


# Heliox for Inducible Laryngeal Obstruction (Vocal Cord Dysfunction): A Systematic Literature Review

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**Objectives:** To perform a systematic literature review on the use of Heliox with patients with inducible laryngeal obstruction/vocal cord dysfunction to: i) identify current evidence base; and ii) establish the methodological quality of published research.

**Methods:** Articles published up to March 2018 were searched for key words and terms using Cochrane Library, MEDLINE, PubMed, CINAHL, EMBASE and Dynamed. Studies were included if they presented original research into the use of Heliox for vocal cord dysfunction.

**Results:** Only three studies met the inclusion criteria for review. All reported favorable results for the use of Heliox as an adjunctive therapy for vocal cord dysfunction but none had sufficient methodological quality to support their conclusions.

**Conclusion:** Despite review articles recommending the use of Heliox in vocal cord dysfunction, there is a lack of good quality research to support this conclusion. There is a need for further research to investigate the effectiveness of Heliox as an adjunctive therapy for vocal cord dysfunction.

**Key Words:** Heliox, inducible laryngeal obstruction, iLO, VCD, vocal cord dysfunction.

**Level of Evidence:** 4

## INTRODUCTION

### Vocal Cord Dysfunction

Vocal Cord Dysfunction (VCD) is an “...intermittent extra-thoracic airway obstruction, mainly during inspiration, leading to dyspnoea of varying intensity”.<sup>1</sup> During a VCD episode, a person’s vocal cords involuntarily adduct during inspiration (or less commonly expiration), leading to wheezing.<sup>2</sup> Up to 50% of patients with severe asthma also have concomitant VCD,<sup>3</sup> and VCD has been diagnosed in up to 22% of people presenting to emergency rooms with symptoms of sudden onset breathlessness.<sup>4</sup> However, VCD is often misdiagnosed as asthma, resulting in a delay in the diagnosis of VCD and unnecessary medical treatment.<sup>1</sup>

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The pathophysiology of VCD is not fully understood, but there are factors which may play a part in its manifestation, specifically laryngopharyngeal reflux (LPR) in excess of three episodes a week, post-nasal drip and psychological factors.<sup>4</sup>

A recent international consensus statement<sup>5</sup> has recommended, for the purposes of nomenclature, the term Inducible Laryngeal Obstruction (ILO) should be utilized. We acknowledge and support this and VCD fits under this classification system. However, to capture all historical references for the purpose of this review, we opted for the term VCD.

### Heliox

Heliox is a mixture of helium and oxygen. It is odorless, nonreactive to body tissues, and has no bronchodilating or anti-inflammatory properties.<sup>6,7</sup> It is nontoxic, noncarcinogenic and has no lasting effects on human organs.<sup>8,9</sup> As Heliox is inert and not metabolized, it can be used safely in most patients,<sup>7</sup> and its use for upper airway obstruction has been documented in the literature since the 1930s.<sup>10–12</sup> However, despite a long history of safe use,<sup>6</sup> it is not widely utilized in the treatment of VCD.

Currently, the most common indication for the use of Heliox is obstruction of the upper airways.<sup>7</sup> Inhaled Heliox can facilitate gas flow through narrow orifices, as it can pass through partial obstruction in the upper and lower airway with ease<sup>13</sup> due to it having lower density than air or oxygen. This decreases turbulent air flow,<sup>6</sup> and leads to more free-flowing laminar flow, with lower overall airway resistance.<sup>9</sup> As a result, less force is required to move Heliox through the airways. This

