Theme: Intensive Care in China

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The 5th meeting of the Chinese Critical Care Society in Guanzhou

The main conference hall was full when Nanshan Zhong, former president of the Chinese Association of Medicine, opened the 5th Chinese Critical Care Meeting.
From fighting to Synchrony

Old generation ventilators left no room for patient interaction or assisted ventilation. The answer was always to sedate and/or administer muscle relaxants as soon as the patient “was fighting the ventilator”. The view that sedation is a problem, and synchronizing the ventilator to the patient effort has since taken precedence. It is therefore timely to present some pioneering background work associated with the effects and consequences of Patient-Ventilator asynchrony, a recurrent theme in this issue.

In this issue you will also meet some individuals, who have been key for the development of critical care in China. We believe it is interesting as critical care has just recently been recognized as an autonomous specialty in the country. Investments in units, research and technology are impressive.

The heritage of excellence in research

Barcelona has been a center for excellence in research in mechanical ventilation for many years. Lluis Blanch, Director of Research and Innovation at the Parc Tauli Corporation, Sabadell Barcelona, has more than 20 years of scientific experience associated with mechanical ventilation. He described his efforts to elucidate the influence of asynchrony on patient outcome, and how the brain and the lungs interact during critical disease.

At the frontier of pediatric and neonatal critical care

Critical Care News covered the proceedings from the European Conference on Pediatric and Neonatal Cardiac Intensive Care (EPNCIC 2011), Montreux. The meeting, which focused on education and new technology for neonatal and pediatric critical care care, also featured hands-on experience during workshops and scientific lectures as part of the proceedings. Although small in format, the advantage for the participants was the focus on education and the close interaction between speakers and the audience. It is a good example of the fact that focused small meetings are important simply by restricting the topics, and penetrating them in more detail.

Critical care in China

The economic developments in China and its impact on the world at large are an established fact today. The expansion of Critical Care follows a similar trajectory.
as the general economic growth, with new hospital constructions being established with large, state-of-the-art intensive care units. Still, Critical Care is a specialty very much in its infancy in China, since Critical Care has only recently become an autonomous specialty in China.

A few observations are of note when attending Chinese Critical Care meetings. The amount of people is always on a different scale, but also, the amount of young, enthusiastic doctors with a curiosity and drive to learn, is simply striking. Sessions regularly end up with countless questions and prolonged discussions afterwards, very often on the practical implications and how to apply the information given by the speaker.

The huge interest in Extracorporeal Membrane Oxygenation (ECMO) and Neurally Adjusted Ventilatory Assist (NAVA) can be seen as symbolic to this vitality. Young people, without prejudice, embracing new technology, applied to a panorama of diseases, which in many ways are different to those in the West. With impressive and prudent leaders like Professor Nanshan Zhong, coupled with enthusiasm and their power in numbers, China will soon emerge as a very important source of new knowledge in Critical Care medicine.

Critical Care News had the opportunity to interview one of the new leaders in Chinese Critical Care, Professor Haibo Qiu, who went from being professor at a large university hospital to working as a fellow in the laboratory of Professor Arthur Slutsky in Toronto for one year. To me this very much represents the importance and mind set of the development in China. Learning is important and if you can, learn from the best!
The 5th meeting of the Chinese Critical Care Society in Guanzhou

Guangzhou is the capital and largest city in Guangdong province. It is situated northwest of Hong Kong on the Pearl River. With an urban population of about 20 million, it is a huge city with a beautiful city center set along the river. During the 17th century, Guangzhou had already emerged as one of the largest trading ports in Asia and was captured by the British in 1841 during the Opium War. One of the resistance leaders, Sun Yat Sen, widely attributed as the Founding Father of the Chinese Republic, received his medical education in Guangzhou. The academic tradition is thus strong in the city, reflected by the Guangzhou Higher Education Mega Center, which can hold 200,000 students and a staff of 50,000. The 5th Congress of the Chinese Critical Care Society, which attracted 5000 intensivists from all parts of China, was held in these impressive surroundings.
One day before the official opening of the congress, the Critical Care Society offered eight postgraduate workshops, with an audience of 500, eager to learn of the latest innovations in critical care. MAQUET participated in 3 of these workshops, demonstrating lung protective ventilation with recruitment, Neurally Adjusted Ventilatory Assist (NAVA) and Extracorporeal Membrane Oxygenation (ECMO). The courses had a practical approach with theoretical background, followed by hands-on demonstrations. The interactive nature of the sessions was very much appreciated and those attending expressed their eagerness to return home to use their new skills to the benefit of their patients.

The opening ceremony filled the grand auditorium leaving standing room only for many attending. The former president of the Chinese Critical Care Society, Professor Liu DaWei was honored for his achievements and the new president, Qiu Haibo was introduced. A much appreciated speech was given by the former president of the Chinese Medical Association, Professor Nanshan Zhong.

Critical Care News had a short discussion with Professor Zhong after the opening ceremony, where he described some of their research strategies and how these had evolved during the SARS epidemic. He concluded that effective antiviral drugs are very hard to produce as the virus mutates frequently, a finding which was confirmed during the outbreak of the SARS epidemic. Professor Zhong's research group had identified the corona virus as a potential human threat, as they had found the virus to spread by infecting wild animals through an animal-to-animal pathway. However, they had also found the rare incident where the virus had infected humans, but this could only be verified in people in close contact with wild animals. During this time they closely monitored the wild animal markets and became aware of how quickly the virus mutated. Suddenly the infection dynamics changed and by choosing a new host, the virus started infecting people through the human-to-human pathway. Following this chain of events, the quickly spreading epidemic started affecting people all around the globe. Professor Zhong immediately instituted steps to close down all wild animal markets in China which quickly removed the source of the epidemic and thus curbed the spread of SARS. With this background, it is not surprising
that the focus of his current research is directed to translational science i.e. from bench to bedside, or from molecular biology to applied medicine. In this context, Professor Zhong emphasized the value of verifying clinical experience in scientific hypotheses.

One of the practical applications of his research interest is the efforts to block the inflammatory response of the host, instead of searching for antiviral agents, which may be elusive as the virus may mutate very quickly. So, mapping out the inflammatory response may give new information on alternative pathways to block the host innate immune response.

A congress presenting the state-of-the-art of critical care medicine

A major event such as this, with a whole host of speakers and varying subjects is of course very hard to follow. Of special interest for the writer was the in-depth coverage of subjects such as sepsis, ARDS, and the results of prolonged patient inactivity giving rise to the ICU-acquired weakness syndrome. The inflammatory nature of ARDS and sepsis was presented from several aspects focusing on the role of sedation, steroids and the use of muscle relaxants. Given the high incidence of ARDS in China, it was not surprising to find an impressive interest in ECMO and continuous renal replacement therapy coupled with lung protective ventilation strategies, including NAVA.

Given the difference in culture compared to western countries, it was interesting to note that there were several sessions on ethics in the ICU, coupled with discussions on the preservation of organs for transplant. Disaster medicine is an important subject of any ICU congress in China, as the country has suffered several earthquakes and landslides with disastrous consequences. Although a team approach with multidisciplinary skills is mandatory for an effective rescue operation, the experience and coordinating skills of the critical care physician was emphasized in the effort to save as many lives as possible. Several international profiles gave presentations at the meeting, among them Professor Jean-Louis Vincent from the Erasmus Hospital, Brussels, Professor Arthur Slutsky of
St Michael’s Hospital, Toronto, Professor Rolf Hubmayr from the Mayo Clinic in Rochester, Professor Kenneth Palmer from Karolinska Hospital, Stockholm and Professor Burkhardt Lachman from the Charitee hospital in Berlin. Their sessions always ended with a storm of questions showing the interest and inclination to learn from the masters.

