

BACHELOR THESIS

OxyGEN project: Emergency ventilator open-hardware project against COVID-19



École Polytechnique Fédérale de Lausanne
Faculty of Computer and Communication Sciences

EPFL

Marc Watine

Supervised by Pr B. Rimoldi (EPFL) and Mr. Lluis Rovira (Protofy)

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Executive Summary

OxyGEN is a social innovation project born to answer the hospitals' need of Emergency Ventilators in Spain in the context of the COVID-19 pandemic. Our purpose was to make an emergency ventilator available anywhere very fast to be able to help in the global sanitary emergency. We decided to use an open hardware approach that made possible a fast-track I+D process; we got medical approvals in 2 weeks when it would have taken us 1 year in a normal situation. OxyGEN is designed to be massively available and simple which is why we focused on a low-tech and low-cost approach to avoid availability issues. As an open hardware project, all designs have been publicly available on our website and free to use at all stage of development. We have been the first project in Spain to receive the AEMPS (Spanish Drugs and Medical Products Agency) approval for clinical trials which allows the use on patients in the hospitals willing to join. We have mass-produced OxyGEN-IP version thanks to our partnership with the Seat-Volkswagen group, who used their Seat León production line in Martorell (Barcelona) to produce the devices at a rate of 300 units/day to be able to reach other Spanish Hospitals. The project started to answer Spain's critical need for emergency ventilators, but it has become an international project, with more than 52 teams working on the design improving it and building it in at least 31 countries. As the first emergency ventilator project to be approved in Spain and, despite the current slowdown of COVID-19's in the country, it is an ongoing process with thousands of engineers, medical personnel and producers working on it around the globe. The project was led by the Barcelona company Protofy and a team of external contributors of which I was a part. We started the project on March 12th (precisely the day EPFL closed down due to the pandemic). From very early on, we had the support of two leading Barcelona hospitals: Hospital Clinic de Barcelona and Hospital Germans Trias i Pujol (HGTP). Dr. Josep María Nicolas (Hospital Clinic) and Dr. David Priego (HGTP) among others were key to make OxyGEN a viable project with every medical requirement. The AEMPS played a critical role in approving a medical device in such a short time. Many individuals -some following the Maker movement and others just wanting to contribute to relieving some pressure to the critical situation- were also key in the success of OxyGEN. The project would not have been possible without the collaboration of a multitude of companies; from the car industry to the motor suppliers, the transportation services and suppliers, public relations managers, testing facilities, FabLabs and many more.

Basic explanation and key links are available here: <https://www.oxygen.protofy.xyz>, all the designs are publicly available and free to use on <https://github.com/ProtofyTeam/OxyGEN> and here is a video of OxyGEN on a patient: <https://www.youtube.com/watch?v=8xA1Cw5RhsE>

1 Context

1.1 OxyGEN's Motivation

This project started with a group of engineers willing to help minimize the effects of the COVID19 pandemic by doing what we do best: innovating, fast problem-solving and prototyping.

OxyGEN is led by Protofy, a Barcelona based company, providing fast software and hardware solutions for other companies. Many outsider collaborators have participated in making this project come true. As an EPFL student, I have been in the core team since the beginning. OxyGEN's website <http://www.oxygen.protofy.xyz> has been updating with all the key steps.

1.2 The Problem

The COVID-19 pandemic has created many challenges that we have been forced to solve very quickly. Ranging from hospital saturation, dealing with a new day to day organization, social distancing or economic challenges. A critical problem that hospitals have faced, is the lack of respirators and healthcare personnel. We decided to focus on this problem to try and come up with a viable solution.

COVID-19 is an infectious disease caused by SARS-CoV-2. Two key factors are central to the source of the problem. First, the strain is relatively highly contagious (it has an R_0 (basic reproductive rate) between 1.4 and 3.9 if no measures are taken). Second, while the majority of cases result in mild symptoms, around 14% develop a severe disease that requires hospitalization and oxygen support and around 5% require admission to an Intensive Care Unit. This can be caused by acute respiratory distress syndrome (ARDS) which causes fluid to build up in the lungs and keeps patients from getting the air they need [17].

1.3 COVID-19 in Spain

The situation in Spain and, in particular, it's need for ventilators was what we focused on in the beginning. It is critical to have accurate and precise information on inventory in each hospital, personnel capabilities, etc. However, a lot of this information was inaccurate or incomplete. As of March 11th, 59,6% (149/250) of the Spanish ICUs had communicated their information to the SEEIUC [12].

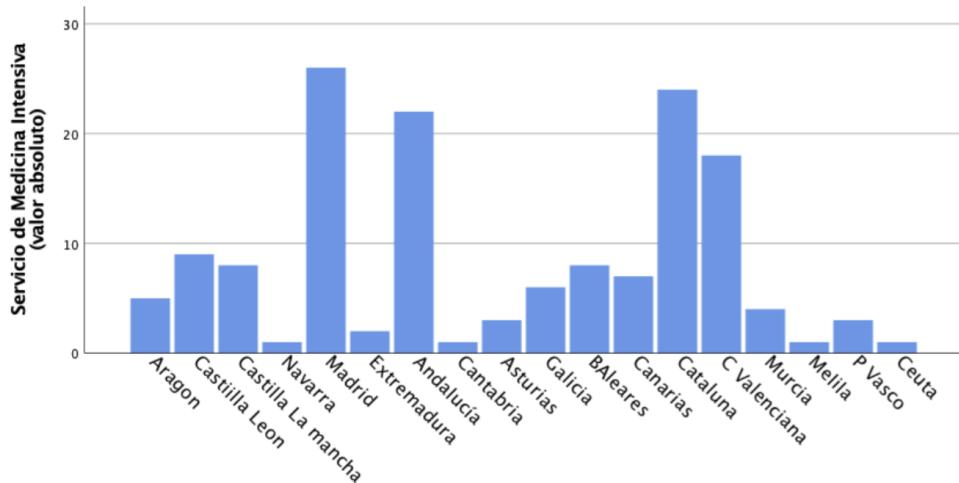


Figure 1: Intensive Care Services distribution by Autonomous Community (SEEIUC)

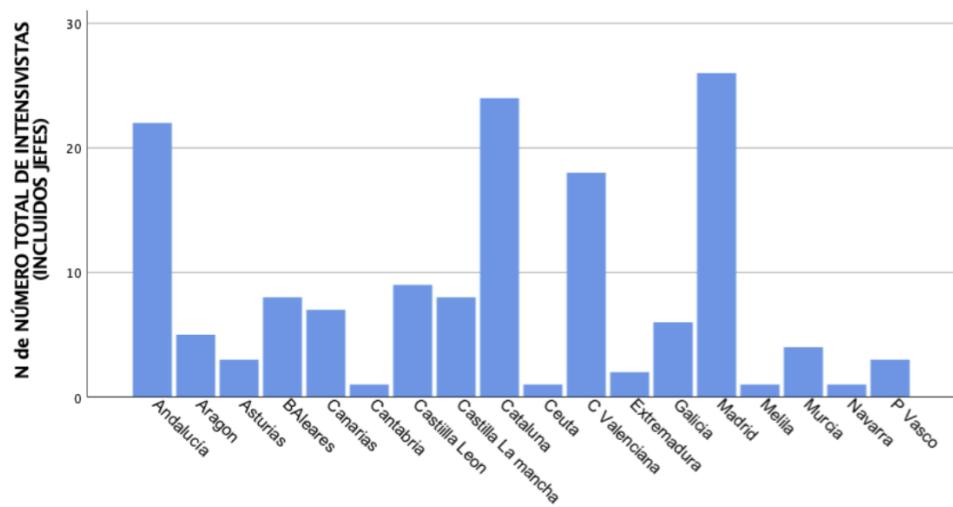


Figure 2: Intensive Care Personnel distribution by Autonomous Community (SEEIUC)

In total, Spain had 2,487 ventilators inventoried. The SEEIUC was expecting to have 9,257 patients hospitalized on the peak epidemic week, with 5,454 patients under mechanical ventilation, which means a 257% of the total expected ICU capacity and a 165% of the total ventilators.

1.4 Medical Challenges of a Ventilator

Building a ventilator from scratch has many challenges. First of all, there are many ways to ventilate a patient depending on its condition. OxyGEN is designed to work with inva-

sive mechanical ventilation (meaning a tube is inserted into the patient’s airways). It’s a positive-pressure ventilator (meaning it pushes air into the patient’s lungs) and it doesn’t assist in the expiration process since the diaphragm will push the air out by elasticity.

Two kinds of pressure are extremely important when designing a ventilator.

The first one is PIP (Peak Inspiration Pressure), which is the highest level of pressure applied to the lungs during inhalation. It is important to control this pressure, since the ventilator is increasing the pressure of the lungs when pushing the air inside, and going above a certain pressure would damage the lungs of the patient [11]. As we will later explain, this pressure is controlled by the cams system of OxyGEN.

The second kind of pressure is PEEP (Positive End-Expiratory Pressure), which is the pressure in the lungs at the end of the expiration. A ventilator typically applies a certain PEEP and it is one of the first settings that must be regarded [15]. PEEP pressure is key in our project because the ARDS (which COVID-19 causes in some cases, as we have shown in section 1.1) is often countered by applying higher PEEP [10]. As we will later explain, we used an already existing medical device to build our respirator and this medical device has a PEEP valve built-in, that can be replaced with the correct pressure valve with ease.

One last point to note is that the ventilator will not just push ambient air into the patient’s lungs. ARDS blocks a fraction of the alveolars and supplemental oxygen therapy is often required, so a FiO_2 injection valve is needed on the ventilator. [17]. Once again, the medical device we used integrates such a FiO_2 injection unit.

2 OxyGEN’s Goals & Approach

2.1 OxyGEN’s Goals

OxyGEN aims at responding to the hospital’s need for respirators and personnel. For that, we have designed an emergency ventilator that has been clinically approved (by the AEMPS in Spain for example), and that is now being actively replicated in all parts of the world. OxyGEN is an emergency ventilator designed to keep patients alive while no other conventional, and much safer ventilator is available and eliminating the need for a human operator. As we will detail in the following sections, it is a low-cost device (as opposed to the 50.000\$ that a regular ventilator would cost [8], not counting the increased cost by the current stress on the market). It also aims at being a low-tech device, under an open-hardware procedure and with the possibility of adding functionalities with ease using a modular approach. It is important to note that OxyGEN does not have sensors built-in. That means that a basic OxyGEN won’t adapt to the patient’s needs on itself,

all parameters are set by the medical professional.



Figure 3: Patient ventilated by an OxyGEN-IP ventilator

2.2 Low-Tech & Low-Cost

Designing a prototype to assist breathing has many challenges, and modern certified devices do multiple things. Obviously, in this kind of situation, you need to sacrifice everything that is not essential to make the device simpler. A device like the one we need must be designed in no time, produced in mass almost immediately, to be up and running in a matter of days.

There are two key points to achieve this with the least possible risk: the design must use parts available anywhere; and the use of complex parts, such as software and electronics, must be minimized.

Advanced control electronics and computer software are the technology on which modern professional devices are built. However, as I am aware of, due to my particular area of study, they require hundreds of man-hours, lengthy testing phases and many quality processes to ensure proper operation and certification. Furthermore, an emergency device such as the one described cannot be supported by complex concepts because it would be

impossible for any team that designed it to provide a “technical service” to the hospitals that are using it. Electronics and their peripherals can also be scarce locally, as is happening with other critical points in the supply chain.

