Is external high frequency oscillation in the treatment of organophosphate poisoning in cats a useful and easily applied method for prehospital ventilatory support?

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Summary

Background: Rapid institution of ventilatory support is mandatory in apneic victims of nerve agents (NA) if fatal outcome is to be avoided. The Hayek oscillator™ (HO)-a high frequency external ventilator can provide non-invasive ventilatory support based on a cuirass tightly fit around the patient chest. Our aim was to investigate the feasibility of provision of resuscitative ventilatory support using the HO to cats poisoned by Dichlorovos (DDVP) an OP and NA-like compound.

Material/Methods: DDVP, 150 mg/kg was administered per os to 10 cats. With the appearance of the first signs of intoxication, the animals were treated with atropine 0.1 mg/Kg. Then, animals were randomly divided into two equal groups: 1) control (no further treatment) or 2) experimental: ventilation using the HO with the following setup: 240 cycles/min, inspiratory and expiratory pressure of –22 and –2 cm H2O respectively and I/E ratio of 1/1.

Results: The control cats died within 4–9 min from the initial appearance of signs of systemic poisoning. The experimental 5 cats survived and regained spontaneous breathing ventilation 3 hr thereafter. The use of the HO enabled also clearance of bronchial secretion saving the need for active suctioning of the airways.

Conclusions: The provision of external high frequency oscillation using the HO may serve as a useful and easily applied mode of ventilation in case of urgent need to resuscitate mass casualties suffering from NA poisoning in the prehospital setting. Its advantages include: lack of need for laryngoscopy and intubation and enhanced clearance of secretions.

Key words: high frequency oscillation • Hayek Oscillator • organophosphate • poisoning • nerve agents • respiratory failure • cats
BACKGROUND

Nerve agents (NA) are among the most deadly chemical compounds known to mankind. In the last two decades their hazardous potential was demonstrated in the terrorist attacks against civilians in Japan in 1994 and 1995 which produced several fatalities and hundreds of casualties [1,2], as well as in the military use of NA by Iraq against Iran and the Kurdish population during the 1980s. NA are chemically organophosphate (OP) compounds, which are irreversible acetylcholinesterase (AChE) inhibitors. The AChE is the enzyme regulating the activity of both nicotinic and muscarinic synapses. NA bind covalently to AChE with the result of its irreversible inhibition and consequently unlimited accumulation of ACh at the neurom-efector junctions [3]. This leads to disruption of normal synaptic transmission in the peripheral as well as in the central cholinergic system leading to the clinical manifestations of severe cholinergic crisis. The immediate cause of death is usually rapid progressive respiratory failure caused by virtue of their poisonous and depressive action on the central respiratory center as well as at the neuromuscular junction and the airways [4]. Irritation of both the upper and lower airways, their blockade by secretion, toxic pulmonary edema and severe bronchoconstriction; all are part of the effects of the NA-induced severe parasympathetic overstimulation that increases airway resistance and poses mechanical obstruction to ventilation. Hence, treatment of respiratory insufficiency is the most crucial step towards salvaging the poisoned patient. This is usually done via intubation and provision of positive pressure ventilation until signs of muscle paralysis disappear. However, in the anticipated scenario of multiple victims and chaos, which might occur in case of mass NA poisoning, shortage in personnel well-trained in airway management is to be anticipated as well as difficulties with performing laryngoscopy while wearing protective gear.

External high frequency oscillation (EHFO) is a relatively new method of non-invasive ventilatory support. The Hayek Oscillator™ (HO) is an external external high frequency oscillator used in conjunction with a specially designed cuirass. Both the inspiratory and expiratory phases are active and the chest is oscillated around a variable negative baseline pressure [5–8].

DDVP (Dichlorovos) is an agricultural pesticide and OP compound, which possesses AChE-inhibitory properties similar to NA thus, serving as a model for NO-intoxication [9]. The aim of the present study was to investigate the effect of ventilatory support to cats poisoned by the OP, using the HO method of non-invasive mechanical ventilation.

MATERIAL AND METHODS

Animals

Institutional approval and veterinary supervision were obtained for the study to assure appropriate animal care. Ten adult mongrel cats weighing 2.8–3.5 kg were studied. Anesthesia was induced by injection of IM ketamine (30 mg/kg) followed by cut-down of the femoral vein and artery. Maintenance of anesthesia was kept thereafter by boluses of IV 10 mg/kg as clinically deemed necessary.

