use of corticosteroids (inhaled and systemic) and the use of nebulisers.

Optimise device technique

Improved delivery of medication results in improved management of CODP. Appropriate use of spacer devices and choice of dry powder inhaler devices that suit the patient's inspiratory capacity are critical steps in improved management.

Reduce different delivery devices

Many people with significant respiratory disease receiving multiple inhaled therapies, often with different devices for different products (e.g. Seretide/ Spiriva). There are a number of modern devices and combination products that incorporate commonly used therapeutic agents and in many cases it is possible to manage patients using a single type of device with an appropriate amount of inspiratory resistance. This reduces variability in delivery systems and may improve compliance and respiratory function.

Minimise number of dose administration times

Many modern inhaler devices for airways disease include quick-onset, long-acting beta agonists which provide significant acute relief from shortness of breath as well as longer-acting bronchodilation. By using devices containing long-acting beta agonists or antimuscarinics, the number of dose administration times can be reduced for many patients. Short-acting beta agonists can often continue to be used in a metered dose aerosol (with spacer) on a prn basis.

Avoid nebulisers

The use of a nebuliser creates fine droplets which can often escape from the face mask being used to deliver the medication. These droplets have been shown to increase the transmission of COVID-19 and the use during an outbreak is to be avoided.[12] Pre-emptively changing people who regularly or occasionally use nebulisers to a different suitable device would be appropriate. Many modern inhaler devices are as or more efficient than nebulised medications.

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