Device maintenance in the event of failure is also affected by complex designs using control electronics. Electronics or software failures are not visible to the naked eye and require specialized tools and training to diagnose and repair the device. On the contrary, mechanical devices can be understood at a glance and there are a large number of people, even with basic knowledge, capable of repairing them.

To overcome all these problems, OxyGEN is a purely mechanical device, with parts widely available from the already existing and highly scalable supply chain. In fact, not using high-tech software and electronics added a huge challenge to the task: Much more thought had to be directed in making our device just as precise as if we were using precise control electronics.

2.3 Open-Hardware & Lean Method

OxyGEN was led by Protofy and the small core team of external collaborators. However, an important factor that made it become a reality was the open-hardware approach. The blueprints were publicly available on our website and constantly updated through a git repository. Anyone, anywhere could start building and OxyGEN, giving us precious feedback that we, with our relatively small team for such a project, would have missed or would have discovered weeks later.

Constantly communicating with all this external help from makers and doctors from all around the world was thus a key factor in the success of the project. We set up a Discord channel where thousands (more than 2100 as of April 14th) of makers, doctors and engineers exchanged with us and with one another. “Have you guys thought of FiO₂ injection”, “We could apply PEEP pressure with a water column, like in the 1850s” or “Use stainless steel instead of wood for asepsis” are a few examples of the inputs of our Discord community.

A critical benefit of this approach was scaling. Protofy is a small company, and we could only produce a single new prototype per day. Having multiple teams working on that same version at the same time was a huge value to instantly detecting what needed to be changed and what could go wrong. This agile way of innovating was key in developing a product in 2-3 weeks that would be approved by Medical Agencies.

The particular world situation also encouraged our “core” team to work in a way that would maximize our productivity, taking into account that some of us, like myself, were not in the “lab”: We needed to work in the most agile way. Every evening, we would meet and discuss new inputs of the day and brainstorm on the next steps and next day’s main

focus, as well as who was in charge of what. This way of working was key. The extremely fast process OxyGEN went through meant that big decisions were to be made every day, if not even hour.

2.4 Modular Approach

OxyGEN is designed to be modular. This means that the emergency respirator has an essential module that can achieve on its own the essential task. From this central module, other functionalities can be added through optional add-ons, which would not affect the basic operation of the system if missing. This approach aims at achieving two goals.

First of all, OxyGEN ventilators need to adapt to different shortage situations. The basic module is built with extremely available parts and could be built with a fully broken supply chain: an isolated Zambian village could assemble it, to give an example.

Modularity is also interesting to adapt to the particular needs of different hospitals. Adaptability is a key factor in this decision. Especially due to the internationalization of the project, hospitals have different FiO_2 injection plugs, different hospital room arrangements, etc. OxyGEN is interesting in the fact that it was not thought for the Spanish hospital system in particular but to be adaptable to any situation.

3 Product Description

3.1 How it Works

Overview

One option to simplify the design of an artificial respirator is to use a medical manual ventilation device, such as the BVM (Big Valve Mask). This is an idea we took from a 2010 MIT paper [1], and that many other COVID-19 emergency ventilator projects have used. Automating an AMBU has the advantages that it is a safe medical device in itself and already provides almost all the functionalities that an emergency automatic respirator would require. The problem is that it is completely manual. To automate it, we designed a system of interchangeable cams pressing on the air bag replicating a traditional respiration cycle, adaptable to each patient's need.

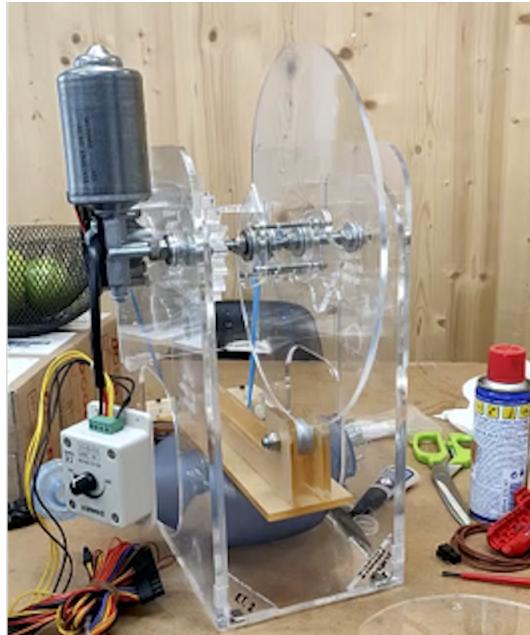


Figure 4: OxyGEN's Maker Version (OxyGEN-M)

The Components

As stated in the previous section, OxyGEN is aimed at tackling the problem of the immediate need for emergency ventilators in the event of a broken supply chain. Thus, the challenge doesn't solely reside in building a functional and reliable emergency ventilator but also in using massively available parts.

The OxyGEN ventilators rely on an already existing AMBU bag, a manual resuscitator. This is a hand-held device commonly used to provide positive pressure ventilation to patients who are not breathing or not breathing adequately. It is ideal for the project because it is widely available (present in large numbers in Hospitals, Ambulances, etc) since it is a required part of resuscitation kits for trained professionals. In fact, the AMBU company chose our project as one of the 3-4 projects they wanted to test internally in Denmark, as they had big demands worldwide for their manual resuscitators and wanted to decide on the most promising projects.



Figure 5: A manual resuscitator (AMBU)

The first step is the motor. In this situation, the obvious choice (and the choice most other teams working on emergency ventilators went for) is using a Stepper Motor: it enables precise rotation and easy control through an Arduino-like Micro-controller. But this kind of motors and their associated drivers would be hard to come by in a stressed supply chain. After a number of tests with micro-waves, drills or juicers motors we thought of wiper-motors. Available anywhere, they are reliable and can be used for long periods of time. I happened to have an old Peugeot 504 in my garage: it soon became the motor of our first OxyGEN functional prototype.



Figure 6: Extraction of the Peugeot 504 wiper motor of our first prototype

A wiper motor needs a 12V power supply. We immediately thought about PC power-supplies: they are not as massive as a car battery and are available everywhere. We also needed to control such a motor. Since a Micro-controller does not fit OxyGEN's philoso-

phy, we used a LED dimmer to control the speed of the motor.

Some assembly materials are needed, but they are really flexible and depend on the particular needs and availability. Our first prototype was made of wood, we then used acrylic and stainless steel to make the sanitation process of the device easier.

The Design

The team created a compact design that can be built in any material (wood, acrylic, stainless steel, etc). Basic screws, bolts and nuts are the only necessary assembly components.

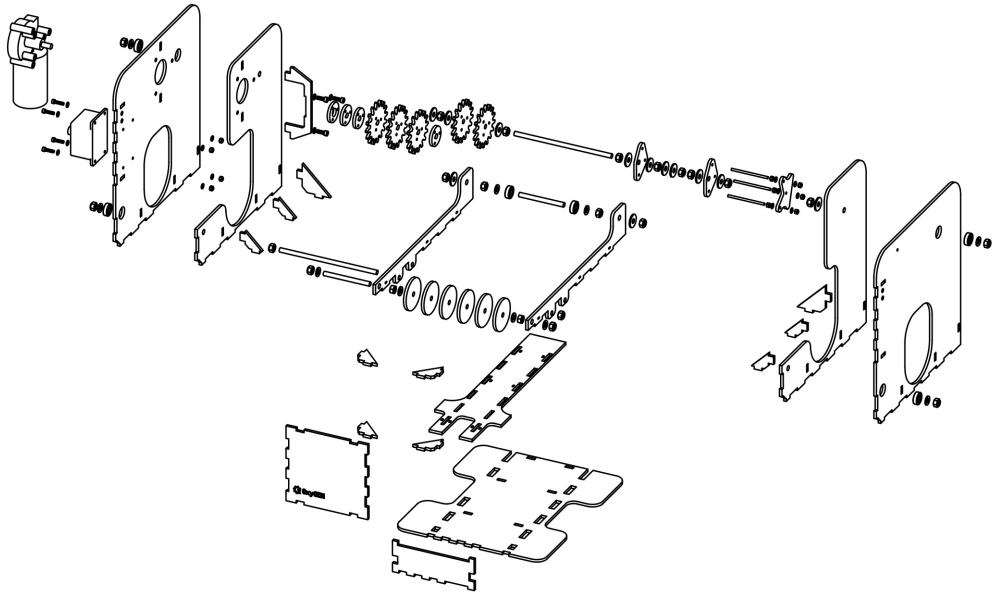


Figure 7: OxyGEN-M 5th version exploded

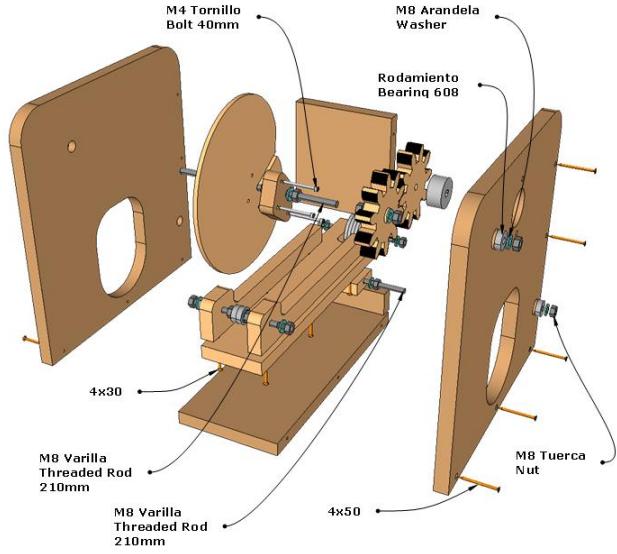


Figure 8: OxyGEN-M wood version 18mm

The Camshaft

Before a deeper thought, one might think that since the AMBU device is used manually, the respiratory cycle curve shape is not a critical point. However, AMBU devices are designed to be used for short periods of time. Long-term use of a ventilator with inaccurate or irregular cycles can generate negative effects on the patient. For this reason, one of the key tasks of the project was to accurately design the respiratory cycle by our cam approach.

Hospital's mechanical ventilators have a large number of adjustment parameters (total volume displaced, airflow rate and duration of inhalation and exhalation phases, waiting time between both phases, etc). That enables them to adapt perfectly to each patient's needs (sex, age, diseases, etc). However, the adjustment of these parameters is carried out with electronics, which we can not do with OxyGEN. Thus we thought about using a camshaft system and pressing a lever on the AMBU with a precise cam.

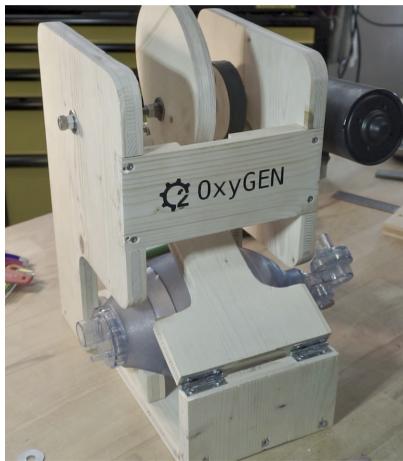


Figure 9: OxyGEN-M1 with it's first cam design



Figure 10: Render of OxyGEN's first version

The team created a Matlab script generating a template to build customized cams, as well as compatible with possible different designs and variations in the dimensions of the device's structure.