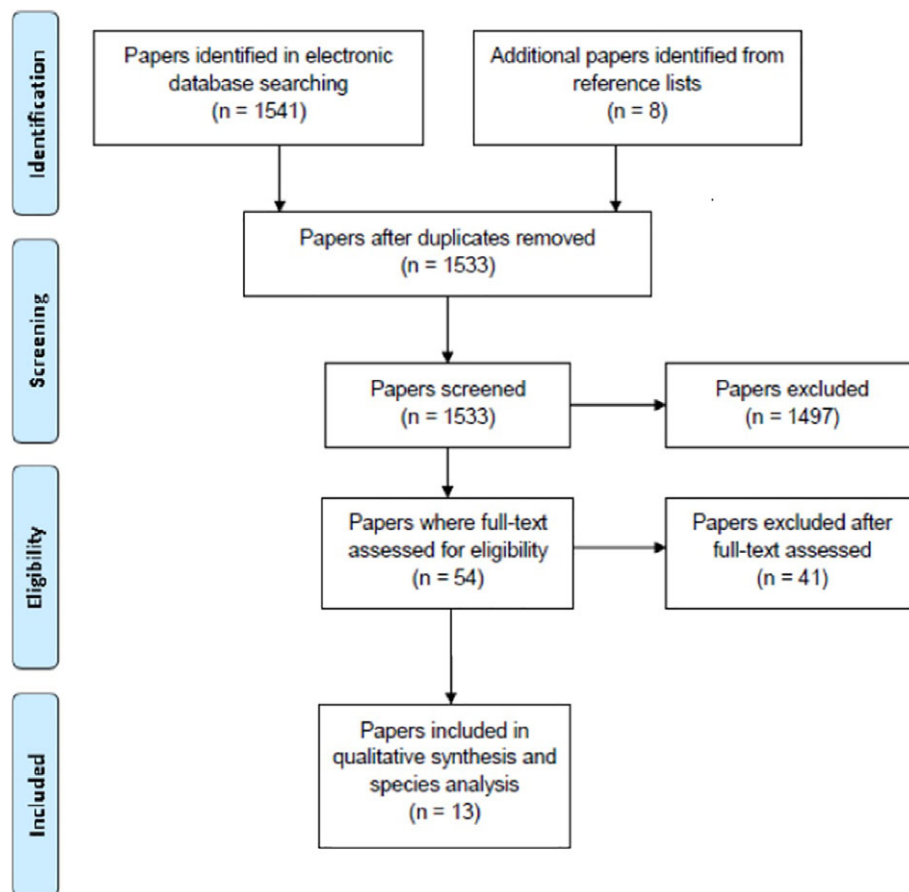


Fig. 1. Literature Search Strategy Using PRISMA Flowchart.

reduction in resistance has been shown to decrease the patient's sense of effort, or work of breathing, and dyspnoea.<sup>7-9,14</sup>

Clinically, the effect of Heliox manifests as a significant decrease in rate of respiration, the work of breathing<sup>14</sup> and decrease in the use of the accessory muscles to facilitate respiration.<sup>13</sup> It is reported that the use of Heliox leads to patients becoming less anxious, more comfortable, and more cooperative as the work of breathing is decreased.<sup>2</sup> Heliox is fast-acting and benefits are usually seen within an hour of treatment.<sup>15</sup>

### **Use of Heliox in Conditions Other Than VCD**

Heliox has been shown in numerous case reports and case series to reduce the work of breathing in patients with obstruction in the extra thoracic and central intrathoracic airways,<sup>9,13,15</sup> and aid the work of breathing and exercise tolerance in people with COPD.<sup>16</sup> However, there is insufficient evidence to support the use of Heliox for acute exacerbations of COPD.<sup>17</sup>

Heliox is not intended to replace other medical treatment, nor is it intended to be curative.<sup>18</sup> Instead, it is intended to "buy time" while the patient is awaiting treatment to alleviate the obstruction.<sup>18</sup> Heliox therefore has no direct treatment effects, and is a "temporizing"

measure until definitive therapies take effect.<sup>9</sup> It can help treat symptoms of respiratory distress, but not the causes.<sup>11,13</sup>

### **Use of Heliox for VCD**

A number of narrative reviews have identified Heliox as a possible therapy for VCD.<sup>1,9,19-23</sup> These papers all state that Heliox can result in improvement of VCD symptoms, proposing that the mechanism is mediated via reduced airway resistance. However, the literature cited to support the use of Heliox within VCD treatment is sparse, with only three separate studies cited across the eight papers as evidence of the effectiveness of Heliox.<sup>2,24,25</sup>

The current paper therefore aims to systematically review the literature to establish whether there is evidence to support the use of Heliox for the alleviation of symptoms of VCD.

## **METHODS**

### **Search Strategy**

A systematic literature search for relevant studies was conducted in March 2018 of major databases: Cochrane Library, MEDLINE/PubMed, CINAHL, EMBASE, and Dynamed. Studies were searched via keywords using terms

of: “vocal cord dysfunction [MeSH], paradoxical vocal fold motion, paradoxical vocal fold motion disorder, paradoxical vocal fold movement, vocal cords [MeSH], Heliox, Heliox therapy, Helium-Oxygen therapy”.

### ***Inclusion and Exclusion Criteria***

Searches were not restricted by dates, were conducted singly or in combination, and key words were searched within the entire article or within the abstract. Search results were restricted to research papers published in peer-reviewed journals, and to papers in English language.

Eligibility criteria for inclusion were that papers discussed the use of Heliox as an adjunctive therapy for patients with VCD, and assessed the effectiveness of Heliox. All types of experimental design were included. Studies were included with participants of any age that had a confirmed diagnosis of VCD.