Maquet satellite symposium

Haibo Qiu from Nanjing Zhongda hospital started the session on the theme “Therapeutic strategies for severe lung injury – A step-by-step approach”. Professor Qiu started by stating the definition and incidence of ARDS. The shifting background of ARDS was discussed with the emphasis on the
inflammatory aspect of the syndrome. Qiu then continued by presenting a six-step approach to treatment.

**Step 1.**
The patient should be ventilated with a low tidal volume, usually 6 ml/kg ideal body weight. Pplat should be limited to < 30 cm H2O.

**Step 2.**
If the patient shows no sign of improvement, or there are oxygenation problems, a recruitment maneuver with titration of best PEEP should be performed. If the plateau pressure cannot be brought down, a trial of prone position or High Frequency Oscillation should be performed.

**Step 3.**
Wait, take a step back and evaluate the effect of the intervention.

**Step 4.**
If no improvement, administer Nitric Oxide in a concentration of 1–10 ppm for 4 days. This may decrease the pulmonary shunt and reduce the pulmonary vascular resistance.

**Step 5.**
If improvement is not satisfactory, administer glucocorticoids at a dosage of 1 mg/kg/day.

**Step 6.**
ECMO.

Professor Qiu finished with the take home message of the importance for a strategy, including specific steps before escalating the treatment. This will allow reflection and evaluation of the timing for the next step.

**ECMO – 24 years of development**

The second speaker of the symposium was Professor Kenneth Palmer from the ECMO unit at Karolinska Hospital in Stockholm. The ECMO unit at Karolinska currently treats 120 ECMO patients per year. They collect patients from all over Europe where they perform on-site cannulation, institute the ECMO treatment before flying the patient back to Stockholm. The most common cause for admission is viral pneumonia complicated by pneumococcal super infection. Bone marrow transplant patients and late stage cancer are regarded as absolute contra-indications to ECMO as the prognosis for survival is close to zero. They have no restrictions on time for accepting patients to the ECMO unit as in their experience the lung will heal given proper time, unless there is some chronic disease, which is irreversible. The Karolinska ECMO center primarily performs respiratory ECMO (veno-venous) with the primary indication for cardiac ECMO (veno-arterial) being right heart failure, often a complication in patients undergoing long term veno-venous support. Professor Palmer stated that the technology has improved substantially during the last years, with fewer coagulation problems and plasma leakage. He underlined the use of proper size and placement of the suction catheter in the right atrium, to avoid problems with flow rate and large shifts in oxygenation between the lower and upper body. The ventilator strategy used is based on the fact that the patient should be awake and communicative. They usually start with a modest Pressure Support with a low PEEP, and then try to adjust this to optimal patient comfort. NAVA is probably the best mode for these patients and they use it on occasion.

Professor Palmer surprised the audience with some seemingly controversial statements:

“If the lungs are really severely injured you may have to accept an arterial saturation of 70%”. The rationale is quite simple - in this situation the lungs must rest to heal and should be interfered with as little as possible. He compared it to the single ventricle circulation, where babies, after a Fontan procedure, will do fine with this low saturation level. Ventilation can then start after gas exchange in the lung is possible. This may take weeks, but somehow some alveoli start to open up, upon which healing of the lungs will proceed at a much higher speed.

“If the patient has a pneumothorax, do not attempt to drain it”. The insertion of a thorax cannula in this situation will always lead to bleeding. This may seriously complicate the course of the patient as he will need blood transfusions and surgical cleaning of the entire thoracic cavity.

The take home message from Professor Palmer was; “Don’t try to solve problems that do not need solving. Given time the body will heal itself, doctors or dramatic interventions cannot do that”

The session was attended by 500 people and there was tremendous interest from the audience. Indeed, there were so many questions that the next session had to wait, and the speakers were immediately approached by several listeners to continue the discussion outside the auditorium.

**Reference**

Bin Du, Xiuming Xi, Dechang Chen and Jinmin Peng; on behalf of China Critical Care Clinical Trial Group (CCCCTG). Clinical review: Critical care medicine in mainland China. Critical Care 2010,14:206.
A short history of critical care medicine in China

Critical Care Medicine is one of the youngest disciplines of clinical medicine in China, initially practiced in postoperative recovery rooms or isolation areas of the general ward. The first official department of Critical Care Medicine was set up in the Peking Union Medical College Hospital in 1984 as a seven-bed general ICU, chaired by Doctor Dechang Chen, acknowledged as the founding father of mainland China’s Critical Care Medicine. In November 1989, the Ministry of Health issued the Regulation of Hospital Accreditation and Management, which required the establishment of an ICU as a prerequisite for accreditation as a tertiary hospital. This led to intensive educational activity where physicians of other specialties were sent to other hospitals, both domestically and abroad, to acquire training before returning back to their home hospital to practice as intensivists.

Development of critical care medicine as a specialty in China

Initially, specialists in other areas, such as surgeons, anesthesiologists or internists were assigned to the critical care of patients. This was based on the interest and skills adopted after experience of patients with urgent need of life-saving treatment.

However, the important role of a specialized critical care physician as a coordinator for critically ill patients has gradually been recognized and respected by other specialties. Junior physicians interested in critical care training can choose to become intensivists after 3 or 4 years of fellowship training in surgery or medicine. However, there has been an interest in related disciplines such as surgery and internal medicine to retain ownership of the critically ill patient, reflected by the rejection of the proposal to set up an autonomous critical care society under the auspices of the Chinese Medical Society in 1996.

Several healthcare crises, such as SARS in 2003, and natural disasters such as the Wenchuan earthquake in 2008 required massive recruitment of doctors knowledgeable in Emergency and Critical Care. The central role of Intensivists to coordinate, collaborate and communicate with regards to patient management and policy-making was well demonstrated during daily work. This was recognized by both the general public as well as healthcare authorities. As a result, critical care medicine was officially recognized as a specialty of clinical medicine in 2009.
Nanjing is a very important city in Chinese history. It is the capital of the Jiangsu region and was the capital of the Chinese Republic before the Chinese Civil War in 1949, and has been the capital of China for several periods in historical times.

The Nanjing Zhongda Hospital, affiliated with Nanjing Southeast University has 1000 beds, which will be expanded to 2000 by the end of the year. The department of Critical Care Medicine (ICU) occupies 20 beds today, increasing to 60 by the end of the year. The director of the ICU is Professor Haibo Qiu, who is also the newly elected president of the Chinese Society of Critical Care Medicine, Chinese Medical Association (CMA).

After finishing medical school physicians are mandated to finish two residency programs before they can autonomously practice medicine. The rotation is 3+2 years and includes 1.5 years of intensive care. After finishing the residency programs it is possible to apply for a specialty. Post graduate training is provided by ICU training programs under the auspices of the health ministry in collaboration with the Chinese Society of Critical Care Medicine (CMA), who arranges training programs for young Critical Care physicians where 200 doctors receive credentials every month. All taken together, I see a very intense and positive development of intensive care here in China.
Zhongda Hospital is an important academic center here in China, does it also imply that you spend a lot of resources on research?

Prof. Qiu: Yes, every unit connected to a university hospital in China are mandated to produce research. This can be either clinical, animal or purely laboratory research. As an academic institution we are obliged to set up both for the Master and PhD programs. We are also obliged to publish the studies in either Chinese or foreign journals. Of course, the planning of these research endeavors take up a lot of time, but I like to see the enthusiasm of the young doctors when they are being enrolled in these programs.

Your personal research has been mainly focused on mechanical ventilation?

Prof. Qiu: Yes and no, I was very early interested in the pathophysiology of ARDS and the effects of lung protective ventilation. So we have for a long time used the esophageal catheter here to measure the trans-pulmonary pressure and titrate PEEP based on these measurements. We also measure the abdominal pressure and follow that in order to better adjust our ventilatory strategy based on these measurements. I also have a great interest in the immuno-regulatory mechanisms of inflammation. It is widely accepted today, that ARDS is primarily an inflammatory disease or syndrome, where immuno-modulation have a central role. We are currently studying the role of the helper T-cells to find out how they are activated and their role in the inflammatory cascade.

