CASE REPORT

Inhaled treprostinil via the Tyvaso Inhalation System through a tracheostomy

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SUMMARY

A 20-year-old man with pulmonary arterial hypertension secondary to systemic sclerosis was admitted to our hospital. Prior to admission, his PAH had been successfully managed with the use of tadalafil, ambrisentan and inhaled Tyvaso. Owing to respiratory failure from vocal cord paralysis, he underwent an emergent tracheotomy. The delivery of inhaled Tyvaso through a tracheostomy tube was explored. Post-tracheostomy, the patient continued his ability to self-administer the medication. His WHO functional classification, brain natriuretic peptide levels, and echocardiograms were not significantly different when Tyvaso was administered via tracheostomy compared with oral administration. This case report summarises the method used to deliver Tyvaso via a tracheostomy tube, which proved to be successful in this patient.

(less septal flattening and improved right ventricular function).

DIFFERENTIAL DIAGNOSIS

Otolaryngology evaluation on admission identified new onset bilateral vocal fold paresis and airway inflammation as the aetiology for the stridor. The PAH team was consulted to assess if the inhaled treprostinil may be a causative factor in his vocal cord dysfunction, though it was suspected that the findings were most likely related to his underlying disease progression. However, due to the severity of the presentation and the possibility that it could be related to the relatively new initiation of Tyvaso, the patient was admitted to the paediatric intensive care unit (PICU), where he was carefully monitored as the inhaled treprostinil was weaned off. Unfortunately, 5 days after admission, the patient required emergent tracheotomy for acute airway obstruction and respiratory failure despite maximal medical management with racemic epinephrine, heliox and intravenous dexamethasone.

TREATMENT

During the course of the next week, the patient's oral PAH medications required alteration in delivery route. Ambrisentan was discontinued and bosentan suspension started. Tadalafil was also switched to a suspension and both medications were given via a gastric tube. Care of the patient included treatment of his systemic sclerosis, pain management, and physical therapy to regain strength and mobility. The patient improved and was able to be weaned off the ventilator and sedation medications. On hospital day 10, the patient was successfully transitioned to a humidified tracheostomy collar (HTC). He was transferred to the technology-dependent ICU (TICU) on hospital day 19, on a 28% HTC.

Owing to his improvement on inhaled treprostinil prior to admission and a desire to maximise his medical management of PAH, the care team discussed restarting the medication. With the patient awake, alert and able to follow commands, the PAH team and TICU respiratory therapist explored the possibility of restarting and delivering Tyvaso via the tracheostomy. On hospital day 30, Tyvaso was reinitiated using the patient's home delivery device and medication. The mouthpiece of the Tyvaso Inhalation System was removed and replaced with 15 mm straight adapters connected to both ends of a 6 inch piece of corrugated tubing to connect the patient's artificial airway to the

BACKGROUND

'Pulmonary arterial hypertension (PAH) is a progressive, life-threatening disease which, if left untreated, can lead to right ventricular failure and possibly death. Several effective therapies are now available to treat pulmonary hypertension, including phosphodiesterase five (PDE-5) inhibitors, endothelin receptor antagonists and prostacyclin analogues¹ either by subcutaneous, intravenous or inhaled route. In 2009, the Food and Drug Administration (FDA) approved treprostinil (Tyvaso) for oral inhalation in adults with PAH administered four times daily with a target dose of nine breaths per treatment session.¹ To date, there is no literature on the use of inhaled treprostinil in patients with tracheostomy tubes. The acute pharmacodynamic effects, safety and tolerability of inhaled treprostinil via tracheostomy has not yet been described or studied.

By presenting this case, medical personnel can explore the option of delivering Tyvaso via a tracheostomy should the need arise.

CASE PRESENTATION

A 20-year-old man with a history of systemic sclerosis-associated pulmonary arterial hypertension (PAH) with progressive stridor and respiratory distress presented to the emergency department (ED). His PAH had been managed with tadalafil and ambrisentan. Six weeks prior to presentation, he was also started on and uptitrated to goal dose (9 inhalations four times daily) of inhaled treprostinil (Tyvaso) with excellent subjective response (improved exercise capacity, less dyspnoea on exertion) as well as improvement in echocardiography

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Figure 1 Tyvaso Inhalation System to tracheostomy.

Inhalation System (figure 1). The initial dose of Tyvaso was three breaths four times daily.

OUTCOME AND FOLLOW-UP

While taking Tyvaso via the tracheostomy, our patient was monitored carefully for any potential side effects (of which there were none). The patient's WHO functional classification, brain natriuretic peptide levels and echocardiograms were not significantly different when Tyvaso was administered via tracheostomy compared with his data when receiving Tyvaso via oral inhalation (table 1).

