Ondine’s Syndrome as a Postoperative Complication of High Cervical Cordotomy: a case series review

Síndrome de Ondine Como Complicação Pós-operatória da Cordotomia Cervical Alta: uma revisão de série de casos

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ABSTRACT

Ondine’s curse is the term used to describe sleep apnea caused by damage to the spinal cord pathways of respiratory control. Despite presenting several causes for this syndrome, Ondine’s syndrome is recognized as a common and fatal postoperative complication of upper cervical cordotomy for malignant pain control. Our objective is to carry out a historical review based on papers linked to PubMed and Scielo databases in order to analyze the frequency and evolution of sleep apnea in patients undergoing upper cervical cordotomy, in addition to observing the anatomical and functional mechanism that triggers it. The results revealed that postoperative Ondine’s syndrome is caused by sectioning of the lateral spinothalamic and spinoreticular tracts, which are located in the anterolateral portion of the spinal cord.

Keywords: Ondine’s syndrome; Sleep apnea; Cordotomy; Respiratory automaticity; Breathing control

RESUMO

A maldição de Ondine é o termo usado para descrever a apneia do sono causada por danos nas vias da medula espinhal de controle respiratório. Apesar de serem apresentadas várias causas, a síndrome de Ondine é reconhecida como uma complicação pós-operatória comum e fatal da cordotomia cervical superior para o controle da dor maligna. Nosso objetivo é realizar uma revisão histórica baseada em artigos ligados aoPubMed e Scielo, de forma a analisar a frequência e evolução da apneia do sono em pacientes submetidos a cordotomia cervical superior, além de observar o mecanismo anatômico e funcional que a desencadeia. Os resultados obtidos revelam que a síndrome pós-operatória de Ondine é causada pela seção dos tratos espinotalâmicos e espiroreticulares laterais, que estão localizados na porção anterolateral da medula espinhal.

Palavras-Chave: Síndrome de Ondine; Apneia do sono; Cordotomia; Automaticidade respiratória; Controle de respiração

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INTRODUCTION

In one of the interpretations of a Greek myth, Ondine is a water spirit who, by falling in love with a human, gives up his immortality to share life with her beloved. At one point, due to her husband's betrayal, Ondine curses him to lose involuntary control of his breathing, so that he dies as soon as he falls asleep\(^1,2\). Due to the correlation with this fanciful story, Ondine Syndrome is the eponym attributed to sleep apnea induced by impairment of the neurological centers of respiration, consisting of loss of respiratory automaticity that culminates in alveolar hypoventilation during the period of sleep\(^3\).

Regarding the etiology of Ondine's syndrome, the congenital origin occurs through mutation of genes intrinsic to the autonomic nervous system, especially the PHOX2B gene considered the gene that causes the syndrome\(^4\). In addition, the medical literature has documented several acquired causes of Ondine syndrome\(^5\), including the postoperative complication of cordotomy\(^6,7\).

Cordotomy is based on the surgical section of the lateral spinothalamic tract and spinoreticular tract, the ascending pathways responsible for the transmission of painful stimuli\(^8\), with the objective of producing the absence of contralateral pain perception and, thus, treating patients with chronic pain\(^9,10\). The aim of this study is to review the anatomo-functional mechanisms that explain Ondine's curse as a postoperative complication of the cordotomy procedure through a series of case reports.

METHODS

The proposed design is a historical literature review. The keywords designated for this study are: Ondine's Syndrome Sleep apnea Cordotomy Respiratory automaticity Breathing control. Thus, the selection of articles to support this review was carried out from the PubMed and Scielo databases between January 2022 and February 2022, using the following search terms: Sleep Apnea AND Chordotomy, Ondine's Curse AND Chordotomy, Respiratory Syndrome AND Chordotomy. The use of the “boolean operator” “AND” proved to be essential to find intersection and correlation between related terms. Inclusion criteria were Research and case reports addressing a correlation between Ondine syndrome and upper cervical cordotomy, written in Portuguese, English or Spanish and published in academic journals. In addition, linked articles were added as a bibliographic reference to other articles present in the databases following the same inclusion criteria to expand the available repertoire. A total of 25 articles were found in the databases, and 7 were considered. The search in the bibliographic references resulted in 6 articles, totaling 13 articles chosen for this analysis.