Sepsis is another area which is one of my primary research interests. As there has been a longstanding and bitter controversy of the use of Corticosteroids in sepsis we are trying to elucidate the role of the cortisone receptor and its influence on the thalamic-pituary-adrenal axis. We frequently see that patients may have a high cortisol concentration in blood and tissues, but the receptor for some reason is not responding. Our current hypothesis is that patients with low cortisol levels in the blood may benefit from supplementation, while patients with high concentrations will not benefit at all due to the absence of receptor response. These patients will probably not respond to the administration of corticosteroids. I personally believe that NAVA will have a big impact on the inflammatory response as I am convinced that it is lung protective by improving gas distribution and decreasing patient-ventilator asynchrony.

How did you come in contact with NAVA?

Prof. Qiu: I read the paper in Nature Medicine by Christer Sinderby a long time ago and was excited by the theory. However, I didn’t understand that this was close to realization. I saw it as an interesting theory of a possible way to ventilate patients in the future. Hence, I was very surprised when Yan Weber from MAQUET China approached me and told me about this new mode of ventilation available in the SERVO-i. Being inquisitive by nature, I was of course willing to try it out and saw that it really worked in the way it was described by the original paper. That sent me home to study the literature and find out more about the theory and practice behind this new mode of respiratory assist.

What was your initial reaction on seeing NAVA in practice?

Prof. Qiu: I could see that NAVA was an extension of patient physiology into the ventilator, and how the response of the ventilator immediately adapted to the patient need. For the doctors, who are not always prone to change, it was very hard to accept initially. As soon as I was out of the unit, somebody had changed the ventilation which was now set to more traditional operation. Several of my colleagues thought that the patient response was too unpredictable and they were not accustomed to the increase in respiratory rate and decrease in tidal volume that sometimes is seen with NAVA. To appreciate what took place in the patient and accept that the patient usually knows what is best for him, took probably more than 6 months. We then had learned that we should talk to the patients and see what they preferred, we also started to pay less attention to the tidal volumes and look more at blood gases and PCO2. If this was stable we realized that the breathing pattern was probably adequate for the patient and could leave the patient with NAVA as this was the mode they accepted the best.

It was even worse for the nurses. They are used to registering the tidal volume and the respiratory rate of the patient. With the variation seen with NAVA this was initially very confusing. I firmly believe that we should spend more time educating the nurses as they always are closest to the patients.

You published work on NAVA in Chinese before NAVA was well known in China. What was the reaction of your colleagues to this?

Prof. Qiu: It was quite an interesting experience. After submitting the paper, the editor called me and said that there was no one that had the experience to properly review the paper. I suspect that 99% of the readers of the paper also didn’t understand either the paper or the physiology described in the paper. Nowadays the understanding has been so much improved as many clinics in China are using NAVA and there has been a lot of people taking part in seminars and courses on NAVA.

You have personally spent a year with Doctor Christer Sinderby in Professor Arthur Slutsky’s laboratory concentrating on the physiology of NAVA. How did this affect your view of NAVA?

Prof. Qiu: This was a very important time for me personally. I realized that NAVA was not only a mode that could be used for respiratory assistance in the weaning phase. I realized that NAVA will be a very important mode for lung protection in ARDS. The current trend to apply low tidal volume ventilation to patients with...
ARDS is enhanced with NAVA as the gas distribution is improved compared to mechanical ventilation and patient ventilator asynchrony is reduced to zero.

Another well known complication of prolonged mechanical ventilation is the atrophy of the diaphragm which may induce prolonged and very frustrating attempts to liberate the patient from the ventilator. I have an example of an elderly lady who had a period of prolonged mechanical ventilation but was deemed ready to wean. However, even though she had a very modest Pressure Support level, extubation was impossible. We put her on NAVA and could follow, how the initially very weak Electrical Activity of the Diaphragm (Edi) increased day by day as a response to a diminishing NAVA level, finally leading to extubation after three weeks on NAVA. Nowadays we always use NAVA in the hard-to-wean patients as we can follow their development so much closer by the use of the Edi signal. The stay in Toronto of course generated a lot of new ideas for research into the pathophysiology of acute and chronic respiratory disease.

It must have felt strange coming to a foreign place and going from professor to more or less working as a fellow.

Prof. Qiu: In fact, the patient and staff may see me as the important professor when I am in the clinic. When being involved in research I always feel like a young fellow as the result we find may be unpredictable and maybe not what we expected. As I have always been interested in the organization of research and clinical trials, I feel that the team-work aspect is really enjoyable. The discussions during the production of a new protocol is not only a mental exercise but something that I really like doing as this give me a feeling of new development not only for me, but also for the rest of the team. It is during such discussions we find new ideas and make us look for ways of implementing the ideas.

The time in Toronto also gave me a lot of new contacts and insights into things I was not aware of before. The exchange of ideas with other institutions are really very fruitful as I always feel that I learn more and frequently find new ideas and new inspiration.

Has the experience from Toronto affected the daily work and practice in your clinic?

Prof. Qiu: Very much so, every morning I joined the morning rounds at St Michael’s Hospital. After seeing how the orders and findings were followed up, I went to the laboratory to conduct my experiments. I realized that in our unit in Nanjing we did not have a consistent way of doing things but left very much of the implementation of the treatment at the discretion of the attending physician. This was in stark contrast to the routines at St Michael’s Hospital, where every procedure was more or less standardized. This made me into a believer of the value of standardizing care in the ICU. Hence, on my return I was very busy writing and modifying protocols for procedures like central vein cannulation, renal replacement therapy, chest drainage and other important procedures regularly performed in the ICU. I also wrote protocols for the order of tests performed to allow a consistent pathway to diagnose specific disease. This has been very appreciated in our ICU and I dare say that we now have improved both the workflow and the consistency of our treatment. Recently I have released a new book with protocols of standardized procedures for the ICU. These guidelines of diagnosis and treatment for the ICU, is the first book of this kind in China. I firmly believe that uniform approach to the medical problems in the ICU has a great value and it will give us a good foundation for the future development of Intensive Care in China.

Now that you are sending fellows from Nanjing both to Europe and North America, do you think that will influence the research efforts of the clinic more than the daily clinical work?

Prof. Qiu: My personal view has always been that all research must be from bench to bedside. By this I mean that you test a hypothesis first in the laboratory, you will then apply the new knowledge to generate a protocol for a clinical study. As I pointed out previously the findings are very seldom what you have expected, which lead you back to the lab either for an animal experiment or a search for more fundamental mechanism which may necessitate an investigation into the molecular mechanisms involved. Anyway, the most interesting aspect of research is this regeneration of new ideas, analyzing what went wrong or right with the experiment, the generation of new ideas and the collaboration with the team.

We are also lucky here in that we can discuss our findings with other colleagues both here in China and abroad. We can thus find new approaches to our research questions which of course is very inspiring.

We find more and more literature appearing underlining the problems with patient-ventilator asynchrony. What is your experience on this issue?

Prof. Qiu: 10 years ago we were only using volume controlled or pressure controlled ventilation. Since then we have seen pressure support becoming more and more common. I believe that patient-ventilator asynchrony is a much bigger problem than we think and the pressures associated with asynchronous ventilation can be very high. I believe that the findings of Papazian’s group (by Papazian L, et al. N Engl J Med. 2010 Sep 16;363(12):1107–16.) in France with a lower mortality for patients receiving neuro-muscular blockade during the first two days of mechanical ventilation should be interpreted in the light of a reduction in asynchronous events. I believe that the lung protective effects we see with NAVA is very much associated with the avoidance of asynchrony. In addition with NAVA we do not have to sedate the patients deeply, which probably also contribute to improvements in outcome. We now pay much more attention to the subjective feeling of the patient as he is much more awake. We currently have a study running to find out the effect of a decrease in patient sedation.
Do you use NAVA today mainly as a tool for research or do you see it as a way of improving the clinical course of the patient?