With the knowledge we got from the Biogear's project [3], we started creating the mathematical function describing the cam's shape. It must be a C^1 function: otherwise, we would have a cam with spikes.

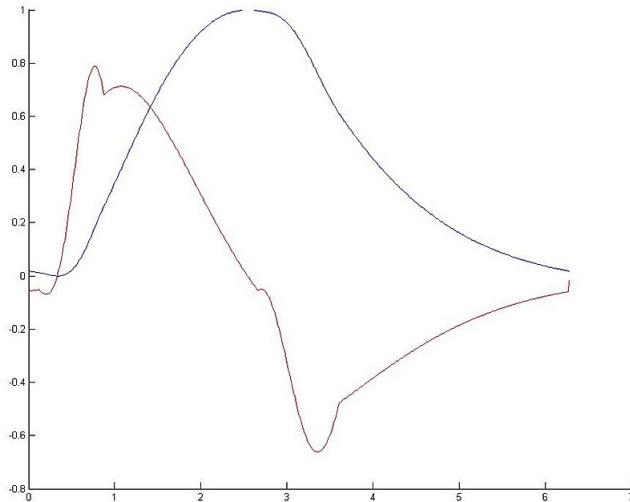


Figure 11: Normalized breathing curve (blue), and its first derivative (red)

Once the function is defined, we normalize it on the vertical axis and adjust it to 2π on the horizontal axis. For the generation of the cam, the normalized curve measurements are adjusted to the minimum and maximum radius necessary for the cam, and then plotted using polar coordinates.

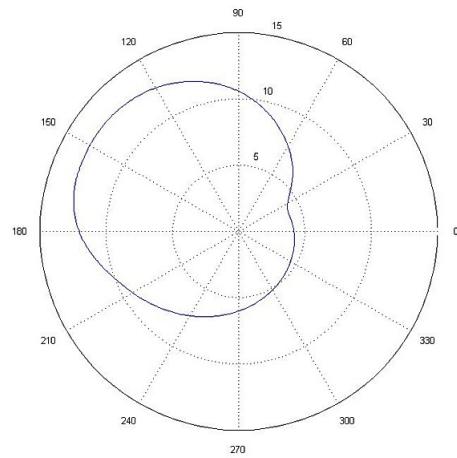


Figure 12: Single cycle cam; minRadius=4cm, travelDistance=9cm

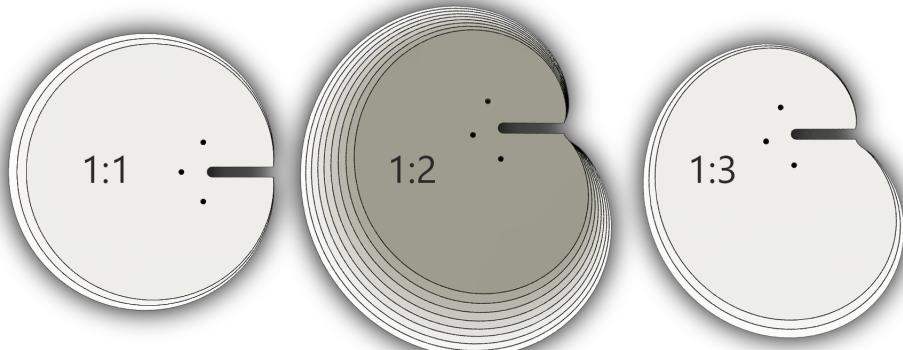


Figure 13: 3 different cams

The cams are very easily interchangeable thanks to a clever system of elastic pressure fixation (a few seconds).

3.2 Multiple Versions

OxyGEN was born with a fast innovation process. Thus, many iterations were needed and a new improved version was made every day in the first weeks, with the constant feedback we got from hospitals, durability tests or the community.

OxyGEN started with the Maker mentality: we wanted our emergency ventilators to be easily assembled by anyone, without the need for special tools. However, as the project grew and became one of the most promising emergency ventilators, we started to be in contact with the car industry sector (I will detail this process further in the Medical approvals & Production section). Thus we designed an industrial version of OxyGEN, adapted to the machines available in car industry factories: OxyGEN-IP. The essential operation of this version is the same. The difference is the material used (stainless steel) and the fact that the cams and lever are surrounded by a stainless-steel cover, to make the device safer to use.



Figure 14: All the different OxyGEN versions

OxyGEN thus has two version branches: the original Maker version (OxyGEN-M) and the Production version (OxyGEN-IP). The international teams working on the projects

are modifying them depending on their needs (different car companies, different medical requirements, etc).

3.3 Drawbacks

As an emergency ventilator project designed for a very particular situation, a supply chain shortage and an immediate need for high scale production, it has drawbacks. Other projects using precise electronics, sensors and software would adapt much better in other contexts.

An important weakness of OxyGEN is that it doesn't adapt to the patient's respiratory rate on its own. That means that we do not have a sensor to detect when the patient is trying to expire, which can be a problem if the patient is not sedated and tries to counter the respiration rate the ventilator imposing on him. This issue could be improved by adding a module with sensors and a micro-controller. This highlights the strength of the modular design of OxyGEN: the essential task that an OxyGEN performs can always be improved by modules.

OxyGEN also relies on a mechanical pressing of the AMBU and physical immutable scheme for its cycle. This means that for each slightly different cycle we want to perform, a new cam needs to be generated, built and exchanged. This is feasible but can be impractical when slight changes are to be applied on short periods of time (varying condition on patients).

4 OxyGEN's Current Status

4.1 Medical Approvals & Production

Two Barcelona hospitals were key to the success of the OxyGEN project: the Hospital Clinic de Barcelona and Hospital Germans Trias i Pujol (known as Can Ruti Hospital). They assigned Dr. Nicolas and Dr. Priego respectively to give their insights and guide the project as we had no medically trained person in the beginning in core team of OxyGEN. Their integration in the core team was critical. Every day, we made trials in both hospitals, testing each new version to improve anything that needed to be. We felt a growing enthusiasm from the medical personnel on each of our trips to the testing labs: this was urgently needed, as hospital beds and ICU's started to be overflowed with COVID-19 patients. This fueled the whole team to keep working hard, as the weeks of stress and sleep deprived days started to pile. We felt a huge responsibility to come with the right solution as fast as possible.

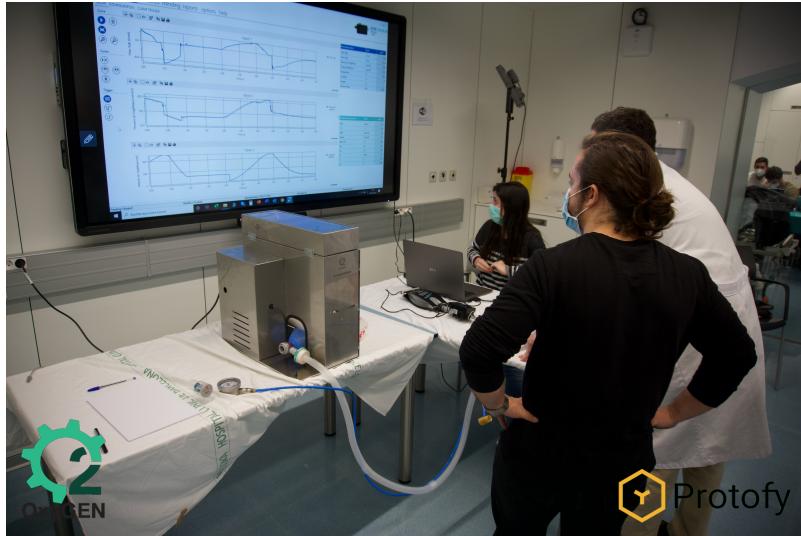


Figure 15: Functionality tests in Hospital Clinic de Barcelona

We started with elementary functionality tests. Then we performed monitoring and longevity testing. As we succeeded those, we then performed tests on live animals (pigs). Finally, some COVID19 patients from Hospital Clinic and Can Ruti were intubated with an OxyGEN.

With these tests succeeding and as the car industry sector started to gain interest in producing emergency ventilator (Tesla, Volkswagen, etc) every puzzle piece was in place to start saving lives.

4.2 Impact & Results

In Spain

With the global pandemic progressing around the globe, and with the lockdown set-up in multiple countries, many business and factories stopped their activity. In particular, the car industry sector stopped producing in Spain mid-march. The Seat León assembly line, located in Martorell, near Barcelona, stopped it's activity on March 13th, with staff layoffs on the table [6].

Luckily for us, the car industry is perfect to build an emergency ventilator: they handle airflow and pressure both in engine parts and with air conditioning, they have rapid and high scale production capabilities and are used to work under strict compliance. As they got interested in producing emergency ventilators, we were undergoing medical tests in our partner Barcelona hospitals and they contacted us, as we were one of the most advanced projects. That's when we forked our designs into 2 separate versions: OxyGEN-M

and OxyGEN-IP. The latter was designed to be easily produced by a car company like Seat. We worked with Seat for several days before getting the AEMPS approvals and they started producing 300 units per day [14].



Figure 16: Seat León production line assembling OxyGEN-IP

The AEMPS approval for clinical trials [2] meant that any hospital wanting or needing to use OxyGEN's emergency ventilator could sign up and Seat would deliver whatever they needed from their Martorell factory.



Figure 17: SEAT León production line preparing the delivery of numerous OxyGEN-IP

Due to the ongoing emergency situation and with the difficulty to have accurate numbers (for instance only 59% of hospital ventilators inventory is known), we do not know the exact impact OxyGEN had in Spain, or how many hospitals ended up using them. However, the COVID-19 peak of hospitalization happened between March 31st and April 9th. Thus, it has to be noted that OxyGEN arrived in production state a bit late in Spain: the situation was less critical than a few days/weeks back and Emergency ventilators were less necessary.

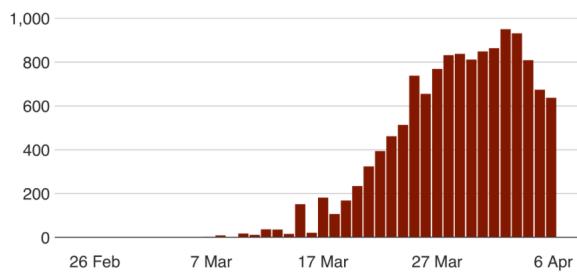


Figure 18: Daily confirmed deaths from COVID-19 (Spanish Health Ministry)

International Impact & Results

From the beginning, we were lucky to count on international collaboration. That was possible through our community organized on a Discord comprising more than 2100 members. From engineers to medical personnel, they were key to the success of OxyGEN. They helped us make OxyGEN a reality because, like us, they were preoccupied with the

critical situation and wanted to help find a solution. That is, most of them didn't only work for the project to be viable in Spain, but also to later be a potential solution for their country as well. That is why OxyGEN is designed to be a very adaptable device: it wasn't only built in the scope of Spanish medical compliance.

