An assistive device for patients with CCHS: clinical study on usability and efficacy

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A magnifying glass in the world of medical device development – 20/01/2022
Congenital Central Hypoventilation Syndrome (CCHS), or Ondine’s curse, is a rare genetic disease (estimated prevalence 1/200000), caused by a mutation in the PHOX2B gene.

It affects the autonomic nervous system and it is mainly characterized by hypoventilation episodes occurring especially during sleep.

This appears to be caused by an anomalous functionality of the respiratory control system made by the chemoreceptors.
Treatment focuses on providing breathing support.

All Patients with CCHS require **lifelong ventilatory support during sleep** and, in some cases, 24 hours per day.

To prevent significant and sustained hypoxia and hypercapnia and their physiologic and neurocognitive sequelae, it is suggested to **monitor oxy-hemoglobin blood concentration (SpO2)**, especially during sleep.
Main issues

Patients, especially in the case of young children, have to be supervised by a caregiver.

The only alarm systems available for patients with CCHS are the ones integrated in the ventilators and monitor devices (e.g. pulse-oximeter).

Most subjects with CCHS did not awaken to ventilator or monitoring alarms and a majority of these patients did not have nighttime nursing (Mathur et al., 2021).

An adequate domiciliary assistance is still not present!
Issues raised by A.I.S.I.C.C.

Habituation problem: both patients and caregivers can become less responsive to frequent and repeated alarm stimuli.

Alarms can be activated both for severe situations and for borderline or less severe ones, interrupting the sleep of both caregivers and patients. Thus, there is the tendency in setting lower and lower alarm-threshold values, to prevent false alarms and the related increase of stress and anxiety.

Achieving independence is a big problem for adolescents and young adults with CCHS that are always dependent on their caregivers.
The awakening device

How can we improve the assistance of patient with CCHS?

Assistive device, coupled with a pulse-oxymeter, which provides multisensory stimulations based on the patient condition and his oxy-hemoglobin (SpO2) blood concentration level.
The awakening device

Main aim:
1. To **wake up** the patient or the caregiver in case of real danger

Secondary aims:
2. To get **gentle awakenings** in case of slight danger
3. To **foster a spontaneous recovery of the SpO2** basal level
4. To obtain a more **personalized monitoring**
5. To reduce the number of **false alarms**
6. To reduce the **habituation** problem
7. To increase the **independence** of adolescents and young adults
The awakening device

- **Software**: SpO\textsubscript{2} Pulse-oxymeter
- **Hardware**: Vibrating pillow, Air fun, Buzzer, Fire alarm
- **SpO\textsubscript{2}**
- **Pulse-oxymeter**

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**ePTRI**

- **EPiCa**
- **la Nostra Famiglia**
- **ASTROLAB**

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The awakening device

How does it work?

Definition of different and custom severity levels (SLs) based on SpO2 threshold and time below that threshold.

Each SL activates one or more actuators that stops when there is a recovery of the SpO2 basal level.
The awakening device

- **Severity Level 0**
  - SPO2 < Threshold 1 (e.g. 94)
  - Effective Device 1

- **Severity Level 1** (Device 1 active)
  - SPO2 < Threshold 2 (e.g. 92)
  - OR Time > Duration 1 (e.g. 12 min)
  - Effective Device 2

- **Severity Level 2** (Device 2 active)
  - SPO2 < Threshold 3 (e.g. 88)
  - OR Time > Duration 2 (e.g. 8 min)

- **Severity Level 3** (Device 3 active)
  - SPO2 < Threshold 4 (e.g. 85)
  - OR Time > Duration 3 (e.g. 4 min)
  - Effective Device 3

- **Severity Level 4** (Alarm active)
  - Effective Device 3
The awakening device

What we did?

1. Development of the device and laboratory tests with simulating signals
The awakening device

What we did?

2. Italian Patent (Application n° MI2011A002324) «Apparecchiatura per il ripristino della ventilazione particolarmente in soggetti affetti dalla sindrome da ipoventilazione centrale congenita (CCHS)“
The awakening device

What we did?

3. Validation of the device on healthy subjects (Biffi et al 2014, Annals of Biomedical Engineering)
The awakening device

What we did?

4. Approval by the Italian Ministry of Health of a multicenter clinical trial on the efficacy of the device in a population of patients affected by CCHS (preliminary results in Biffi, Piazza et al, IFMBE proc 2016)

Preliminary Data on the Usability and Efficacy of an Assistive Device for the Congenital Central Hypoventilation Syndrome: An Observational Study

E. Biffi¹,* C. Piazza¹,2,* F. Morandi³ P. Avantaggiato¹, F. Formica¹, A. Carcano⁴, R. Borgatti¹, and G. Remi¹
The clinical trial

Involved centers:

• Scientific Institute Eugenio Medea, Bosisio Parini (LC), Italy

• Pediatric Pain and Palliative Care Service of the University of Padua, Italy

• Meyer children’s hospital, Florence, Italy
The clinical trial

Patient recruited: **15 subjects**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Gender</th>
<th>Age (years)</th>
<th>Gene Mutation</th>
<th>Type of ventilation</th>
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</table>
The clinical trial

Study protocol

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<th>Devices used</th>
<th>REFERENCE NIGHT</th>
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<th>TEST NIGHT 2</th>
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<tr>
<td></td>
<td>• PSG</td>
<td>• Awakening device</td>
<td>• Awakening device</td>
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<tr>
<td></td>
<td>• Actigraph</td>
<td>• PSG</td>
<td>• Actigraph</td>
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<tr>
<td></td>
<td></td>
<td>• Induced desaturations</td>
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Randomized order

Only one actuators was associated to each SL in a random way

The fire alarm was always associated to SL4
The clinical trial

Results

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<tr>
<th>Number of activation per subject</th>
<th>Median</th>
<th>IQR</th>
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<tbody>
<tr>
<td>Air fun</td>
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<tr>
<td>Buzzer</td>
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<td>28</td>
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<td>Vibration</td>
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<td>10</td>
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<td>Fire allarm</td>
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<td>2</td>
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</table>

- 4 children (2 females, 2 males) mean age: 8,7 years (sd = 3,7)
- 11 adolescents and young adults (8 females, 3 males) mean age: 23,4 years (sd = 6,8)
The clinical trial

Results

% arousal

- air fun
- buzzer
- vibration
- fire allarm

ADULTS

CHILDREN
The clinical trial

Results

% recovery from spontaneous desaturations

%  
0 20 40 60 80 100

with device  
without device

*
The clinical trial

Results

Sleep efficiency

With device: 80% ± 5%

Without device: 75% ± 5%
The clinical trial

Conclusion

• Promising results in awakening adolescents and young adults

• Low efficiency in awakening children

• The multisensory stimulations foster the spontaneous recovery

• The device didn’t affect the sleep efficiency
Thanks for your attention!