Prof. Qiu: Both, we use NAVA more and more in patients with ARDS and have only positive experience on this. We also use NAVA immediately if we have patients that are difficult to wean or if we suspect that we will have weaning problems with the patient. We can control muscle training in this patient group and have excellent experiences in patients that probably otherwise might be chronically ventilator dependant. We have also good experience of patients with spinal cord injuries were the Edi signal may be very week initially, but through the gentle assist provided by NAVA we can see how the patients own breathing is returning day by day. Of course we have several studies running on NAVA of which the sedation study is a very important one.

Extracorporeal Membrane Oxygenation (ECMO) is very much discussed here in China. How do you see this therapy developing in your unit?

Prof. Qiu: ECMO is now an accepted technique in China for patients with very severe lung failure. Initially, before we were familiar with the technique we hesitated to use it because of the high costs involved and we felt it was very complicated to use. Now we find it very easy to use and we see more indications as we gather more experience. Today if we have a patient with severe ARDS we believe is reversible, we do not hesitate to start the ECMO treatment. Currently, we treat around 1 patient/month with ECMO. We do expect an increase in the amount of patients we treat on ECMO. Naturally it is a big cost issue, but with the health reforms and the focus the health ministry is giving to the ICU, we believe that the economic problem will diminish.

There are some interesting studies combining NAVA and ECMO. How important will this form of combined therapy be in the future?

Prof. Qiu: This is probably a very good idea. By avoiding CO2 stimulation, the tidal volume can be kept low thus avoiding ventilator induced lung injury. I think this new approach may very well become an important therapy for seriously ill patients.

Selected references


A newborn baby with E.Coli and Group B Streptococcus septicemia and hypoxemic respiratory failure – successful treatment with NAVA

Pediatric patient case report with Doctor Robert Lee, Hong Kong

Clinical background and situation

A male newborn was born at gestation age of 41+4 weeks with a birth weight of 3.2 kg. The mother had a high temperature and the birth was complicated by a prolonged rupture of the membrane. Moderately meconium stained fluid was noted at birth and endotracheal intubation was performed twice to clear fluid from the baby’s lung. Blood cultures showed the growth of two organisms: E Coli and Group B Streptococcus. Placental swab, ear swab and umbilical swab showed growth of the same organisms.

Intervention and course of ventilator therapy

Respiratory distress was noted at birth and the baby was transferred to the NICU. The baby was intubated due to respiratory acidosis. Surfactant was administered once intraoperatorily. The ventilator requirement escalated resulting in a drop of systemic blood pressure requiring repeated doses of normal saline boluses and inotropic supports. Eight hours after birth, the baby was started on high frequency oscillation (HFO) and nitric oxide (NO). The chest X-ray at this time revealed ground-glass appearance. (X-ray day 1). Dopamine, dobutamine and adrenalin were required to stabilize the blood pressure.

During the subsequent 12 days the baby’s respiratory problem was managed by HFO with a Mean Airway Pressure (MAP) of 16–25 and an FiO2 of 1.0, resulting in escalated hyper-inflation and an increasingly reticular appearance of the lung fields on the chest X-ray (X-ray day 14 and 18). Several attempts were made to decrease Mean Airway Pressure (MAP) in view of the obvious hyper-inflation seen in the chest X-ray. However, these interventions only resulted in an acute plummeting of oxygen saturation, requiring reversion to the high MAP. Nitric Oxide (NO) was started at 20 ppm and attempts were made to decrease NO on day 4 but due to oxygen desaturation, the NO concentration was again increased back to 20 ppm. Methylprednisolone was administered from day 4 to day 14 at a dose of 2 mg/kg/day. After day 12, oxygen saturation became more stable and NO was gradually weaned off on day 14 with ventilator settings FiO2 100 %, MAP 18.5 cm H2O, amplitude 45 cm H2O. Chest X-ray on day 14 evidenced that hyperinflation was an increasing problem on HFO with the appearance of pulmonary interstitial emphysema and a bulla in the right lung.

HFO was switched to SIMV with Pressure Support (PS) mode (SERVO-i ventilator, MAQUET, Solna, Sweden) and the setting was FiO2 100 %, pressure of 30/5 cm H2O, rate 45. On day 18, pressure was gradually weaned down to 22/3 cm H2O, FiO2 90 %. Chest X-ray (X-ray day 18) still showed persistent pulmonary interstitial emphysema and bulla in right lung. On day 18, NAVA was initiated. The initial NAVA level was 3 cm H2O/µV. The alarm was set to cut off peak inspiratory pressure at 23 cm H2O and back up PS and Pressure Control (PC) was set at pressure of 23/4 cm H2O.

Over the days a declining Edi signal was noted requiring a gradual increase in the NAVA level from 3 on day 18 to 8 cm H2O/µV on day 25 in order to generate adequate pressure to ventilate the baby. On day 25, the patient had a very irregular breathing pattern. After prolonged apnea periods, regular breathing recommenced, resulting in peak inspiratory pressure of 15 to 18 cm H2O. However, breathing was irregular with sighs generating a high Edi, potentially resulting in high pressures, were attenuated by the upper alarm limit (set to cut off at 23 cm H2O). At this time FiO2 had been decreased from 0.9 to 0.6.

It was then concluded that the lung function had improved substantially, and that the current high NAVA level was the cause of the irregular breathing pattern and the intermittently recurring pressure limitation. Hence, the NAVA level was decreased to 5 cm H2O/µV. The Upper Pressure limit was re-set to allow a maximum pressure of 20 cm H2O and backup PS and PC were adjusted accordingly. On day 27, the NAVA level was further reduced to 3 cm H2O/µV with the Upper Pressure limit set to allow a maximum pressure of 18 cm H2O. FiO2 by then was 0.35 coming down from 0.9 on day 18.

The baby was extubated successfully on day 28. Chest X-ray on the day of extubation showed almost complete resolution of pulmonary interstitial emphysema and bulla (X-ray day 27).
X-ray day 1.
Baby admitted and on CMV. Chest X-ray shows ground glass appearance of the lungs.

X-ray day 14.
Baby on HFO since day 1 with x-ray showing progressive hyper-inflation with interstitial emphysema and bulla in the right lung.

X-ray day 18.
Baby back on CMV, persistent interstitial emphysema and bulla in the right lung.

X-ray day 27.
After nine days on NAVA Chest X-ray showing almost complete resolution of interstitial emphysema and bulla.
Case summary:

A newborn baby with severe hypoxemic respiratory failure due to E. Coli and Group B streptococcus septicemia who required high distending pressure during HFO and NO. HFO resulted in barotrauma as evidenced by pulmonary interstitial emphysema and bulla, which resolved with NAVA. NAVA provided gentle and appropriate ventilation allowing the lungs to recover from the incident leading to Barotrauma.

Fig 1. To the left in the picture, titration procedure identifying three distinct response patterns. Note the increase in airway pressure and tidal volume at a NAVA level corresponding to NAVA high. To the right in the picture an example of the irregular breathing pattern described in the text. Adapted from Brander1.
Editor’s Comment

This case has significance for a number of reasons. First, it illustrates that high tidal volumes is not the only culprit in inducing lung injury. Second, we can deduct that high mean airway pressure per se might lead to serious over inflation of the lung (see x-ray day 14). In line with Gattinoni’s theory of stress and strain², chronic hyper-inflation to TLC or above, may be injurious to the lung tissues. Third, the initial NAVA level selected (3 cm H₂O/µV) was probably already high as indicated by the description of the irregular breathing pattern including apnea, small regular tidal volumes and sighs.