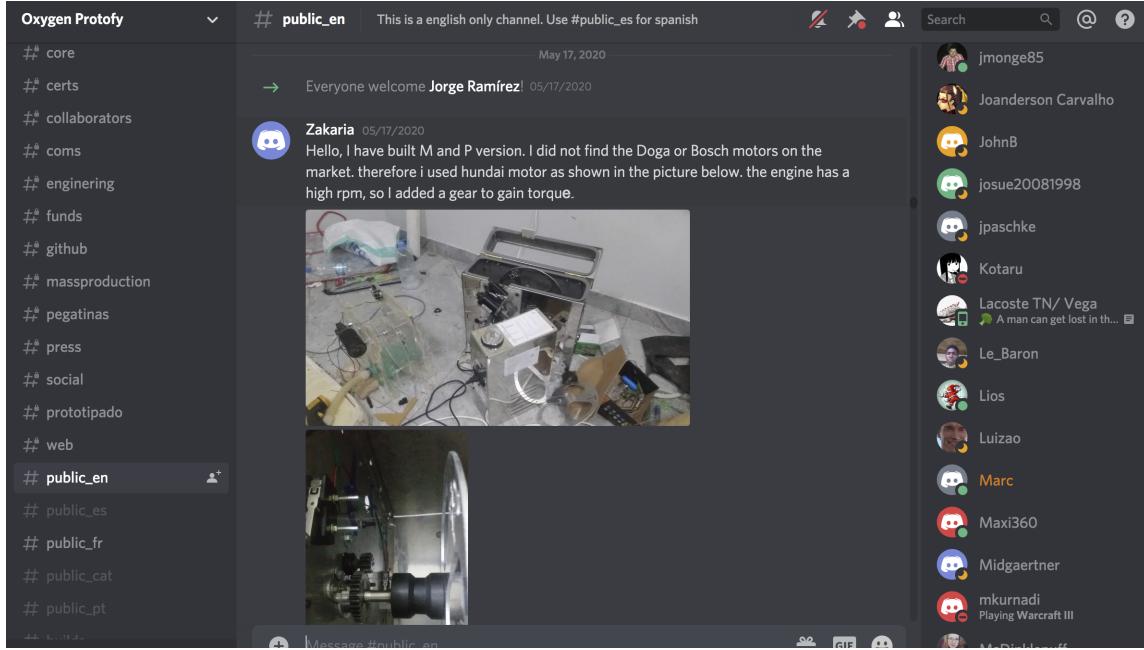


Figure 19: A view of the Discord's organisation

Many teams of engineers, working with local hospitals and producers, emerged all around the world. I will detail this part in Next Steps section.

5 Key Learnings

5.1 The unprecedented situation brought strong collaboration

The 2020 Pandemic caused a global social and economic disruption, with half of humanity on lock-down. This has had many effects on citizens and companies, from panic buying causing widespread supply shortages or a rise in racial discrimination to important donations to the medical sector or daily acts of bravery by essential workers. As a project that started during the Pandemic and that aimed at fighting it, OxyGEN was deeply impacted by this social and economic disruption.

The community, amounting to thousands of helping hands from all over the world, were all there for the same reason: doing its bit to help solve the global crisis. Some were

doctors dedicating some time at the end of their exhausting day to share their precious point of view with us. Others where makers or engineers concerned by the effects would have in their community. The maker movement, driven by solidarity, emerged from every part of the world.

Many companies also engaged in this solidarity movement. SEAT-VOLKSWAGEN dedicated Seat Leon's assembly line to produce OxyGEN, IDNEO issued the Electromagnetic tests and certifications, DOGA gave us every wiper motor we needed for production, Recam Laser built the first 20 OxyGEN-IP units, LF channel managed OxyGEN's public relations and the media, and many others. Brand image can be a strong factor in firm solidarity, especially considering the high media attention the project had in Spain and internationally. Nevertheless many helped without issuing any public statement.



Figure 20: The first 20 OxyGEN-IP units, assembled by Recam Laser



Figure 21: Seat León production line assembling OxyGEN-IP

5.2 Working with the Medical Sector

The medical sector has the enormous responsibility of keeping humans alive. Thus, safety always comes first and to produce innovation in such a sector is a long and tedious task. A battery of tests, medical compliance and n-tuple checks are necessary to ensure that no one's life is at risk. And for a medical device that aspires to be in charge of such a critical zone as is the respiratory system, this is even more true.

However, due to the urgency that the COVID19 pandemic created, extreme measures had to be taken. Hospitals were out of ventilators and were starting to have to choose whom to let go. At the time, we knew this was the case in Italy, but were not aware it was also the case in Spain. The project was stressful and intense since the beginning, but the day we got a call at 2 am from Can Ruti Hospital, the reality of the impact OxyGEN could have was revealed to the whole team. They told us that they were going to be out of respirators the next day and asked us how many units we could produce during the night. There was urgency in their call for help and it drove our efforts from then onwards.

The Spanish Agency for Medicine and Medical Devices (AEMPS) key. A few weeks after passing the tests in our partnered Barcelona hospitals, OxyGEN was the first emergency ventilator to be approved for clinical trials in Spain. That meant that any hospital that wanted or needed one could request one from the Seat-Volkswagen supplier and use it on patients. These few weeks might sound like a lot, but as stated, this process generally requires years of tests before being approved.

However, as exceptional as the situation was, it could also have been faster. As OxyGEN was ready to be used in patients in Spain thanks to all the tests we did in the Clinic and the Can Ruti Hospitals, and all the improvements we did on the ventilator, the AEMPS could have sped the process even further instead of taking 2-3 weeks to approve it. The need was high during these 2-3 weeks and OxyGEN ended up arriving slightly late in Spain, as the curve slowly started to flatten as it got the medical approvals.

5.3 Fast Innovation Process & Team Management

Protofy, as a fast prototyping start-up, was the perfect team to lead the OxyGEN project. But the combining factors of working on a medical device and the pressure of having to do it in the smallest possible time stepped up the difficulty of the project. Lives were on the line and, as the most advanced emergency ventilator project in Spain, we had the responsibility to do everything that we could to make OxyGEN available fast.

The core team of OxyGEN counted several external collaborators with very different backgrounds and was composed of around 14 people. The goal was to accelerate the process as much as possible. Every single night for 1 month and a half, we had a team video-call where each of us would share the day's inputs and discuss the next steps. Sometimes, a quick 1-hour call was enough, but more often, we would go on until late at night: things developed so quickly. Every I+D step that would've normally spanned in a year was condensed in 3 weeks.

5.4 Social Innovation

The OxyGEN project was set as a Social Innovation project. As a team we decided that we would work on the project without any commercial purpose and all the team has worked with no economical reward. As an open-hardware project, the designs are publicly available on our Github repository and anyone can use them. OxyGEN is licensed as a Creative Commons. The goal of a social innovation project is to have a social purpose before an economical one. In our case, it came from a group of people that wanted to help bring a solution to the critical problem of ventilator shortage. The whole team was fully dedicated to the project for 2 months. Many of us had jobs or studies to pursue but were so passionate about contributing to helping at this critical situation that we focused on it full-time. Some of us placed their holidays, others delayed their daily obligations.

In April, in order to support the expenses of the project and international deployment and to continue to improve the design we decided to set-up a fundraising campaign. We used GoFundMe, raising 21,000 euros. The success of the project needed an active engineering team and Protofy, as a relatively small business, couldn't continue to set aside its economically profitable projects indefinitely.

6 Next Steps

6.1 International Support

Right now, we are giving comprehensive advice to 52 projects distributed in 31 countries. We know that there are even more, that have not contacted us for additional information since all that is needed is publicly available on our repository. These international teams are reproducing similar processes of fabrication, certification and production we endured in Spain. We are thus actively helping them in the engineering side as well as the industrial and certification protocol.

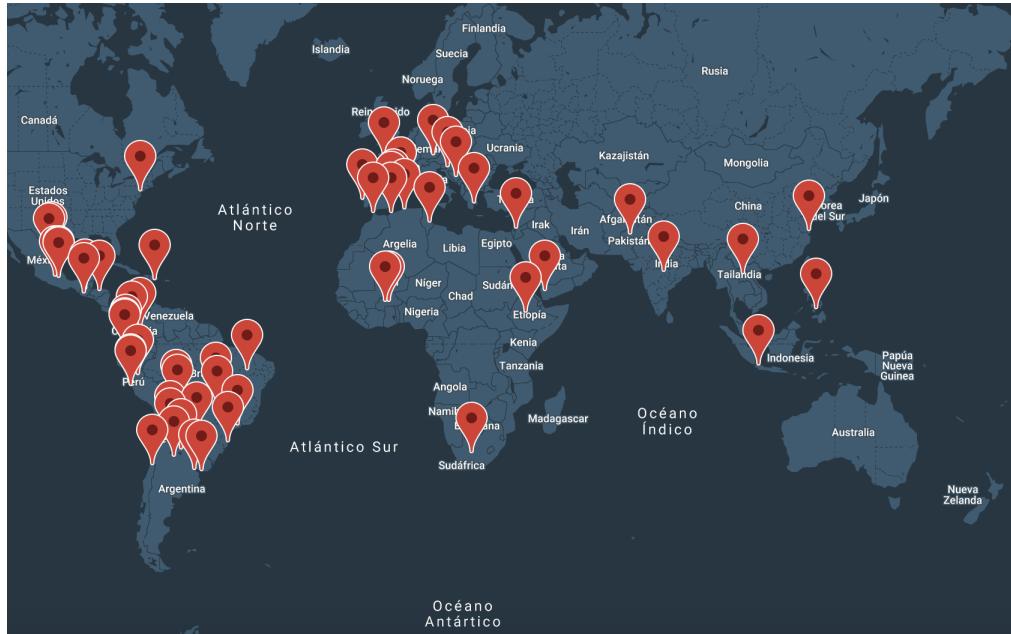


Figure 22: Every active OxyGEN project around the world

In Brasil for example, they are currently in talks with Volkswagen, Scania and local car industry to produce OxyGEN-IP locally. In parallel, they are conducting medical trials on animals. In Guatemala, they have received a prize for innovation and, under the leadership of El Pilar Hospital, they are also conducting medical trials on animals. In some cases, in addition to advice, we shipped an OxyGEN machine to accelerate the reproduction

(Pakistan, Rwanda and some South American countries).

We are also collaborating with international organizations like the WHO, MSF (Médecins Sans Frontières), the Skoll Foundation or even Acumen. They have been critical to speed up the networking process, especially in third world countries, where it would have been much harder to find them ourselves. MSF, for instance, was critical to have the field expert's view on the real needs of these countries. We are currently assessing with the PAHO (WHO in South America) to send spare OxyGEN machines from SEAT's production to South America.

6.2 Module Extension

Various module extensions have been implemented for OxyGEN both from the core OxyGEN team and from external and international teams using the device. The first add-on we implemented was an alarm system to warn the medical personnel should the motor fail. We also made it easy to incorporate a number of sensors to the device to monitor a number of ventilation data like the total volume displaced or the airflow rate.

We also considered the problem of asepsis relatively early on. Emergency ventilators do not contain viruses: on normal use, the virus will spread in the form of aerosols, on expiration [7]. The goal is to eliminate the virus from said aerosols before they spread in the room where the patient is being treated. A member from the CoronaVirusMakers had an idea: since Biocidal agents inactivate the COVID-19 virus [9], we could set-up a bubble column reactor with said agents at the expiration end. This could be possible by connecting an easy-to-build one-way valve at the expiration end and managing the correct water height to achieve hydrostatic pressure. As the expired air would go through the bubble column, the biocidal agents (bleach for example) would inactivate the virus and thus achieve asepsis.