The patient was discharged from the hospital 2 days after the re-initiation of Tyvaso. Up-titration continued at home by increasing the breaths by three every week until he successfully reached his preadmission dose of nine breaths four times daily. The patient continued the use of Tyvaso through his tracheostomy until he was able to occlude his tracheostomy tube and inhale the treprostinil orally.

DISCUSSION

Initially, there was concern that this patient's airway inflammation and bilateral vocal cord paresis may have been a side effect of the Tyvaso. In TRIUMPH 1, a 12-week double-blind placebo controlled study looking at the safety and efficacy of Tyvaso in 235 patients with Pulmonary Arterial Hypertension (WHO Group 1), 25% of the patients experienced throat irritation or pharyngolaryngeal pain compared to 14% in the placebo group.² Krishnan *et al* conducted a retrospective analysis of 29 paediatric patients receiving inhaled treprostinil along with other PAH therapies. Of the 20 patients who were able to achieve the goal dose of nine breaths per treatment four times daily, 6 (30%) of the patients complained of a sore throat but

the therapy was not discontinued.³ After the laryngoscopy in our patient, the medical teams felt the narrowing was not due to the inhalation of Tyvaso but, rather, disease progression from his systemic sclerosis, thus justifying re-initiation.

The pharmacodynamics, safety and tolerability of Tyvaso via tracheostomy has not yet been described or studied. Takatsuki *et al*⁴ utilised inhaled Tyvaso on patients in the catheterisation lab to assess its use in acute pulmonary vasodilator testing. Inhaled treprostinil was delivered by the OPTINEB-ir Model ON-100/7 ultrasonic nebulizer. For sedated patients breathing through a natural airway, the medication was delivered via an anaesthesia mask with a flow-inflating bag. For those anaesthetised and breathing through an endotracheal tube or laryngeal mask airway, the medication was delivered via the manual mode of the anaesthesia system in synchrony with the OPTINEB's inhalation indicator.⁴ The authors reported that "inhaled treprostinil had acute haemodynamic effects similar to those of inhaled nitric oxide and was well tolerated with an acceptable safety profile".⁴ The authors also stated "although the exact treprostinil dose administered to the patient may have decreased slightly by the delivery system dead space, the hemodynamic response suggests adequate drug delivery".⁴

Since Tyvaso is only FDA approved for oral inhalation, altering the mode of delivery must be performed with extreme caution. The dose delivered and particle deposition is unknown. The authors could not find any publications related to particle deposition from nebulised aerosols adhering to the surface of an artificial airway in the literature. It remains unknown if Tyvaso particles adhere to the inside of the tracheostomy tube, which may cause narrowing or occlusion of the lumen. Bypassing the pharyngolaryngeal portion of the airway and delivering the medication directly to the trachea may alter the absorption of the medication or cause inflammation in the trachea. The Tyvaso Inhalation System can only deliver medication using room air. If the patient requires oxygen supplementation, saturations should be monitored as desaturation may occur and lead to worsening of the pulmonary hypertension. In our patient, condensation occurred in the connector tubing, which may have altered the dose of the medication delivered to the airway.

Tyvaso was initiated in our patient via his tracheostomy temporarily, until he was able to occlude it and return to using the inhaled Tyvaso by mouthpiece. We carefully monitored the patient during his hospitalisation. Since the patient had previously used Tyvaso, he and his family were familiar with its side effects and told to call the PAH team if any arose.

Table 1 Patient data

	1 week prior to admission (PTA)	Hospital day 1	Hospital day 31 (1 day after initiation of Tyvaso via tracheostomy)	10 weeks after Tyvaso inhalation (taking via mouthpiece)
Tyvaso dose (inh QID)	9	9	3	9
Tricuspid regurgitation (TR) (mm HG)	40	35		42
Septal flattening	None	None		None
RV function	Normal	Normal		Normal
TAPSE (cm) (z score)	1.77 (−3.33)	1.89 (−2.76)		1.60
BNP (pg/mL)	20 (1 month PTA)	132	60	71
WHO class	4			4

inh QID, inhalations four times daily.

BNP, brain natriuretic peptide; RV, right ventricular.

Learning points

- ▶ Pulmonary arterial hypertension (PAH) is a progressive, life-threatening disease which, if left untreated, can lead to right ventricular failure and possibly death.
- ▶ There are three classes of drugs used to treat PAH: phosphodiesterase five inhibitors, endothelin receptor antagonists and prostacyclin analogues.
- ▶ Tyvaso is the inhaled formulation of treprostinil, a prostacyclin analogue.
- ▶ Delivering inhaled treprostinil via the Tyvaso Inhalation System through a tracheostomy proved successful in this patient.

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Neonatal and Childhood Pulmonary Vascular Disease in 2014. JH reviewed the current literature and developed the abstract into the initial manuscript of this report. AC, PL and DS read the manuscript for accuracy of details of the case, expanded the table and made contributions to the editing of the manuscript.

Competing interests None declared.

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