The increase in NAVA level to 8 cm H₂O/µV in order to increase the assist pressure, probably further aggravated the problem. Animals and humans will show a progressive decrease in the Edi with increments in the NAVA level. However, it will not go down to zero unless a controlled or semi-controlled mode of ventilation is used. Hence, the described increase in the NAVA level left the Edi signal at the same level, but the assist pressure increased (P=NAVA level x Edi). Fig 1 shows how an increase in the NAVA level from 0 and upwards results in a progressive decrease in the Edi (1st phase) until a plateau is reached (2nd phase). An increase in the NAVA level beyond the plateau phase will lead to an increase in assist pressure, but also a very irregular breathing pattern, as seen on the right in the figure. An example of the aberrant breathing pattern can be seen in the left part of Figure 1. Note that if the increments in the NAVA level are large, the plateau phase may not be detectable.

What can be learned?

The case illustrates the safety of NAVA. It is comforting to see that the patient continued to improve and that there were no further respiratory complications, despite the very high NAVA level set (the upper pressure limit attenuates the pressure, but maintain synchronous cycling). The remarkable improvement in the patient, with resolution of the gross pathology, coupled with the fact that it was possible to extubate the patient without complications, shows that even if the NAVA level is not always optimized, the patient will modify his respiratory pattern to promote healing.

References


The need for more research pertaining to ventilatory assist

– perspectives from Doctor Lluis Blanch at Sabadell Hospital, Barcelona, Spain

Sabadell Hospital in Barcelona province is a 600-bed public and teaching hospital just north of Barcelona. It provides the medical and surgical specialties for a population of 400,000 people. The hospital has an excellent record for research in mechanical ventilation, and we were curious to find out how they are organized to keep the tradition alive.

Critical Care News interviewed Doctor Lluis Blanch, Director of Research and Innovation at the Parc Tauli Corporation, Sabadell Barcelona and Chief of a CIBER group on Respiratory Diseases. His research is on two different lines, one focused on biomedical science exploring the association between lung injury and the brain, a connection that has been known for years, but still the mechanisms involved are obscure as it has not been possible to analyze the pathways and the biochemical markers involved until fairly recently. The second project, where they are now running pilot trials with clinics all over Spain, allows them to watch the progress of patients in far away locations with only a few seconds of delay, totally synchronized on a unique interface, including all waveforms from the patient monitor and ventilator. For this project Doctor Blanch has spent 5 years of work with his engineering group creating algorithms for automatic detection of asynchrony, hyperinflation, secretion and other events important for the care of the patient.

The Parc Tauli Corporation has shown great appreciation for the projects by supporting the formation of a company, Better Care, which provides expertise and innovations for the industry. Collaboration between Better Care and the Spanish company GMV has resulted in a product for telemedicine, which features transmission of high resolution physiologic waveforms including ultrasound scanning, directly from the ambulance. Installations in ambulances make it possible to apply care and carry out interventions immediately, on the advice of qualified, remotely located physicians.

It is striking to see the amount of research in Mechanical Ventilation that has come out of Barcelona. How did this tradition evolve?

Dr. Blanch: I did my residency in Sant Pau Hospital, Barcelona, which has a long tradition of research in mechanical ventilation. Doctors Net, Benito and Artigas were my mentors and promoted research associated with mechanical ventilation. I immediately got interested and started my research career collaborating with Jordi Mancebo and Rafael Fernandez with whom...
I published several articles relating to applied respiratory physiology and mechanical ventilation.

You have done scientific work associated with mechanical ventilation for more than 25 years, can you tell us a bit about your career?

Dr. Blanch: After I had achieved my MD degree, I trained in the Critical Care department at Sant Pau hospital in Barcelona for five years, then stayed as a fellow at the Meakins-Christie laboratory in Montreal, to study mechanical ventilation under the guidance of Charis Roussos. I then came back to Barcelona and could continue my research here at Sabadell interrupted by a sabbatical in St. Paul at Professor John Marini’s institution to collaborate with Avi Nahum on the effects of tracheal gas insufflation. During the last five years I have been working on my project of registration and integration of physiological signals. During this time I have learned to appreciate collaborating with engineers who are devoted and enthusiastic. Bernat Sales and Jaume Montaña have been fantastic collaborators and I have realized that with the currently available technology it is possible to do virtually what you want and the only limit is your own fantasy. Besides that they are great sources for new ideas as they will look at problems with a different angle than me.

Networking between academic institutions has expanded a lot in the last ten years. Physiologic studies are a bit overlooked, while Randomized Clinical Trials, RCT, seem to be where all the weight is concentrated, both in terms of economy and prestige. What is your comment on this?

Dr. Blanch: The RCTs are important as they should be the logical ending of a research hypothesis. But, the physiologic studies are maybe even more important as they will map out the response of an intervention and they will generate new angles and research hypotheses associated with the initial question. The RCT design must take the background physiologic knowledge into consideration in order to be successful.

For example, it was well recognized that small tidal volumes and low pressures was preferable and should be used before the ARMA trial (ARDSnet low/high tidal volume trial) was published. However, the ARMA trial had an impact in all institutions around the world. This is the important outcome of the RCT.

In spite of all the information obtained by the capnogram, volumetric CO₂ is very much underused in the ICU, this is in sharp contrast to the situation in Anaesthesia where CO₂ monitoring is mandatory. Do you have a theory for this fact?

Dr. Blanch: Essentially I believe that there are two problems. First there is the question of the instrumentation and stability of the signal. Ideally the sensor should be placed at the middle of the tracheal tube, where it wouldn’t interfere with patient care at all, this is obviously not today. In addition, current technology may not work on a continuous basis as secretion and humidity may make measurements difficult to interpret. So, this has to do with application and trust in the signal.

Secondly, the interpretation of the curve shape and variations in output is not easy to interpret if not integrated in routine care. So it might be a knowledge gap, which is unfortunate as the CO₂ curve will give a lot of information and will give good guidance of the effect of interventions.

Recommendations for Controlled Mechanical Ventilation in severely ill patients, are very much focused on tidal volumes, with the ARMA trial seen as leading the way. In your work you have emphasized the interaction between lung mechanics and gas distribution. How can these seemingly conflicting theories be reconciled?

Dr. Blanch: The low tidal volume strategy is very important. Some people will argue that in patients with more

Sabadell Hospital north of Barcelona.
compliant lungs, it is beneficial or not important if larger tidal volumes are used. However, for the setting of PEEP it is important to take into consideration the lung mechanics of the patient and not be restricted by a large tidal volume for the appropriate setting of the PEEP. I believe that one of the most important studies recently published is the paper from Pesenti’s group (Bellani G, Guerra L, Musch G, et al. Am J Respir Crit Care Med 2011;183:1193–1199.), showing how inflammation is associated with plateau pressures below what is currently recommended as the upper limit, especially if it is delivered in the presence of a low FRC. If the patient is a recruiter, it is important to be able to give an adequate PEEP without excessive pressure delivery.

Assisted breathing has become much more common for treatment of severe lung injury. Is this a result of the discussion on reduction of sedation or purely a reflection of the improvements in ventilator technology?

**Dr. Blanch:** It is probably more complex than so. I believe that critically ill patients should be properly sedated and probably given muscle relaxants during the, maybe for the first 24–48 hours. A recently published article (by Papazian L, et al. N Engl J Med. 2010 Sep 16;363(12):1107–16.), indicates that this strategy is also associated with an improved outcome. It is implied in the paper that the reduction in asynchrony is an important factor for the improvement in outcome, this is interesting, but it needs to be tested. To me however, the most important factor is the presence of the physician at bedside during the critical period. He is needed to continuously assess the progress of the patient, allowing for prompt intervention if something happens. This is the situation where the knowledge and the collaboration of the team is really tested and where they can make the most difference.