RESULTS

From the selected 13 articles, according to Table 1, it was highlighted the following aspects of each study: author, method used and final result obtained.

In general, the papers mentioned, mostly case reports, pointed to a correlation between upper cervical cordotomy and sleep apnea through the disruption of pathways that circulate in the anterolateral portion of the spinal cord, such as the spinoreticular tract, which are responsible for involuntary breathing control.

DISCUSSION

Ondine's syndrome is characterized by the automatic deactivation of breathing during sleep and is one of the main postoperative complications of cordotomy, a procedure that aims to treat patients with chronic pain.

Cordotomy is usually performed using two techniques: the open technique and the percutaneous technique. Open technique cordotomy requires general anesthesia and hemilaminectomy or total laminectomy to access the patient's spinal cord in the contralateral portion and 3 to 4 spinal cord levels above which pain attenuation is desired. Then, the anterolateral segment of the spinal cord is exposed and a cordotomy hook\(^24\), as shown in Figure 1. The percutaneous cordotomy technique is more used and less invasive when compared to the open technique, consisting of disruption of the spinal pain through radiofrequency ablation.
**Table 1. Results of selected studies.**

<table>
<thead>
<tr>
<th>Author</th>
<th>Method</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lahuerta et al.</td>
<td>Case reports of 12 patients who died after unilateral cordotomy</td>
<td>Unilateral high cordotomy causes destruction of spinoreticular tract fibers in the anterior and lateral cords of the spinal cord that are related to the process of reticular activation of the respiratory center of the brainstem</td>
</tr>
<tr>
<td>Krieger et al.</td>
<td>Case reports of 10 patients who developed sleep apnea after bilateral cervical cordotomy</td>
<td>The upper cervical cordotomy is responsible for causing the rupture of ascending reticular fibers in the anterolateral cord of the spinal cord that establish a connection with the respiratory center of the brainstem</td>
</tr>
<tr>
<td>Kanpolat et al.</td>
<td>Retrospective study of 207 patients who underwent CT-guided cordotomy between 1987 and 2007</td>
<td>CT-guided cordotomy is associated with considerable pain relief on the Karnofsky scale for patients with malignant conditions and intractable pain, requiring 1 week interval between procedures if it is a bilateral approach</td>
</tr>
<tr>
<td>Polatty et al.</td>
<td>Case report of a 33-year-old man who developed Ondine’s syndrome after cordotomy to treat chronic pain</td>
<td>Cordotomy causes injury to the involuntary descending pathways of respiratory control in the anterolateral segment of the spinal cord, predisposing to Ondine’s syndrome</td>
</tr>
<tr>
<td>Chevrolet et al.</td>
<td>Case report of a 46-year-old man who developed ventilatory disorders after bilateral cordotomy</td>
<td>Bilateral cordotomy usually presents with apnea due to respiratory control dysfunction or respiratory muscle dysfunction, which are reversed with the administration of aminophylline</td>
</tr>
<tr>
<td>Tranmer et al.</td>
<td>Retrospective study of 112 patients who underwent upper cervical cordotomy since 1977</td>
<td>About 5% of the 112 patients evaluated developed sleep apnea due to injury to the afferent and/or efferent respiratory fibers of the spinal cord</td>
</tr>
<tr>
<td>Nathan</td>
<td>Retrospective analysis of eight case reports</td>
<td>Most of the descending fibers responsible for respiratory activity are located in the most anterior part of the lateral cord of the spinal cord and are partially or totally interrupted in the cordotomy procedure</td>
</tr>
<tr>
<td>Hitchcock and Leece</td>
<td>Case reports of respiratory functions through spirometry in 14 patients before and after upper cervical cordotomy</td>
<td>Voluntary and involuntary control of breathing occurs through distinct nerve pathways, which corroborates the fact that many patients develop sleep apnea after high cervical cordotomy</td>
</tr>
<tr>
<td>Mullan and Hosobuchi</td>
<td>Case reports of 9 patients who died due to upper cervical cordotomy</td>
<td>Vital pathways for respiratory control circulate in the anterior portion of the anterior cord of the spinal cord and are extremely compromised during the cordotomy procedure, with sleep apnea being the most common manifestation during the first 5 nights after the procedure</td>
</tr>
<tr>
<td>Lema and Hitchcock</td>
<td>Case reports about changes in breathing patterns in patients with opioid-resistant pain after surgery at the upper cervical level</td>
<td>Involuntary airways are affected during upper cervical procedures, which led to changes in breathing pattern in 11 of the 15 patients evaluated</td>
</tr>
<tr>
<td>Tenicela et al.</td>
<td>Case report of ventilatory changes in 13 patients who underwent cervical cordotomy at C2 level</td>
<td>Of the 13 patients, 3 developed sleep apnea in the period after bilateral cordotomy, showing that the level of respiratory failure and the number of respiratory fibers affected are directly associated</td>
</tr>
<tr>
<td>Belmusto et al.</td>
<td>Case reports of 20 patients who underwent cervical cordotomy with observation of respiratory functions</td>
<td>Bilateral upper cervical cordotomy is contraindicated for patients with previous lung disease because it causes changes in breathing pattern through injury to the descending airways</td>
</tr>
<tr>
<td>Rosomoff et al.</td>
<td>Randomized study to evaluate changes in respiratory functions in 48 patients undergoing cervical cordotomy</td>
<td>Both unilateral and bilateral cordotomy promoted a reduction in respiratory capacity and respiratory muscle strength and an increase in respiratory rate</td>
</tr>
</tbody>
</table>