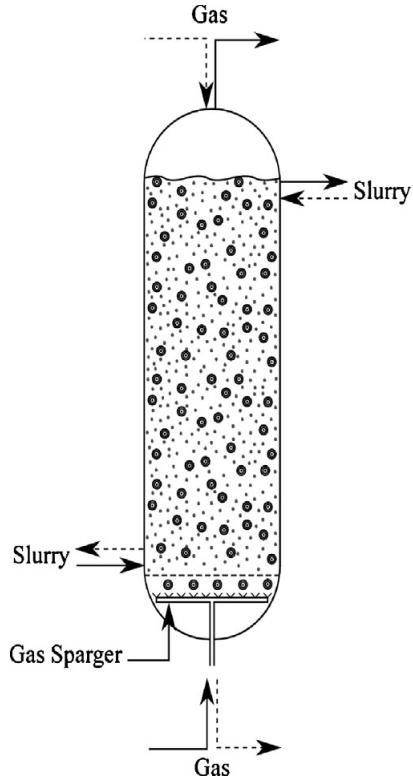


Figure 23: A simple bubble column reactor

We did not implement this module due to the lower priority it had for doctors at the time, and the relative complexity a water column would bring to an environment where patients were moved around often due to hospital's overflow.

Many other modules have been implemented by international teams to adapt to their medical agencies' requirements and to extend OxyGEN's capabilities.

6.3 Viability in post - COVID-19 Context

As developed, OxyGEN's primary concern is responding to an urgent need of emergency ventilators under very special broken supply chain situations. Under different circumstances, other approaches (using precise electronics for example) become way better options in many cases. However, working with MSF and other NGOs, we realized that our low-cost and low-tech approach could make sense in some of these countries.

Ventilators and intensive care units are not only used for respiratory disease treatment [16]. Major surgeries often require the anesthetist to ventilate the patient [5]. He must be careful to do the patient no harm, particularly when using the ventilator. That becomes a huge problem in places where the necessary equipment is not found. The overall

anesthesia-related mortality in developing countries is still a big issue, especially in pediatric care. The most common pediatric anesthesia method is general anesthesia with manual ventilation or spontaneous breathing. Most pediatric-related mortality is due to airway-related complications [13]. OxyGEN could potentially have a big impact on such scenarios.

But as we developed in the “Medical challenges” section, proper mechanical ventilation requires a mixture of air and oxygen, even for surgical procedures [4]. Thus, it is important to have an oxygen intake, and these are often not available in remote places. This is a challenge we are currently investigating together with MSF.

7 Conclusion

The OxyGEN project was a real challenge. Building an emergency ventilator from scratch that needed to be approved by the national medical agencies and ready to ventilate patients in a matter of weeks seemed unfeasible in the beginning. With the already existing constraints, we had to work with a broken supply-chain that forced us to have a low-tech approach. In addition to the fact that we had to design a low-cost device.

Many factors were keys to the success of OxyGEN. Firstly, the core team was small (14 people) but we complemented each other very well. Crucially, we all worked with passion and purpose, fully committed to this social innovation project. Secondly, the Maker movement, represented by the 2100+ international community that participated, followed and then produced OxyGEN, was an essential success factor. This was not only key for the realisation of the project, but also for the additional motivation it brought to the team and everyone involved in the project. The community believed in the project and the impact it could have. Another fundamental actor was the public and private organizations support. Hospitals endorsing the project; national and international health organizations approving the device; NGOs helping us reach remote populations and companies providing industrial facilities, components, transportation, legal support or public relations management etc.

As a result of this national and international support, OxyGEN became the first emergency ventilator project to be approved in Spain by the medical agency (AEMPS) on April 3rd 2020. The entire Seat León (Volkswagen group) production line was adapted to produce OxyGEN devices at a rate of 300 units/day, to make them available for any Spanish hospital that would require them. The international community built around OxyGEN, as well as the cooperation with international organisations like the World Health Organization or Doctors Without Borders (MSF) stimulated the creation of more than 52 teams in at least 31 countries working on, improving and building the OxyGEN design with the support from the core team to guide them in the medical approvals.

As a personal note, I would like to add that this project was life-changing for me. I was

lucky enough to be a part of the core team of OxyGEN and was able to experience every step of the process. It was exciting to be an actor of a project that evolved extremely fast. A new big decision that could change the outcome of OxyGEN had to be made every day, if not every hour. But most importantly, I was deeply moved by the amount of people that genuinely wanted to help, giving us everything that they could to help turn the project into a reality and save lives. It would be amazing to see this solidarity movement continue past the COVID-19 crisis.

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A Appendix: Official Documents

A.1 AEMPS Clinical Approvals



PS/CR798/20/EC v.3

AUTORIZACION DE INVESTIGACIONES CLINICAS

Visto el procedimiento iniciado por Germans Trias i Pujol Research Institute (IGTP), como promotor de la investigación clínica “ESTUDIO RES-COVID: BALÓN RESUCITADOR AUTOMATIZADO MECANIZADO COMO ALTERNATIVA A LA COMPRESIÓN MANUAL PARA LA VMI DE PACIENTES CRÍTICOS EN SITUACIÓN DE ALARMA. PROTOCOLO DE USO COMPASIVO.” Versión 3(30/03/2020), nº expte. 798/20/EC v.3, en solicitud de autorización de la misma.

Tramitado el procedimiento conforme a lo dispuesto en el Título IV de la Ley 39/2015, de 1 de octubre, del Procedimiento Administrativo Común de las Administraciones Públicas y, consideradas las disposiciones establecidas en el capítulo VIII del Real Decreto 1591/2009, de 16 de octubre, por el que se regulan los productos sanitarios y el Real Decreto 1275/2011, de 16 de septiembre, por el que se crea la Agencia estatal “Agencia Española de Medicamentos y Productos Sanitarios” y se aprueba su estatuto.

En su virtud, a propuesta del Departamento de Productos Sanitarios, y en el uso de las atribuciones que me están conferidas, he resuelto

AUTORIZAR la realización de la investigación clínica indicada en las condiciones y términos que figuran en el expediente, en los centros sanitarios siguientes:

- Hospital Germans Trias i Pujol
- Hospital Clinic de Barcelona

Contra esta resolución que agota la vía administrativa puede interponerse potestativamente recurso de reposición ante la Directora de la Agencia Española de Medicamentos y Productos Sanitarios en el plazo de un mes, conforme a lo dispuesto en los artículos 123 y 124 de la Ley 39/2015, de 1 de octubre del Procedimiento Administrativo Común de las Administraciones Públicas, o interponerse recurso contencioso-administrativo ante el Juzgado Central de lo Contencioso-administrativo de la Comunidad Autónoma de Madrid, en el plazo de dos meses a contar desde el día siguiente a la recepción de la presente notificación, conforme a lo dispuesto en la Ley reguladora de la Jurisdicción Contencioso-Administrativa de 13 de julio de 1998, y sin perjuicio de cualquier otro recurso que pudiera interponerse.

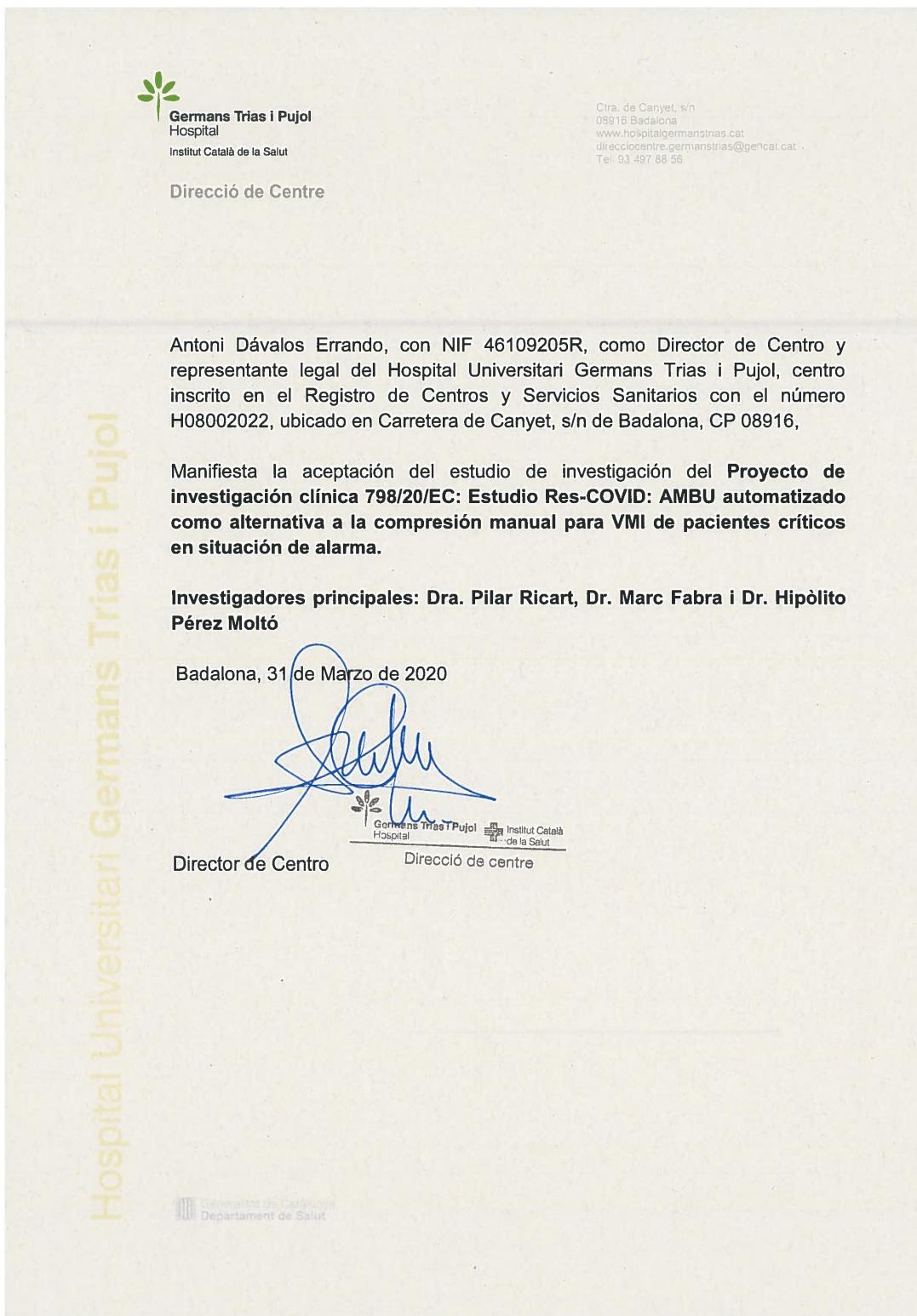
Mediante este documento se Notifica a D. Manel Puig Domingo, MD, PhD, (Acting Director and Professor of Endocrinology – Germans Trias i Pujol Research Institute (IGTP) Universitat Autónoma de Barcelona; Campus Can Ruti; Carretera de Can Ruti, Camí de les Escoles s/n; 08916 Badalona, Barcelona), la presente resolución, según lo exigido en el artículo 40 de la mencionada Ley 39/2015.