Sedation is a problem of its own and prolonged sedation without any real indication is bad especially as it has a big impact on patient ventilator interaction and outcome. I believe that the very severe patients should be sedated and given neuromuscular relaxants during the acute crises and these drugs should be discontinued as soon as the crises is over, to allow spontaneous breathing, but always keeping an eye on patient-ventilator synchrony.

You have recently been working a lot on the effects of patient-ventilator asynchrony. Can you give us some insight into this fairly new investigative field?

**Dr. Blanch:** We have now collected continuous data from 50 patients. The collected data represents more than 7000 hours of ventilator treatment. Hence, the data spans an average time of more than 5 days/patient. We have several interesting hypothesis associated with the impact of patient ventilator asynchrony. However, as the data is not yet fully analyzed, I am not able to say directly how asynchrony is affecting outcome. However, we can see that asynchrony is very common and I do believe that it is so important that it should be registered and classified in the patient chart like any other value like for example, blood gases or biochemical data. Unfortunately this is not possible with current systems as you need a dedicated system that will guarantee vigilance for 24 hours and 7 days a week. This is obviously not possible for a human, so there is a need for an automatic function interpreting the waveforms, attached to an appropriate storage capacity to be able to make analysis of the important events afterwards. We have tested our system (Better Care®) against the Edi signal in many patients and can see that we have a sensitivity close to 70 % with very high specificity. We are consciously conservative in our approach as we would like to avoid false positives. Accordingly, our analysis show that we have almost no false positive events, which indicates that the system is robust. We believe that our system has adequate performance as an expert clinician will detect missed efforts with similar sensitivity and specificity.

The health economic and commercial implications of patient ventilator asynchrony is potentially huge. Hence, I believe that we need to test systems to recognize and classify asynchronies in single institution trial, then do it in a randomized clinical trial in multiple institutions. We are close to the first step at the moment and we will be ready to start the multicenter trial by the end of this year in collaboration with Jesus Villar, Bob Kacmarek, Umberto Lucangelo and the Spanish clinical trial group for this project, encompassing 5 university hospitals in Spain.

How is patient-ventilator asynchrony currently diagnosed, and is it common to discuss the phenomenon as an important factor for patient outcome in daily practice?

**Dr. Blanch:** Currently, analysis is done from the ventilator display. Of course, the analysis is only done sporadically, which by nature leads to under diagnosis of the problem. We know that sedation and other interventions diminishing the respiratory drive might induce an increase in the frequency of asynchrony, but on the other hand, a low drive will make the asynchrony harder to detect. I believe that asynchrony is discussed a lot today and we will probably be overwhelmed by studies on this issue. However, although in vogue, from a practical, bedside perspective interventions based on patient ventilator asynchrony is not common. Unless it is obvious that the patient is actively fighting the ventilator.

Sedation is currently very much discussed. How is this problem associated with asynchrony?

**Dr. Blanch:** As alluded to earlier, interventions which diminishes the respiratory drive might increase the frequency of asynchrony. However, sedation and/or relaxation may be necessary sometimes, as stated previously in critical situations, but also in patients who has a pathologic respiratory drive. These patients may show up with very high tidal volumes if they are on a flow regulated mode and may show frequent double triggering if on a continuous flow mode. This is especially important for patients subjected to permissive hypercapnia, where the drive must be suppressed for the treatment to be effective.
Passive inflation after triggering the ventilator seems to be very much the rule. Charles Bryan (Anesthesiology. 1974 Sep;41(3):242–55.) pointed out the difference in gas distribution between passive and active inflation of the lungs in the early 70s, can this be regarded as another aspect of asynchrony.

The ability to detect patient-ventilator asynchrony seems to be very low. How may this affect patient outcome?

Selected references:


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Montreux, Switzerland, is one of the most beautiful towns in the world. The view of snow on the mountains, in stark contrast to the palm trees and abundance of flowers by the lake, offers a breathtaking experience of beauty. In these gorgeous surroundings, there is not only a world famous Jazz Festival that is held regularly, but also a high level Pediatric and Neonatal Intensive Care Meeting.

In the year 2004, the European Conference on Pediatric and Neonatal Ventilation (EPNV), organized and chaired by Professor Peter Rimensberger from the University Hospital of Geneva, was organized for the first time in Montreux, and from then on this high level educational meeting has been held bi-annually. Since 2009, a second conference, the European Conference on Pediatric and Neonatal Cardiac Intensive Care (EPNCIC), arranged in collaboration with the Working Group of Pediatric Cardiac Intensive Care (WGPCIC) from the Association for European Pediatric Cardiology (AEPC) and the European Society of Pediatric and Neonatal Intensive Care (ESPNIC) has joined the program of “The Montreux Meetings” that has become highly recognized worldwide. The
common objective of both meetings, which alternate nowadays on a yearly basis, is to provide education on state-of-the-art practice and to discuss new available technology. The small format of the meeting, with a limit set at 250 participants, encourages discussions where experts and speakers are easily available. Discussions are frequent not only during sessions, but also informally, after presentations. The conferences also offer a variety of practical pre-conference workshops, most of them with hands-on possibilities, which are always highly appreciated by the participants.

As this year’s meeting was more devoted to cardiac issues the next conference will again emphasize ventilation management in children and neonates. All meetings attended by Critical Care News have been highly thought-provoking and offer an excellent opportunity to acquire new knowledge while facilitating contacts and discussions with opinion leaders, and last but not least to experience the beauty of Montreux. MAQUET contributed at this year’s meeting with three major events: two workshops on basic and advanced mechanical ventilation, including specific aspects of mechanical ventilation in the cardiac ICU setting, and a NAVA symposium stressing the importance of patient-ventilator interaction. The symposium focused on the problems associated with the very high incidence of asynchronous assist in pediatric and neonatal practice.

“You cannot beat physiology”

The workshops were led by Professor Peter Rimensberger who started off with the observation that the way mechanical ventilation is administered has a large impact on patient outcome. Still, the way it is practiced is largely influenced by old traditions and many extrapolations from old literature, primarily conducted on healthy adult patients undergoing general anesthesia. This promotes reliance on “cook-book medicine” with very little room for an individual approach based on patient physiology to the setting of the ventilator. Professor Rimensberger rebuked standard practice and offered an alternative approach based on the continuously changing lung mechanics of the patient, which requires continuous respiratory monitoring. His very persuasive argument for this view was that nobody would administer any inotropic drug without some hemodynamic monitoring, i.e. at least a continuous blood pressure reading. He promoted the view that just as the modification of inotropic administration is based on blood pressure readings, the ventilator settings must be carefully and repeatedly adjusted, not according to random numbers, but to changes in patient respiratory mechanics as principally characterized by the time constant (Resistance x Compliance) of the respiratory system. This is not as complicated as it may seem, and Professor Rimensberger gave a beautiful demonstration using a simple lung model to demonstrate how this can be easily accomplished at the bedside. In practice, through observation of flow at end-inspiration (should decelerate to a short zero period) and end-expiration (flow reverting to zero again, signaling absence of Auto-PEEP) cycle times can be optimized. This will allow for the identification of the individual maximal respiratory rate for each patient. Correct settings according to the mechanical behavior of the patient’s respiratory system, allow for the use of the lowest possible plateau pressure, coupled with the most efficient carbon dioxide removal. In this context he also emphasized the importance of patient and disease-specific tidal volumes (Vt), exemplified by the risk of standard settings (i.e. 5 to 6 ml/kg) for babies with diaphragmatic hernia who may have an important reduction of their total lung volume (i.e. severely reduced total lung capacity in relation to their body weight). These patients are severely at risk if standard Vt settings, according to body weight, were to be applied. The latter would, assuming a reduction of TLC by 50%, result in a situation similar to applying 10 to 12 ml/kg to a baby with normal sized lungs. An approach of 5 to 8 ml/kg or less was recommended (biology tells us that a physiologic tidal volume is about 6 to 7 ml in all vertebrates) with a reduction of this target for special circumstances, remembering that each restrictive lung pathology is associated with a reduced inspiratory capacity (i.e. the “baby lung concept” indicating that “stiff lungs” may not be
of cardiopulmonary depression during Vascular Resistance (PVR) is lowest at the lung volume at which Pulmonary Functional Residual Capacity (FRC), patients to restore normal physiologic levels, as might be required in some than the traditional, increasing PEEP resulting in lower inspiratory pressures and stiff, but functionally small. Growing adult, pediatric and neonatal experience strongly indicates that an approach to limit inspiratory pressure to well below 30 cm H2O (in patients with normal lungs even below 20 cm H2O) might help in overcoming, in part, the difficulty of choosing the most appropriate lung protective tidal volume for any single patient at any stage of lung disease.