The Hayek oscillator

The HO (Flexco Medical Instruments AG, Zurich, Switzerland) consists of a flexible, lightweight plastic cuirass that covers the anterior part of the chest and upper abdomen, having foam skirt edges, which create an airtight seal. It has a backplate and is secured by Velcro straps [10]. The cuirass is connected by wide-bore flexible tubing to a mobile and microprocessor-controlled power unit. Within the power unit is a diaphragmatic pump, which generates an oscillatory pressure that operates over a wide range of frequencies, 8–999 cycles per min. Additional pump enables these oscillation to be superimposed on a negative pressure baseline, permitting to control lung volume. The frequency, inspiratory and expiratory pressure in the cuirass chamber and inspiratory-expiratory (I/E) ratio can be set at the automatic control unit, which then adjusts the performance by negative feedback from a pressure transducer connected to the inside of the cuirass [11]. Since both the inspiratory and expiratory phases are controlled, high frequencies can be achieved. This is in contrast to regular negative pressure ventilation, which depends during the expiratory phase on passive recoil of the chest, limiting sharply attainable frequencies.

Animal treatment

Ringer solution, 10 ml/kg/h was infused through the femoral vein throughout the experiment. Dichlorovos (DDVP) a 2.2 Dichlorovinyl dimethyl phosphate (MAFU fly-killer, Bayer Agro-chemicals, UK), 150 mg/kg was administered per os. At the appearance of first signs of AChE inhibition: cramps, muscular fasciculation, bronchorrhea, wheezing, excessive salivation, miosis and lacrimation, animals were treated with atropine 0.1 mg/kg. The 5 control cats received no further treatment. The 5 cats of the experimental group were connected to the HO as soon as apnea and tongue cyanosis appeared.

RESULTS

All values are given as means ± SD. Differences among groups were analyzed using the two-tailed paired Student’s t-test. P<0.05 was considered significant.

Statistical analysis

Based on preliminary experience [12] ventilatory parameters were set as follows: 240 cycles/min, inspiratory and expiratory pressure of –22 and –2 cm H2O respectively and I/E ratio of 1/1. Samples of arterial blood were taken for blood gases analysis.
festations typical to the anticipated cholinergic hyperstimulation included: miosis, bronchorrhea, lacrimation, excessive salivation, diarrhea, skeletal muscle fasciculation and convulsions.

Table 1 presents data on arterial blood gases of the ventilated cats. These were measured at the following time points:

1. with the first appearance of clinical signs of the poisoning,
2. when cyanosis appeared 8 min thereafter and just before the start of mechanical ventilation,
3. ten min after the start of the mechanical ventilation,
4. two min after arrest of ventilation and reappearance of cyanosis,
5. ten min after resuming the ventilatory support.

It can be seen that before the initiation of mechanical ventilatory support, all cats in the experimental group developed severe combined (hypoxemic and hypercarbic) respiratory failure. The cats continued to be ventilated for a period of 3 h after which they resumed their spontaneous breathing and were disconnected from the HO.

Throughout the period of mechanical ventilation an enhanced clearance of airway secretions was observed saving the need for airway suctioning. The severe bronchorrhea disappeared gradually as time elapsed since the start of the poisoning.

**DISCUSSION**

NA are OP compounds similar to those used as pesticides but with much higher toxicity. Victims are intoxicated by absorption of the toxin via exposed skin or, more commonly, via inhalation of the poisonous gas. The resultant clinical picture is of hyperstimulation of both the nicotinic and muscarinic cholinergic system which, if not promptly treated, leads to severe muscle paralysis, hypersecretion from secretory glands, respiratory failure, seizures, coma and death.

We used the DDVP poisoning to create a model for severe and multi facet (central apnea, bronchorrhea, bronchospasm and pulmonary edema) respiratory failure that occurs following exposure to NA. The results of our experiment prove that the use of the HO in the early phase of resuscitation following acute poisoning with OP compounds can be life-saving in view of its potential to prevent death by suffocation [4]. Blood gases normalized few min after the institution of the respiratory support using the HO and expulsion of large amounts of secretions was accomplished without the need for active suctioning of the airways. The use of the HO was proved to be safe for as long as 3 h of the acute intoxication.