DIRECTORA DE LA AGENCIA ESPAÑOLA DE MEDICAMENTOS Y PRODUCTOS SANITARIOS

M^a Jesús Lamas Díaz

Agencia Española de Medicamentos y Productos Sanitarios Fecha de la firma: 03/04/2020 Puede comprobar la autenticidad del documento en la sede de la AEMPS: https://sede.aemps.gob.es	Localizador: K B Y A B 7 S B 8 6
CORREO ELECTRÓNICO sgps@aemps.es	Página 1 de 1 C/ CAMPEZO, 1 - EDIFICIO 8 28022 MADRID Tel.: (+34) 91.822.54.99 Fax: (+34) 91.822.52.89

A.2 Hospital Acceptance Documents



A.3 Animal Clinical Validation



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Instituto de Investigación Germans Trias i Pujol

INFORME DEL PROJECTE RESCOVID - OxyGEN

27/03/2020

Avaluació de la capacitat del respirador OxyGEN en model porcí, per compensar diferents escenaris patològics respiratoris, i aconseguir uns nivells adequats d'oxigenació i ventilació: PaO₂ Pa CO₂ i pH en sang. Codi DMAH 10681.

Marc Fabra Raduàⁱ, Adrià Escudero Teixidóⁱ, David Priegoⁱ, March Cusachsⁱⁱⁱ, Jordi Grífols Rondaⁱⁱ, Sara Capdevila Larripaⁱⁱ, Osvald Pinoⁱⁱ, Martí Pons Òdena^{iv}, Fritz Diekmann^v, Elena Baltà^{vi}, Ignasi Plaza Álvaro^{vii}

- i- Hospital Universitari Germans Trias i Pujol
- ii- Centre de Medicina Comparativa i Bioimatge – IGTP
- iii- Institut de Recerca Germans Trias i Pujol (IGTP)
- iv- Hospital Sant Joan de Déu
- v- Hospital Clínic de Barcelona
- vi- Seat
- vii- OxyGEN

Informació prèvia

L'equip "OxyGEN" correspon a un ambú mecanitzat per a actuar com a ventilador en situació d'emergència. L'equip ha estat validat al laboratori de fisiologia respiratòria de l'Hospital Clínic de Barcelona, amb un simulador respiratori, en situacions de diferent compliment i resistència, simulant una mínima patologia fins a simular una patologia extrema asimilada a un pneumotòrax.

Material i Mètodes

L'estudi en fase animal es realitza al Centre de Medicina Comparativa i Bioimatge de Catalunya, de l'Institut de Recerca Germans Trias i Pujol, registrat com a centre d'experimentació animal amb el codi B9900005, després de ser aprovat pel Comitè d'Ètica d'Experimentació Animal del propi centre.

El dia 23/03/2020 es realitza una prova de concepte amb un porc de raça Largewhite x Landrace de 35 kg de pes, seguint el cronograma detallat més endavant.

Durant tot l'estudi l'animal es manté anestesiat de forma contínua amb una infusió de propofol (5-20mg/kg/h), paralitzat mitjançant lús de besilat d'atracuri (2mg/kg IV), i sondat endotrachealment i connectat a una màquina d'anestèsia Wato-Ex35 de Mindray que controla l'aportació d'oxigen i aire.

S'estableix una via venosa permeable a la vena auricular ventral per a fluïdoteràpia de manteniment (Sèrum salí fisiològic a 100-300 mL/h segons requeriment), i una via arterial heparinitzada a l'artèria auricular dorsal per al mostreig i estudi analític de la gasometria arterial (les mostres es preserven amb gel durant el trasllat fins l'aparell analitzador localitzat a l'HUGTiP).

Es fa suport tèrmic de l'animal mitjançant estora elèctrica sota el cos i amb escalfador automàtic de fluids. El control anestèsic es fa per connexió a un aparell multi paramètric Mindray ipn 12-Vet, controlant els següents paràmetres: ECG, freqüència cardíaca, EtCO₂, SpO₂, freqüència respiratòria, temperatura rectal i pressió arterial no invasiva.



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Es grava tot l'estudi (el funcionament del respirador OxyGEN i la pantalla del multi paramètric) per tenir constància dels valors mesurats de forma contínua. Hora d'inici 17:30h – Hora final 19:50h.

- 1. Mesura de paràmetres amb la màquina convencional d'anestesia Wato-Ex35 de Mindray (equipada amb respirador) i amb l'equip multi paramètric de control Mindray ipn 12-vet.**

17:30h Es mesuren els paràmetres del model en situació basal:

Manteniment en modus Volum Control Pressió amb PPI de 15 cm H₂O i PEEP de 3 cm H₂O, amb la resta de constants estables. EtCO₂ de 45 mm Hg. SpO₂ del 100%.

Es canvia a la modalitat de Pressió Control, simulant model experimental de l'equip OxyGen amb la lleva nº2 (en proves prèvies subministra 550mL de Volum corrent a boca de simulador/patient).

Pressió PPI de 20 cm H₂O; PEEP de 10 cm H₂O; EtCO₂ de 46; SpO₂ del 100%; FiO₂ de 90%. Freqüència Respiratòria de 16rpm (es mantindrà constant durant tot l'experiment). Volum Corrent mesurat a boca de 550mL.

S'obtenen les següents variables fisiològiques: Saturació 100% . EtCO₂ 46 mm Hg. Constants hemodinàmiques estables.

- 2. Connexió i estabilització amb el prototip de respirador OxyGEN, i control en diferents situacions amb l'equip multi paramètric de control Mindray ipn 12-vet.**

- 2.1 Model de ventilació en animal sà, anestesiat i connectat amb el prototip OxyGEN a avaluar.**

17: 47 Canvi de respirador Mindray a respirador OxyGEN amb la lleva nº2 i FiO₂ fixa a 100% durant tot l'experiment.

17: 50 Presa de mostra basal de 1 mL de sang arterial amb xeringa de gasos.

L'analítica de gasos en sang es realitza a HUGTiP a les 18:25: pH 7,55; pCO₂ 37 mm Hg; pO₂ 523 mm Hg; sO₂ 99.1%.

18: 00 2a Presa de mostra de sang.

L'analítica de gasos en sang es realitza a HUGTiP a les 18:26: pH 7,54; pCO₂ 38 mm Hg; pO₂ 550 mm Hg; sO₂ 98.6%.

18: 16 L'animal torna al respirador Mindray durant 1 minut per lubricar l'equip OxyGEN.



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2.2 Model d'obesitat: afectació a la conformitat ("compliance") de la caixa toràcica aconseguit per compressió de l'abdomen amb un pes de 5 Kg. Mesura dels paràmetres respiratoris durant 30 minuts.

- 18:17 Es connecta l'animal al respirador prototip OxyGEN.
- 18:18 Inici del model d'obesitat afegint 5kg de pes a la zona abdominal de l'animal en posició decúbit lateral.
- 18:28 S'incrementa el pes en el model fins a 10Kg de pes zona abdominal de l'animal en posició decúbit lateral, s'afegeix inclinació aproximada de 10 graus descendant caudo-craneal a la taula quirúrgica.
- 18:31 S'intensifica la compressió toràcica canviant l'animal a decúbit supí amb els 10kg de pes a la zona abdominal.
- 18:49 Presa de mostra basal de 1mL de sang arterial amb xeringa de gasos.
L'analítica de gasos en sang es realitza a HUGTiP a les 19:32: pH 7,54; pCO₂ 36 mm Hg; pO₂ 565 mm Hg; sO₂ 98.8%.

2.3 Model animal sa amb canvi de Volum Corrent:

- 18:52 Canvi de lleva, a la de mida nº3.
Fins al moment el Volum Corrent era de 500mL i EtCO₂ de 33 mm Hg. Després del canvi de lleva el Volum Corrent és de 380mL, EtCO₂ de 39 mm Hg, Pressió PPI de 18 cm H₂O i PEEP de 10 cm H₂O.
- 19: 00 Mostra de 1 mL de sang arterial amb xeringa de gasos.
L'analítica de gasos en sang es realitza a HUGTiP a les 19:35: pH 7,46; pCO₂ 45 mm Hg; pO₂ 556 mm Hg; sO₂ 98.7%.
- 19:05 EtCO₂ de 41 mm Hg.

2.4 Model animal de síndrome de dificultat respiratòria aguda moderada (SDRA):

- 19:06: Canvi de lleva a la de mida nº2.
Inici model SDRA (Am J Respir. Crit. Care Med. Vol 199, Iss 5, pp 603–612, Mar 1, 2019): S'estableix una ventilació per Volum Control. Es realitza un rentat alveolar amb 700mL de Sèrum Salí Fisiològic (30mL/kg), temperat i introduït a través de la sonda endotraqueal mitjançant una sonda de nutrició enteral pediàtrica fins que s'aconsegueix un P/F (pO₂ / FiO₂) inferior a 250 mm Hg.



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19: 15 Pressió PIC a 35 cm H2O; PEEP de 10 10 cm H2O; EtCO₂ espirada de 50 mm Hg, i Volum Corrent de 430mL.

19:30 Mostra de 1 mL de sang arterial amb xeringa de gasos.

L'analítica de gasos en sang es realitza a HUGTiP a les 20:16: pH 7.37 ; pCO₂ 52 mm Hg; pO₂ 386 mm Hg; sO₂ 98.7%.

2.5 Model SDRA amb obesitat: afectació a la conformitat (“compliance”) de la caixa toràcica aconseguida per compressió de l’abdomen amb un pes de 10 Kg amb l’animal posicionat en decúbit supí):

19: 34 S’afegeix compressió toràcica al model, afegint un pes abdominal de 10Kg en decúbit supí.

EtCO₂ espirada de 51 mm Hg.

La corba de EtCO₂ espirada, mostra una petita empremta al final de l’espació, coincidint amb un petit artefacte de la lleva (tall d’introducció de la lleva).

S’observa un descens de volum corrent a 410mL.

19: 40 Mostra de 1 mL de sang arterial amb xeringa de gasos del model SDRA + compressió (model obès).

L'analítica de gasos en sang es realitza a HUGTiP a les 20:19: pH 7,31; pCO₂ 58 mm Hg; pO₂ 221 mm Hg; sO₂ 98,7%.

S’aconsegueix un pO₂ / FiO₂ aproximat de 200, en el límit alt de la definició de SDRA moderat.

2.6 Valoració de la resposta d’hipercàpnia a l’augment de freqüència respiratòria:

19:42 Freqüència respiratòria augmenta a 20 rpm; EtCO₂ de 46 mm Hg.

19:46 Mostra de 1mL de sang arterial amb xeringa de gasos del model SDRA + compressió + augment de Freqüència Respiratòria.

L'analítica de gasos en sang es realitza a HUGTiP a les 20:19. pH 7,41; pCO₂ 42 mm Hg; pO₂ 425 mm Hg; sO₂ 98,9%.

19:48 Retirada dels 10Kg de pes.

20:00 Eutanàsia del model animal.