**How to set PEEP?**

Traditionally, the use of PEEP in controlled mechanical ventilation is regarded as the limiting factor for venous return and to increase pulmonary vascular resistance, thus additively exerting a negative influence on cardiac output. In this context, Professor Rimensberger discussed the observations from an echocardiography study by Vieillard-Baron A et al. (J Appl Physiol 1999; 87:1644-1650) which clearly indicated that right ventricular output depression does not take place during the PEEP phase, but during inspiration when intrathoracic pressure is at its peak.

With the advent of small Vt ventilation resulting in lower inspiratory pressures than the traditional, increasing PEEP levels, as might be required in some patients to restore normal physiologic Functional Residual Capacity (FRC), the lung volume at which Pulmonary Vascular Resistance (PVR) is lowest will in fact allow for the minimization of cardiopulmonary depression during positive pressure ventilation. Hence, Professor Rimensberger argued forcefully on the importance of setting respiratory time cycles (i.e. Ti and Te) and a “physiologically correct” PEEP properly to re-establish FRC in the diseased lung. He argued that optimal PEEP should be set after a slow and step-wise recruitment maneuver, best administered by first incremental then decremental PEEP-steps of 1 cm H2O. This can be easily achieved in the Pressure Control mode. A step-wise increase in PEEP resulting in a rising tidal volume should be interpreted as pulmonary recruitment, resulting in improvement in dynamic compliance and oxygenation, hence an incentive to further increase PEEP. As tidal volumes start to decrease with further increase in PEEP, this usually indicates that the flat part of the Pressure-Volume curve has been reached and further recruitment will be marginal. PEEP has to be titrated down again in small steps, until tidal volume, as a marker of worsening dynamic compliance, and saturation start to drop. This will indicate the beginning of important lung collapse (closing pressure) and PEEP should be set now after a second recruitment maneuver maximally 2 cm H2O above this point of closing. After successful re-recruitment and setting the optimal PEEP level, Vt and cycle times and respiratory rates (because of induced compliance changes by recruitment) have to be re-adjusted, aiming again at the smallest Vt affordable. This will result in low inspiratory pressures and subsequently minimized cardiopulmonary depression. In the acute phase of lung disease this may have to be done repeatedly as lung disease, like any other biologic function, will have an evolution. As put by Professor Rimensberger: “When the ventilator settings are still the same when I come in the morning as they were when I went home in the evening, I will get nervous as this implies that there was no progress in the patient, or more likely, that the status of the patient has not been re-assessed for the last 12 hours”.

As alluded to previously, PEEP should be set with the objective to reach physiologic FRC, as this coincides with the lowest pulmonary vascular resistance and thus lowest right ventricular afterload. It is probably not a coincidence that in this situation the respiratory muscles will have optimal working conditions allowing for a better chance for the patient to succeed in being weaned from mechanical ventilation as early as possible.

“New trends and development in mechanical ventilation”

This symposium was arranged outside of Montreux in the famous Gruyere cheese factory. Chairing the session, Professor Peter Rimensberger also gave the introductory talk entitled “Assisting Spontaneous Ventilation”. He described the chain of events leading to respiratory muscle activation in health and disease and the principal concepts of various ventilatory assist modes. He continued by explaining the most frequently occurring types of asynchrony during ventilatory assist. Examples of missed efforts, out of phase cycling, auto-cycling, and inappropriate flow termination (cycle off) settings leading to inappropriate tidal volumes, increased respiratory rate with sometimes even double cycling events, increased work of breathing, and patient discomfort during pressure support ventilation. He stressed the fact that, although it is sometimes very difficult from the classic ventilator display of pressure and/or flow readings, to determine the incidence, it has been shown that the occurrence of asynchrony is intimately linked to patient
outcome. The introduction of Neurally Adjusted Ventilatory Assist (NAVA) in clinical practice represents a big leap forward in the treatment of children with respiratory failure, as it can assure proportional synchronous assist to every patient effort, allowing, already in a first step, the improvement of patient comfort, resulting in the possibility to reduce sedation. He reported that in his experience the reaction of parents is often one of astonishment after their baby has been started on NAVA, as improved comfort in the baby is obvious.

“NAVA: Experience from the CICU”

Doctor Philippe Pouard from Bordeaux France gave the second presentation in this symposium. His group has extensive clinical experience with NAVA in the CICU setting, having data from more than 50 patients in an ongoing study. He sees the possibility to monitor the Electrical Activity of the Diaphragm (Edi) as a breakthrough in postoperative care, as it allows for the monitoring of sedation and analgesia, and can also be used as a guide for weaning. He stated, that in a baby in whom it is not possible to close the chest after cardiac surgery “it is the ideal tool for monitoring the respiratory function”.

As tidal volume, driving pressure and FiO2 are generally lower during NAVA, still resulting in normal or slightly reduced PaCO2, when compared to pressure support or controlled ventilation, he argued that NAVA fits well in the actual concepts of lung protective mechanical ventilation, which ultimately may lead to a decline in Acute Lung Injury (ALI) and Bronchopulmonary Dysplasia (BPD). In babies with single ventricle hearts undergoing a Fontan procedure, ventilator assist by NAVA is an important asset as pulmonary flow is inversely related to intrathoracic pressure. Doctor Pouard advocated the use of NAVA after cardiac surgery, stressing how its use in neonates will allow improvements in monitoring and outcome.

“Non-invasive Ventilation – Synchronisation with NAVA”

Doctor Davide Colombo showed, in the final presentation of this symposium, that non-invasive ventilation (NIV) is now an accepted treatment in both adults and children. In the adult field, COPD and cardiac failure are the current primary indications for NIV, and this is accepted almost universally. Although some centers have reported success with NIV in hypoxic respiratory failure, this latter indication remains controversial. In babies, a trial of CPAP and/or NIV seems to be indicated in most cases of acute respiratory failure before proceeding to intubation. After presenting the literature in support of these conclusions, Doctor Colombo went on to describe some of the problems with interfaces during NIV. He stated that patient acceptance of the chosen interface is critical and that patient acceptance is significantly correlated to the outcome of the treatment. For long-term treatment, skin abrasions and eye irritation are major reasons for a patient's non-acceptance of NIV, hence he proposed the helmet as the interface of choice in situations where patient adaptation is problematic.