In case of exposure to non-conventional warfare agents, mass casualties are to be anticipated. The safest mode of airway protection in the case of NA poisoning is probably endotracheal intubation. However, some concerns may arise from a possible low success rate of intubation when performed by physicians called upon in a mass casualty scenario who are not familiar with the procedure on a daily basis and required to perform it in the prehospital setting with less than ideal conditions. In this regard the application of the HO saves the need for laryngoscopy and intubation, acts which may also be cumbersome in the described scenario due to protective gear wear by the medical personnel which impair visual acuity and manual dexterity [13]. In addition, cross contamination of the acute caring team can cause ocular signs and symptoms, such as severe miosis, dim vision and persistent rhinorrhea which, although not lethal, can compromise physician’s ability to function [14]. In addition, providing non-invasive respiratory support saves the use of muscle relaxants, which are sometimes needed for intubation. These medications might act unpredictably in cases of underlying systemic inhibition of AChE [15].

Systemic toxicity of OP or NA is invariably associated with severe bronchorrhea [15]. Hence, repeated active drainage of bronchial secretions is a major component of the respiratory care of the intoxicated patient. Clearance of secretions has been shown to be enhanced by using EHFO and attributed to reduction in sputum viscosity and enhancement of ciliary clearance [16]. In the prehospital setting where mass casualties are need to be treated simultaneously and when medical personnel is expected to be limited and probably will not be available for every patient to perform airway suctioning periodically emergency ventilation using the HO might serve as a useful solution.

The EHFO is a relatively new modality of non-invasive ventilation which controls both phases of respiration...
In EHFO both inspiratory and expiratory phases of ventilation are active and the peak inspiratory chamber pressure and the end expiratory chamber pressure are controllable. The expiratory pressure will always be negative to expand the chest and inflate the lungs, but the expiratory pressure may be negative, atmospheric or positive to produce an end-expiratory lung volume above, at or below functional residual capacity respectively [18]. Tidal volume is determined by the pressure difference between the expiratory and peak inspiratory chamber pressure and frequency. Increasing the above-mentioned pressure difference increases tidal volume while increasing frequency reduces it. Since minute ventilation is the product of frequency and tidal volume, minute ventilation increases as long as the increment in frequency is higher than the decrease in tidal volume [19]. As both inspiratory and expiratory phases are controlled high respiratory rates (up to 999 oscillations/min) may be achieved in contrast to normal negative pressure ventilation (without an active component of expiration). Nevertheless, optimal carbon dioxide removal is achieved with a rate of 90/min. The 1/E of 1/I is optimal although, in patients with inspiratory or expiratory obstruction, increasing that phase of respiration with the increased resistance may be needed for optimal ventilation [19].

Trials in animals and humans proved the efficacy of the HO in ventilating normal and sick lungs [6,7,12]. The potential to preserve cardiac output using EHFO as compared to its reduction when conventional positive pressure ventilation [6] is instituted might be favorable facing the NA-induced negative inotropic effects [15].

Resuscitative respiratory support in the case of mass casualties from NA poisoning has been given before using intubation followed by positive pressure ventilation [1,2]. Recently, the possible role of supraglottic devices (i.e. comibute and laryngeal mask airway) in the prehospital management of respiratory failure caused by toxic inhalation has been discussed and the potential use of the laryngeal mask tested on a monkey model by gear-protected physicians [20]. Nevertheless, although easy to insert by trained as well as untrained medical personnel, all supraglottic device affords only partial protection against aspiration of regurgitated gastric content a fact that may minimize the utility of their use in the case of NA poisoning. The current medical literature has no reports on the use of any type of negative pressure ventilation in the mentioned toxic inhalation mass-casualty scenario. Nevertheless, giving the technical simplicity of applying the cuirass, it is expected that after a short training period, medical as well as nonmedical personnel could operate the ventilator easily and respiratory support instituted in short time periods even when wearing protective gear in the prehospital setting. This will able to give respiratory support using fewer medical staff as compared to the case when hand-operated respirator (self-inflating bag) is used to ventilate large number of victims. In this regard, the development of a more compact and light-weight version of the HO will be helpful to minimize logistic encumbrment.

**CONCLUSION**

Being non-invasive and easily applied, the EHFO using the HO might be a safe and useful method for early provision of respiratory support in case of urgent need to resuscitate mass casualties from NA poisoning in the prehospital setting. Further tests are needed for determining optimal ventilatory parameters for humans suffering from NA poisoning.

**REFERENCES**