CMCiB

Centre de Medicina Comparativa
i Bioimatge de Catalunya



Instituto de Investigación Germans Trias i Pujol

INFORME DEL PROJECTE RESCOVID - OxyGEN

27/03/2020

Avaluació de la capacitat del respirador OxyGEN en model porcí, per compensar diferents escenaris patològics respiratoris, i aconseguir uns nivells adequats d'oxygenació i ventilació: PaO₂ Pa CO₂ i pH en sang. Codi DMAH 10681.

3. Resum i conclusions:

En aquesta prova de concepte s'ha mantingut l'animal anestesiat i amb respiració assistida amb el prototip OxyGen, de forma continuada, des de les 17:47h fins les 19:48h (2 hores). Durant aquest període de temps i en les diferents circumstàncies respiratòries testades, s'ha observat:

L'animal ha mantingut unes constants, variables no invasives i paràmetres analítics de gasos arterials dintre d'un context d'estabilitat i seguretat aplicable a l'ésser humà.

El funcionament del dispositiu OxyGEN ha estat correcte durant tot el procés sense falles mecàniques.

Volem destacar la capacitat del dispositiu de modificar les pressions PPI en un context coherent com adaptació als canvis clínics simulats preservant de forma acceptable els volum corrents (caigudes del 10%).

Essent aquest un dispositiu amb un generador de baixa pressió, la capacitat del motor de modificar les pressions per a mantenir volums corrents estables dintre d'un rang acceptable l'aproparia a un mode teòric de Volum Control regulat per pressió amb gran avantatge sobre un model simple de pressió control.

La modificació de la freqüència respiratòria és de realització senzilla amb resposta clínica immediata en el model.

La modificació del volum corrent programat (implica canvi de lleva) es pot realitzar en un temps curt, però en el prototip definitiu no hauria de precisar d'us d'elements mecànics i garantir sempre una sola posició correcta de les peces.

Finalment, encara que no és atribuïble al model, la condensació sobre la vàlvula de PEEP pot fer que la vàlvula no mantinguï la pressió programada, per tant s'ha de garantir que aquesta quedi posicionada més elevada que el cap del pacient i no pugui retenir humitat.

A.4 Human Clinical Validation



**Validación traslacional del nuevo dispositivo de ventilación mecánica invasiva
OxyGEN en modelo humano**

Informe elaborado por Marc Fabra, Hipòlit Pérez Moltó y Pilar Ricart

Promotor: Institut de Recerca germans Trias, Badalona

Equipo investigador:

Josep Maria Nicolás, director del Institut clínic de medicina, Hospital Clínic
Sara Capdevila, veterinaria, directora del CMCiB
Jordi Grífols, veterinario, jefe del área quirúrgica y de Bioimagen del CMCiB
Marc Cusachs, biotecnólogo, jefe de innovación del IGTP
David Priego, cirujano, Dpt de innovación del Hosp germans Trias
Carol Gálvez, veterinaria, investigadora en el grupo de cardiología experimental, IGTP
Martí Pons, jefe de cuidados intensivos, Hosp Sant Joan de Deu
Marc Fabra; intensivista, Hospital germans Trias
Hipòlit Pérez Moltó, intensivista, Hospital germans Trias
Pilar Ricart, jefa de cuidados intensivos del Hospital germans Trias
Lluís Rovira, ingeniero, OxyGEN
Ignaci Plaza, ingeniero, OxyGEN
Ferran Cáceres, ingeniero, OxyGEN
Oriol Estrada, director de innovación, Hosp germans Trias
Manel Puig Domingo, director del IGTP

CEiC: Hospital germans Trias, Badalona

Presidente: Magí Farré

Con el fin de comprobar que el nuevo dispositivo OxyGEN es funcional y adecuado para su utilización clínica, se ha realizado una prueba de validación en humano en el Hosp Germans Trias de Badalona.

Previa obtención del Consentimiento Informado por parte de la familia del paciente, dicha validación se ha llevado a cabo en un varón de 61 años y de 61,5Kg de peso, afecto de infección grave por COVID19, siguiendo el protocolo elaborado por el equipo del estudio de validación. Dicha prueba se ha realizado en la Unidad de Cuidados Intensivo. El paciente fue sedado con Morfina 2mg/h ev y Midazolam 15mg ev iniciales y 10mg/h ev a partir de la primera hora, con relajación neuromuscular con Rocuronio 50mg/h ev para facilitar la ventilación invasiva.

Inicialmente, el paciente se encontraba conectado a un respirador volumétrico de uso convencional en modalidad Asistida/Controlada (A/C) por volumen. Para poder analizar los parámetros basales de referencia, se incluyeron: saturación de O₂ (SO₂), presión positiva al final de la espiración (peep), porcentaje de O₂ inspirado (FiO₂), Presión Pico, frecuencia respiratoria (FR), así como los valores de pH, PaCO₂, PaO₂, PaFiO₂, SatO₂ y lactato en gasometría sanguínea arterial. Estos parámetros se analizaron en las siguientes situaciones:

0. Paciente conectado a respirador volumétrico convencional en modalidad A/C: Los valores ventilatorios fueron de: Presión pico 20, Peep 12, SO₂ 95%, FiO₂ 35%, FR 20, VCorriente de 600ml (VMinuto de 12l). (Tabla 1)

	pH	PaCO ₂ (mmHg)	PaO ₂ (mmHg)	PaFiO ₂	SatO ₂ (%)	Lactato (mmol/l)
Basal	7.45	40	78	222	95.6	1.2

Tabla 1. Valores de gasometría sanguínea basales bajo ventilación de forma invasiva con respirador volumétrico convencional en modalidad A/C, antes de iniciar prueba de ventilación invasiva con OxyGEN en paciente Covid-19.

Una vez determinados los parámetros basales, se ha procede a conectar el paciente al nuevo dispositivo de ventilación invasiva OxyGEN, para validarla en condiciones fisiopatológicas de síndrome de distrés respiratorio agudo (SDRA) en el contexto de Neumonía secundaria a Infección por Covid-19.

1. Ventilación Inicial: ventilación del paciente con OxyGEN, leva 3 (650ml y relación I:E 1:2) y FR 22, con válvula de Peep de 10 cmH₂O y FiO₂ de 100% en reservorio de oxígeno del balón resucitador. Se realizan dos gasometrías sanguíneas, una a los 30 y a los 60 minutos de iniciar la ventilación con OxyGEN. Los valores ventilatorios fueron de: Presión pico 22cmH₂O, Peep 10cmH₂O, SO₂ 99%, FiO₂ 100%, FR 22, VCorriente de 475ml (VMinuto de 10.5l). (Tabla 2)

	pH	PaCO ₂ (mmHg)	PaO ₂ (mmHg)	PaFiO ₂	sO ₂ (%)	Lactato (mmol/l)
30 minutos	7.45	37	456	456	99.0	1.1
60 minutos	7.47	34	378	378	98.2	1.2

Tabla 2. Valores de gasometría sanguínea a los 30 y 60 minutos de iniciar ventilación invasiva con OxyGEN en paciente Covid-19.

2. Variación de parámetros ventilatorios: ventilación del paciente con OxyGEN, leva 3 (650ml y relación I:E 1:2) y FR 20, con válvula de Peep de 10 cmH₂O y FiO₂ de 100% en reservorio de oxígeno del balón resucitador. Se realiza una gasometría sanguínea a los 90 minutos de iniciar la ventilación con OxyGEN. Los valores ventilatorios fueron de: Presión pico 21cmH₂O, Peep 10cmH₂O, SO₂ 99%, FiO₂ 100%, FR 20, VCorriente de 500ml (VMinuto de 10l). (Tabla 3)

	pH	PaCO ₂ (mmHg)	PaO ₂ (mmHg)	PaFiO ₂	SatO ₂ (%)	Lactato (mmol/l)
90 minutos	7.42	39	380	380	99.0	1.0

Tabla 3. Valores de gasometría sanguínea a los 90 minutos de iniciar ventilación invasiva con OxyGEN en paciente Covid-19, tras 30 minutos de modificación de los parámetros ventilatorios.

3. Variación de parámetros ventilatorios y de oxigenación: ventilación del paciente con OxyGEN, leva 3 (650ml y relación I:E 1:2) y FR 18, con válvula de Peep de 10 cmH₂O y FiO₂ de 48% sin reservorio de oxígeno del balón resucitador. Se realiza una gasometría sanguínea a los 120 minutos de iniciar la ventilación con OxyGEN. Los valores ventilatorios

fueron de: Presión pico 19cmH₂O, Peep 10cmH₂O, SO₂ 95%, FiO₂ 48%, FR 18, VCorriente de 350ml (VMinuto de 6.3l). (Tabla 4)

	pH	PaCO ₂ (mmHg)	PaO ₂ (mmHg)	PaFiO ₂	SatO ₂ (%)	Lactato (mmol/l)
120 minutos	7.28	59	102	212.5	97.6	0.9

Tabla 4. Valores de gasometría sanguínea a los 120 minutos de iniciar ventilación invasiva con OxyGEN en paciente Covid-19, tras 30 minutos de modificación de los parámetros ventilatorios y de oxigenación retirando el reservorio del balón resucitador.

En esta fase del estudio observamos que, al desconectar el reservorio de oxígeno del balón resucitador para poder administrar una FiO₂ diferente del 100%, se pierde parte del Vcorriente efectivo con las compresiones con el árbol de levas del propio balón, con la consecuente hipoventilación del paciente. Al observar esta incidencia decidimos prolongar el estudio aplicando un dispositivo que nos ha permitido administrar una FiO₂ diferente del 100%, manteniendo el reservorio de oxígeno del balón resucitador. Conectamos en Y un caudalímetro de Aire Medicinal y un caudalímetro de O₂, que nos permitieron administrar un alto volumen de gas a diferente FiO₂ en el reservorio del balón resucitador, para evitar la pérdida de Vcorriente.

4. Variación de parámetros ventilatorios y de oxigenación con dispositivo en Y: ventilación del paciente con OxyGEN, leva 3 (650ml y relación I:E 1:2) y FR 20, con válvula de Peep de 10 cmH₂O y FiO₂ de 50% con dispositivo en Y mezclador de Aire Medicinal y O₂ conectado al reservorio de oxígeno del balón resucitador. Se realiza una gasometría sanguínea a los 150 minutos de iniciar la ventilación con OxyGEN. Los valores ventilatorios fueron de: Presión pico 21cmH₂O, Peep 10cmH₂O, SO₂ 97%, FiO₂ 50%, FR 20, VCorriente de 480ml (VMinuto de 9.6l). (Tabla 5)

	pH	PaCO ₂ (mmHg)	PaO ₂ (mmHg)	PaFiO ₂	sO ₂ (%)	Lactato (mmol/l)
150 minutos	7.34	49	86	172	96.8	0.6

Tabla 5. Valores de gasometría sanguínea a los 150 minutos de iniciar ventilación invasiva con OxyGEN en paciente Covid-19, tras 30 minutos de modificación de los parámetros ventilatorios y de oxigenación con

dispositivo en Y mezclador de Aire Medicinal y O₂ conectado al reservorio de oxígeno del balón resucitador.

5. Punto final del estudio. Desconexión de la ventilación invasiva con OxyGEN y reconexión del paciente a la ventilación invasiva con respirador volumétrico convencional en modalidad A/C

Conclusión:

Los datos analizados muestran unos parámetros de dinámica respiratoria y gases en sangre dentro de lo esperado en la Ventilación Invasiva de un paciente afecto de síndrome de distrés respiratorio agudo (SDRA) en el contexto de Neumonía secundaria a Infección por Covid-19 con el dispositivo a validar (OxyGEN), superponibles a los resultados encontrados en el mismo paciente conectado a un respirador volumétrico de uso convencional en modalidad Asistida/Controlada (A/C) por volumen.