By injuring the respiratory control pathways in the anterolateral segment of the spinal cord, respiratory control or respiratory muscle dysfunction may occur<sup>17</sup>. This occurs because when sectioning the spinoreticular tract, chronic pain would be relieved, but this tract contains fibers that establish the connection with the respiratory center of the brainstem and, when injured, causes apnea<sup>12</sup>.

Depending on the number of respiratory fibers affected, respiratory compromise can be variable<sup>21</sup>. Bilateral upper cervical cordotomy, for example, consists of sectioning more than one fiber pathway, which can cause more severe respiratory failure and, therefore, is contraindicated in patients with lung disease<sup>22</sup>. In some cases, a one-week interval between procedures may be necessary<sup>13</sup>.

Unilateral cordotomy, despite breaking a smaller number of fibers compared to bilateral, also causes respiratory dysfunction, as the fibers of the spinoreticular tract in the anterior and lateral cords of the spinal cord are sectioned in the same way<sup>11</sup>.

Both the bilateral and the unilateral approach affect the fibers responsible for respiratory activity and can cause varying degrees of respiratory failure, but mainly sleep apnea, which characterizes Ondine’s syndrome. The Lema Ane Hitchcock study (1986)<sup>20</sup> found that about 74% of the patients undergoing the procedure suffered from some alteration in their breathing pattern.

Despite the dysfunction of respiratory control after the procedure, the use of bronchodilators, such as aminophylline, can reverse apnea<sup>15</sup>.

**CONCLUSION**

Cordotomy is a procedure aimed at relieving chronic pain, either unilaterally or bilaterally, and consists of sectioning the lateral spinothalamic and spinoreticular tracts (Figure 1), at the level of the lateral and anterior cord of the spinal cord. Such tracts contain fibers that are directly related to the respiratory center and their section can cause different degrees of respiratory dysfunction, depending on the number of fibers affected. Although there is a difference in the degree of respiratory distress, sleep apnea or Ondine’s curse is the main postoperative complication of cordotomy.

**REFERENCES**


Case Report


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