Doctor Colombo indicated that asynchrony is another big problem associated with NIV. In fact, Vignaux et al. (Intensive Care Medicine 2009 May) showed recently that a high Asynchrony Index (AI) >10 % was found in 43 % of the patients on NIV. Such a high AI is mainly associated with leakage at the patient interface and results in a lack of patient compliance with NIV. With NIV NAVA, the presence of a leak will not have the same deleterious influence, as ventilator triggering does not depend on a pneumatic signal but on recognition of the excitation of the diaphragm muscle. This will virtually eliminate the incidence of various types of asynchrony events. Hence with NAVA, leakage is not a limiting factor for using NIV and the trigger delay, usually an important problem with the helmet, due to the high capacitance of the device, can be minimized. It is frequently maintained that NIV is associated with an increased workload for the staff. Doctor Colombo refuted this, claiming that if the patient is properly introduced to the treatment, the time needed for the nurse to spend with the patient becomes limited, mainly because the patient can be kept awake and cooperative.
Doctor Colombo finished his presentation by stressing how hard it is to diagnose patient-ventilator asynchrony by showing data from a recent study, which has just been accepted for publication in Critical Care Medicine. Analyzing strips of pressure and flow gave a correct assessment in less than 50% of the cases, even for specialists of mechanical ventilation. Properly detecting asynchrony early in the course of mechanical ventilation may be an important improvement in the care of patients with respiratory failure. The Edi signal is currently the best tool available for diagnosing patient-ventilator asynchrony.

During the questions following the session, the audience was interested in methods for weaning patients after NIV. Doctor Colombo recommended incremental periods without assist and strict evaluation of the patient response to the withdrawal. If the patient has an Edi catheter in place this is of course very easy to follow as the Edi signal will allow for indirect quantitative evaluation of the patient’s respiratory work.

Some highlights of the sessions

Other sessions in the main conference program covered early heart transplant, ECMO, care of the baby with a single ventricle physiology, brain protection (did you for example know that erythropoietin may be an effective brain protecting agent?) and peri- and postoperative care following repair of congenital heart disease.

As editor of Critical Care News, one presentation was of special interest to the readers. Professor Desmond Bohn from the Sick Children’s Hospital in Toronto discussed the current recommendation of cooling patients after cardiac arrest. He delivered a word of warning that the practice, which is an extrapolation from the adult field, may not show the outcome we might expect as the patophysiology of cardiac arrest is totally different between children and the adult population. Adults usually suffer a cardiac arrest as a result of a primary cardiac problem. In this situation – the tissue is still normally oxygenated when the heart stops. In contrast to this, the most common situations where the heart of a baby will arrest is either after an unobserved period of apnea (sudden infant death syndrome) or a severe hypoxic event due to acute respiratory failure, ultimately leading to an ischemic insult not only to the heart, which subsequently stops, but also to the brain. Therefore the neurologic outcome of pediatric cardiac arrest is extremely poor. This topic has been one of the special interests of Professor Bohn for a long time. His arguments were substantiated by previous research, and he pointed out the fact that there is ongoing research in this area which may give a definite answer to the concerns.

The Montreux Meetings (EPNV and EPNCIC) with speakers and lectures at the frontier of pediatric and neonatal intensive care practice are highly recommended, not only to trainees, but also to fully trained intensive care specialists working in a PICU, CICU or NICU. The beautiful setting definitely adds an extra dimension.

Selected references:


New Publications Relevant to Mechanical Ventilation

**Papazian L, Forel JM, Gacouin A, et al.**


This multi-center randomized, controlled clinical trial included 340 patients with severe ARDS. The study compared the administration of Cisatracurium, a neuromuscular blocking agent (NMBA), to placebo during the first 48 hours of Intensive Care. The Cisatracurium group showed more ventilation-free days, less pneumothorax, improved gas exchange and improvement in the adjusted 90-day survival rate. It is assumed that the improvement in outcome for the NMBA group is due to less patient-ventilator asynchrony.

**Bellani G, Guerra L, Musch G, et al.**

**Lung Regional Metabolic Activity and Gas Volume Changes Induced by Tidal Ventilation in Patients with Acute Lung Injury. Am J Respir Crit Care Med 2011;183:1193–1199.**

The metabolic activity, determined by cross-registration of lung computerized tomography and positron emission tomography (PET). The hypothesis being that the increased metabolic activity reflects inflammation. This is correlated to the tidal volume and even more strongly to the tidal volume over end expiratory lung volume. The paper also implies that lung injury may be induced at lower plateau pressures than previously thought. It is recommended to read the paper together with the work of Protti et al.

**Protti A, Cressoni M, Santini A, Langer et al.**

**Lung stress and strain during mechanical ventilation: Any safe threshold? Am J Respir Crit Care Med 2011;183:1354–1367.**

Long-term animal study showing that strain, defined as Vt/FRC, is not linear even in healthy lungs. The non-linear relationship between strain and subsequent injury suggests a threshold phenomenon where an apparently “safe” tidal volume is dependant on the size of the lung compartment receiving the tidal volume. The observations are entirely in line with the Stress Index hypothesis, which states that the preferred volume range over which the lungs of patients with respiratory failure should be ventilated is defined by the linear portion of the pressure-time curve. Several previously healthy animals have died from pulmonary stress failure after a period where no injury was detected.

**Pelosi P, Ferguson ND, Frutos-Vivar F, et al.**

**Management and outcome of mechanically ventilated neurologic patients. Crit Care Med Vol.39, No 6.**

This multi-center observational study indicates that Assist-control Volume controlled ventilation is the most utilized mode of ventilatory assist, independent of disease. It further indicates that very little adaptation or adjustment to specific disease or patients between different diagnostic groups is done. The rate of tracheostomy is more influenced by time on mechanical ventilation than disease, and that prolonged mechanical ventilation in neurologic patients is more determined by convention than by current evidence. The low PCO2 in neurologic patients probably relates to less initial lung injury and conventional ventilatory settings.

**Colombo D, Cammarotta G, Alemani M, et al.**


This study establishes that the detection rate of patient-ventilator asynchrony by traditional means is very low, even when the evaluation is done by experienced ICU physicians. At higher levels of Pressure Support the detection rate is lower in spite of a higher incidence of asynchrony. The authors conclude that alternative means besides analysis of pressure and flow curves should be used to detect patient-ventilator asynchrony.

**Foronda F.A., Troster E.J., Farias J.A.**

**The impact of daily evaluation and spontaneous breathing test on the duration of pediatric mechanical ventilation: A randomized controlled trial. Crit Care Med 2011 Vol. 39, No.11.**

This RCT shows that a waning protocol consisting of daily evaluation of predefined criteria instead of physician evaluation followed by a spontaneous breathing test, using a low level of pressure support shortened the time of mechanical ventilation by 25% in pediatric patients.

**Armstrong R.K., Carlisle H.R., Davis P.G., Schibler A., Tingay D.G.**

**Distribution of tidal ventilation during volume-targeted ventilation is variable and influenced by age in the preterm lung. Intensive Care Med (2011) 37:839–846.**

The article shows that the pre-term infant exhibits marked breath-to-breath variability in regional ventilation which is influenced by age, and the tidal volume cannot be predicted by a global measure of flow at the airway opening.

**Blum JM, Maile M, Park PK, et al.**

**A Description of Intraoperative Ventilator Management in Patients with Acute Lung Injury and the Use of Lung Protective Ventilation Strategies. Anesthesiology 2011;115:75–82.**

Patients undergoing surgery fulfilling the criteria for Acute Lung Injury are not given lung protective treatment during anesthesia. FiO2 and plateau pressure are higher and PEEP lower than recommended guidelines. Anesthesiologists do not appear to use low tidal volumes intraoperatively.

**Sundar S, Novack V, Jervis K, et al.**

**Influence of Low Tidal Volume Ventilation on Time to Extubation in Cardiac Surgical Patients. Anesthesiology 2011; 114:1102–10.**

In a study comparing low tidal volume (6 ml/kg) to high (10 ml/kg) in patients undergoing elective cardiac surgery, there was no difference in time to extubation, but there was a reduced incidence of intubated patients at 6 hours postoperatively and lower reintubation rate in the low tidal volume group.
The views, opinions and assertions expressed in the interviews are strictly those of the interviewed and do not necessarily reflect or represent the views of Maquet Critical Care AB.

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