Concluimos que, a pesar de las limitaciones de la ventilación invasiva con OxyGEN, que sólo permite la modalidad ventilatoria controlada por volumen de Ventilación Invasiva y que por ello debe aplicarse únicamente a pacientes sedados y relajados, en la situación actual de Emergencia Sanitaria y dado el déficit extremo de dispositivos de Ventilación Mecánica Invasiva disponibles para hacer frente a la misma, el dispositivo a validar (OxyGEN) puede ser una muy buena alternativa de uso compasivo para intentar salvar vidas a la espera de poder disponer de dispositivos más complejos.

Badalona, 26 de marzo de 2020

Dr Marc Fabra
Especialista en Medicina Intensiva

Dr Hipòlit Pérez Moltó
Especialista en Medicina Intensiva

Dra Pilar Ricart
Jefa, Unidad de Cuidados intensivos

Dr Manuel Puig Domingo
Director y representante legal del IGTP

A.5 Example of International Approvals: Brazil Animal Test

Relatório do teste pré-clínico em animal do sistema de automatização da ventilação com Balão-Válvula-Máscara da INOVA

Prof. Dr. Luiz Antonio Rivetti

Doutor em Cirurgia e Diretor do IPITEC/Santa Casa de São Paulo

Dr. Mauro Prado da Silva, TSA/SBA

Mestre e Doutor em Medicina e Chefe Do Serviço e Disciplina de Anestesiologia e Dor da Santa Casa de São Paulo

Dra. Valéria Vieira Chida, Médica Veterinária

Mestre em Técnica Cirúrgica pela UNIFESP e Coordenadora da UTECE/Santa Casa de São Paulo

Sra. Ana Cristina de Lima Cardoso Delbellis

Farmacêutica e Bioquímica, Coordenadora IPITEC – Santa Casa de São Paulo

Introdução

Em virtude da pandemia do vírus SARS-COVID 19 e as graves implicações pulmonares que essa infecção pode acarretar, e, ainda, considerando a urgência da possível necessidade de desenvolvimento, produção e início de operação de ventiladores pulmonares em nosso meio, onde a falta deste tipo de equipamento foi responsável por cuidados inadequados a uma parcela da população em países atingidos antes do nosso, como por exemplo a Itália (Remuzzi & Remuzzi, 2020) associada ao impacto desta doença na cadeia mundial de suprimentos, com o consequente aumento de preços nos produtos e desabastecimento no setor hospitalar (Carvalho & Batista, 2020), soluções de produção destes equipamentos em território nacional inovadoras com menores custos de produção e facilidade de aquisição de peças produzidas internamente são essenciais para este enfrentamento. A equipe Ventila O2 INOVA que se apresenta como “uma Equipe Multidisciplinar, seguindo a metodologia de Gestão e Inovação e Tecnologia com Médicos e Fisioterapeutas, Técnicos e Engenheiros, de entidades como o Hospital Dante Pazzanese, CREMESP, Inov@ SCS e FGV; MIW soluções, outras empresas coligadas e equipe do seu Laboratório Otimiza Industria 4.0, para criar o projeto Ventila O2. Tem como objetivo desenvolver equipamentos pulmonares e, em ritmo de crise, apoiar entidades que buscam recuperar equipamentos hospitalares. O projeto é sem fins lucrativos; os profissionais trabalham de forma voluntária, na busca de ajudar o sistema de saúde brasileiro.” Esta entidade nos solicitou que realizássemos um teste pré-clínico em modelo animal de seu protótipo de Sistema de automatização da ventilação por Balão-Válvula-Máscara (também conhecido como AMBU® - nome derivado do equipamento deste tipo desenvolvido pela empresa homônima, onde o emprego de seu nome é corrente pelos profissionais de saúde para se referir a equipamentos análogos produzidos por outras empresas). O equipamento que foi utilizado no teste se trata de um ventilador mecânico cujo projeto foi desenvolvido na Espanha, durante a pandemia de COVID-19, com o projeto liberado para uso em outros países. A intenção da equipe é disponibilizar o projeto para a produção interna deste equipamento, com a devida submissão à ANVISA.

Objetivo

Avaliar a funcionalidade do protótipo do sistema de automatização da ventilação por Balão-Válvula-Máscara/AMBU, da Ventila O2 - Inova.

Material e Método

Esta avaliação foi realizada nas dependências da Unidade de Técnica Cirúrgica e Cirurgia Experimental da Irmandade da Santa Casa de São Paulo no dia 01 de junho de 2020, após a aprovação do Comitê de Ética em Pesquisa com Animais da mesma instituição.

- 1- Breve descrição das características operacionais do protótipo do sistema de automatização da ventilação por Balão-Válvula-Máscara/AMBU, Ventila O2 da Inova, com uma visão de profissionais de saúde.**

a. Descrição do equipamento

Se trata de um sistema de automatização mecânico da ventilação por Balão-Válvula-Máscara/AMBU ciclado a tempo que usa este balão como força propulsora de gases medicinais, com modalidade ventilatória controlada, com a possibilidade de limitação da ventilação à pressão e com o recurso de Pressão Expiratória Final Positiva, sendo os dois últimos recursos com válvulas devidamente instaladas no circuito ventilatório (Figura 1).

Apresenta em sua face anterior, um manômetro aneroide conectado distalmente ao tubo corrugado, para monitorar as pressões em vias aéreas em tempo real, apresenta um controle de frequência respiratória e um botão vermelho para interromper o fluxo de energia elétrica. O volume corrente e a relação inspiração/expiração (relação I:E) pode ser modificado se trocando os discos de engrenagens dentro do equipamento com cada engrenagem apresentando um determinado volume e relação I:E (Figura 4).

O circuito ventilatório possui uma válvula unilateral ligada em série com outra, por meio de um tubo corrugado, na válvula distal é acoplada uma válvula manual de Pressão Expiratória Final Positiva, e no sistema é acoplada uma válvula para limitar o Pico de Pressão Ventilatória. Ainda é acoplada um filtro de barreira distal ao sistema (Figura 2).

A Fração Inspirada de Oxigênio (FiO_2) pode ser regulada por meio de um *Blender* de Oxigênio/Ar Comprimido, com a saída de gases conectada ao sistema balão/válvula máscara/AMBU, nos limites de 21% a 100%.



Imagen 1: Visão anterior do protótipo.



Imagen 2: Visão do circuito do protótipo.



Imagen 3: Visão posterior do protótipo.



Figura 4: Visão dos diferentes discos.

b. Programação do equipamento

O equipamento pode ser programado manipulando o controle de frequência respiratória, a Fração Inspirada de Oxigênio (FiO_2) por meio do *Blender*, e o Volume Corrente e a relação I:E trocando-se o disco da engrenagem do equipamento. A Pressão de Pico Inspiratória e a Pressão Final Expiratória Positiva (PEEP) são reguladas manipulando-se as repetidas válvulas no circuito ventilatório.

c. Variável Medida pelo Equipamento

Se mede as pressões de vias aéreas continuamente, por meio do manômetro aneroide.

d. Ventilação Assistida

O equipamento não é capaz de fornecer ventilação assistida.

2- Preparo do animal

Um suíno, fêmea, de 60 kg e raça *Large White* recebeu Midazolam 10 mg e Cetamina 500 mg intramuscular como medicação pré-anestésica, após cinco minutos foi levado ao centro

cirúrgico, onde foi realizada a instalação de cateter de teflon número 22 em orelha direita, foi realizado Fentanil 300 mcg e Propofol 150 mg endovenosos. Após, foi realizada a intubação traqueal com sonda 9,0 com balonete, sendo a anestesia mantida com Propofol 100 mcg.kg⁻¹.min⁻¹ e Fentanil 0,03 mcg.kg⁻¹.min⁻¹ em infusão contínua, além de bôlus intermitente de Midazolam de 0,1 mg.kg⁻¹ e Fentanil 5 mcg.kg⁻¹. O bloqueio neuromuscular foi realizado com Atracurílio 0,3 mg.kg⁻¹ em bôlus a cada 30 minutos. Após a intubação o animal foi ventilado com sistema válvula-balão-máscara/AMBU de pressão positiva com oxigênio a 21 % por dez minutos, colhido os exames iniciais e, logo após, colocado em ventilação mecânica no equipamento que foi realizado o teste. Foi monitorado com oximetria de pulso (SpO_2), Fração Expirada de Gás Carbônico (ETCO₂), temperatura nasal e pressão arterial invasiva (aneroide), sendo esta instalada a partir da dissecção da artéria femoral do animal, com implante de cateter 22G, tanto para ser utilizada tanto para a monitoração contínua da pressão arterial, como para a coleta de sangue arterial para a análise gasométrica seriada e de bioquímica sanguínea inicial. O volume de soro fisiológico infundido foi de aproximadamente 500 ml com o intuito de apenas dar *flush* após a infusão dos fármacos.

3- Variáveis

As seguintes variáveis foram tabeladas e relacionados em cinco momentos diferentes:

- a. Do ventilador mecânico: Modo Ventilatório (Volume), Pressão Inspiratória, Volume Corrente, Frequência Respiratória, Pressão Expiratória Final Positiva (PEEP), Fração Inspirada de Oxigênio e relação inspiração/expiração.
- b. Análise inicial gasométrica e da bioquímica sanguínea.
- c. Análise Gasométrica: pH, pCO₂, pO₂, BEefc, HCO₃, TCO₂, SO₂ e Lact.
- d. Parâmetros monitorados do animal: Saturação de oxigênio, Fração Expirada de CO₂, Pressão arterial média invasiva, Fração Inspirada de Oxigênio (FIO₂), Frequência Cardíaca e Temperatura.

4- Parâmetros Iniciais

Foram definidos como parâmetros iniciais com o modo controlado a volume ou pressão, com Volume Corrente de 575 mL ou pressão de platô de 18 cmH₂O, limite de pressão de 30 cmH₂O, Pressão Expiratória Positiva de 0 cmH₂O, Fração Inspirada de Oxigênio de 21% e relação inspiração/expiração de 1:2.

5- Momentos com diferentes programações do Ventilador Mecânico

Foram definidos os seguintes momentos para teste e avaliação do protótipo, com diferentes programações do ventilador pulmonar, realizados sequencialmente e com duração de aproximadamente dez minutos após a respectiva programação do ventilador.

- a. Momento 1: Ventilação Controlada a Volume com parâmetros iniciais*.
- b. Momento 2: Ventilação Controlada a Volume com PEEP de 5 cmH₂O.
- c. Momento 3: Ventilação Controlada a Volume com PEEP de 10 cmH₂O.
- d. Momento 4: Ventilação Controlada a Volume com PEEP de 0 cmH₂O.
- e. Momento 5: Ventilação Controlada a Volume com PEEP de 5 cmH₂O.
- f. Momento 6: Ventilação Controlada a Volume com relação de 1:2, com 10kg de peso sobre o abdômen do animal, para simular uma restrição à ventilação por aumento da pressão intra-abdominal e PEEP de 10 cmH₂O