Papers were excluded if they did not discuss the use of Heliox as an adjunctive therapy for VCD specifically, when participants did not have a diagnosis of VCD, were not published in peer review journals, or were not published in English.

### ***Selection of Studies***

Papers were initially screened by an independent librarian according to the eligibility criteria, following the process outlined in the PRISMA guidelines.<sup>26</sup> Two review authors (CS and RS) then read the full-text study reports of all potentially eligible studies identified and independently screened them for inclusion, recording the reasons for exclusion of ineligible studies.

### ***Data Extraction and Critical Appraisal***

Data were sought that compared any measure of VCD severity and/or impact before and after the use of Heliox. Two review authors (CS and RS) assessed risk of bias independently for each reviewed study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions.<sup>27</sup>

## **RESULTS**

The search returned 1541 possible papers, with an additional eight papers identified from reference lists. Once duplicates had been removed, 1533 papers remained. Titles and abstracts were reviewed for relevance to the review topic, which removed 1497 papers. Full text copies of the remaining 54 papers were studied for relevance, and a further 41 papers were removed, leaving a total of 13 relevant papers that met the broad inclusion criteria. Of these, 10 were narrative reviews that stated Heliox could be effective for VCD. However, none of these presented original research or data on the effectiveness of Heliox and were therefore removed, leaving three papers for inclusion.

The three reviewed papers were the same as those cited within previous narrative reviews as evidence of the effectiveness of Heliox.<sup>2,24,25</sup> The systematic review

therefore identified no further original published research in this area. Characteristics and results of the three identified studies are described below.

Christopher et al.<sup>24</sup> present a case review of five adult patients with a diagnosis of VCD without asthma. They state that wheezing and dyspnoea were improved in all patients following use of Heliox. However, no data are reported to support this improvement, and due to the low participant numbers no statistical analyses are presented.

Weir<sup>2</sup> presents a retrospective case review of five pediatric patients with acute VCD. The paper states that four of the five patients had a favorable response to the use of Heliox, with no therapy complications. It argues that the role of Heliox in acute VCD treatment can be viewed as similar to that of beta agonists for the treatment of asthma, and that it may reduce acute care visits. Heliox is viewed as being more effective than other medical interventions, which can have a poor risk–benefit profile, such as botulinum toxin, tracheostomy, intubation and mechanical ventilation. However, no measures are used to measure VCD improvement and no data or statistical analyses are reported within the paper.

Reisner and Borisch<sup>25</sup> state that in the authors’ clinical experience “Heliox is particularly efficacious in the treatment of an acute episode of vocal cord disease”. However, they do not present any data such as number of participants, methodology, or results to support this statement.

Three papers therefore support and recommend the use of Heliox for VCD for adults and children. However, there are many methodological weaknesses within these papers.

The reviewed studies were assessed using a quality appraisal checklist for case series studies.<sup>28</sup> Of the 18 quality indicators within the appraisal checklist, Weir<sup>2</sup> contained three, Christopher et al.<sup>24</sup> contained two, and Reisner and Borisch<sup>25</sup> contained none.

All three papers were judged as having a “high” risk of bias according to the Cochrane Handbook.<sup>26</sup> Methodological issues with the papers include: no information is presented as to how the participants were selected for inclusion; no measures were reported to evidence the diagnosis of VCD, the baseline severity of VCD, or measure improvement; the intervention (ie, use of Heliox) is not standardized; no comparisons were made with a control group; no statistical analyses were performed.

In summary this systematic literature review found only three papers claiming to provide evidence of Heliox as an adjunctive therapy for VCD, but none were of adequate methodological quality to support this assertion.

## **DISCUSSION**

Heliox has been shown to be effective for patients with upper airway obstruction,<sup>9,13,15</sup> and its use for VCD/ILO has a clear clinical rationale. However, despite a number of narrative reviews recommending the use of Heliox for VCD, the results of this systematic literature review produced little evidence relating to the effectiveness of Heliox for VCD. It cannot be concluded, therefore, that there is a current evidence base for the use of Heliox for VCD in either adult or pediatric populations. There is a need for good quality

research to investigate the effectiveness of Heliox as an adjunctive therapy for VCD.

Future research needs to be of an appropriate methodological quality that addresses the shortcomings within the current evidence base. Research should involve greater participant numbers that allow for the use of appropriate statistical measures, the use of pre- and post-treatment standardized clinical measures (eg, Pittsburgh Vocal Cord Dysfunction Index<sup>29</sup> or VCDQ<sup>30</sup>), and methodological controls (eg, comparison groups and/or intention to treat analyses).

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