LITERATURE-SERVICE 09 | 20

Dear ladies and gentlemen, dear ADVOS users and interested parties,
we are pleased to present you another issue of our ADVOS Literature Service. We regularly select one or more papers from international journals which might be of interest to you in connection with our ADVOS procedure. This month we have selected the following:

ADVANCED ORGAN SUPPORT (ADVOS) IN THE CRITICALLY ILL: FIRST CLINICAL EXPERIENCE IN PATIENTS WITH MULTIPLE ORGAN FAILURE.

Fuhrmann et al.

Key message

In this paper, Fuhrmann et al. show first clinical data of patients with multiple organ failure treated with the ADVOS device. The ADVOS therapy was able to remove water-soluble and albumin-bound substances, correct acid-base imbalances, remove CO_2 and improve the hemodynamic status in patients with liver failure, septic shock or ARDS in need of extracorporeal support.

Background

Multi organ failure (MOF) is one of the most challenging problems in critically ill patients. Despite significant progress in the management of MOF, the mortality rate still remains high. Extracorporeal organ support is a huge help in the management of MOF. These procedures are usually indicated as a bridge to recovery or transplantation.

Methods

Between December 2014 and August 2016, 34 critically ill patients with MOF received 102 ADVOS treatment sessions in the Department of Intensive Care Medicine of the University Medical Center Hamburg-Eppendorf. Markers of metabolic detoxification and acid base regulation were collected and blood gas analyses were performed on samples from the inlet and outlet of the dialyzers. A subgroup analyses was performed in patients with severe acidemia (pH < 7.2) and liver failure (ARDS).

Patients

Critically ill patients with a median SOFA Score of 17, resulting in an expected mortality rate > 80% were treated. Their main admission diagnostic was Septic Shock (47%), ARDS (26%), Cardiogenic Shock (12%) and Liver Failure (15%).

At the time of the first ADVOS treatment 44% had acute-on-chronic liver failure and 56% acute liver failure - either acquired (44%), post-transplant (9%) or primary (3%).

73% of the patients were on vasopressors, 76% needed mechanical ventilation and 100% had an indication of renal replacement therapy.

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ADVOS treatments

102 treatments were performed, with a median of 2 (1-9) treatments/patient and a median duration of 18.5 hours. Median blood flow was 100 ml/min, concentrate flow 160 ml/min and dialysate pH was 8.3.

Unfractionated heparin (UFH) was used in 44 treatment sessions, regional citrate anticoagulation (CiCa) in 45 treatment sessions, antithrombin III (AT III) in 10 treatment sessions and no anticoagulation was applied in 3 sessions.

Results

The median removal rate per ADVOS treatment for bilirubin was 17.0%, for creatinine 7.1%, for BUN 17.6% and for ammonia 16.4%. The reduction rate was concentration dependent and was higher during the first treatment. Blood pH, bicarbonate, pCO_2 and base-excess were significantly improved.

In patients with ARDS, blood pH increased from 7.21 to 7.40 and pCO_2 decreased from 68.8 to 49.5 mmHg during the first ADVOS treatment (Table 2).

In patients with severe metabolic acidosis the pH increased from 7.19 to 7.40, bicarbonate from 15.4 to 20.4 mmol/l and base excess from -12.4 to -4.9 mmol/l (Table 2).

Improvement of driving pressure was observed in up to 75% of treatment sessions and was related to baseline driving pressure prior to ADVOS treatment.

Norepinephrine could be reduced in 73% of all treatments and in all patients requiring doses < 0.100 µg/kg/min. No NE was required in 43% after ADVOS treatments.

Safety

Treatments were well tolerated. A non-significant reduction of platelets was observed. Major bleeding complications were observed in 3 patients with acute-on-chronic liver failure grade III. None of these bleeding complications appeared to be related to the ADVOS treatment.

Mortality

Median length of the ICU stay was 9 days (IQR: 3–22). The 28-day mortality rate was 50% and the 90-day mortality rate 62%.

	Before ADVOS treatment	After ADVOS treatment	Relative elimination for each ADVOS treatment	Rate of treatments showing a reduction of serum levels
Creatinine (mg/dl)	1.65 (1.15; 2.36)	1.13** (0.87; 1.82)	- 24% (- 49%; - 5%)	69%
BUN (mg/dl)	28 (17; 44)	16** (11; 23)	- 48% (- 62%; - 17%)	84%
Ammonia (µmol/l)	65 (58; 87)	58** (45; 72)	- 19% (- 60%: - 8%)	91%
Bilirubin (mg/dl)	4.5 (0.9; 19.1)	4.1** (0.9; 12.6)	- 20% (- 34%: - 4%)	76%

Table 1: Elimination of water-soluble substances and bilirubin during the first ADVOS treatment of each patient.
Median (IQ25; IQ75). Non-parametric paired Wilcoxon test; **p < 0.01. Median treatment duration was 18.5 h (range 8.25; 22.0).

	All (n=34)		ARDS (n=10)		Severe metabolic acidosis (n=11)	
	before	after	before	after	before	after
Blood gas						
Blood pH	7.29 (7.19; 7.35)	7.40 (7.32; 7.46)**	7.21 (7.11; 7.29)	7.40 (7.33; 7.48)**	7.19 (7.09; 7.19)	7.40 (7.33; 7.45)**
HCO_3^- (mmol/l)	19.0 (17.5; 23.1)	22.8 (20.0; 27.4)**	24.1 (18.6; 26.7)	32.5 (28.1; 39.6)**	15.4 (13.8; 16.8)	20.4 (18.0; 24.3)**
$PaCO_2$ (mmHg)	40.6 (32.9; 60.8)	36.8 (31.6; 43.6)**	68.8 (58.4; 73.2)	49.5 (42.3; 56.1)**	37.5 (31.0; 42.9)	36.8 (32.5; 40.6)
PaO_2 (mmHg)	81.1 (65.9; 97.8)	78.6 (73.4; 93.2)	73.0 (65.0; 83.3)	84.7 (74.8; 96.9)	88.4 (61.5; 108.2)	77.6 (65.1; 84.2)
Base Excess (mmol/l)	-6.7 (-9.3; -1.6)	-1.5 (-6.6; 3.1)**	-0.4 (-7.0; 2.8)	7.8 (1.6; 15.5)**	-12.4 (-14.9; -10.5)	-4.9 (-8.5; 0.9)**
Lactate (mmol/l)	2.20 (1.15; 9.40)	2.50 (1.50; 8.15)	1.90 (0.85; 3.45)	1.95 (1.75; 2.55)	9.60 (5.85; 12.60)	7.40 (5.10; 10.15)
SID (mEq/l)	31.4 (27.2; 35.4)	32.8 (27.5; 39.0)	38.7 (31.2; 40.7)	41.5 (33.4; 47.2)	23.2 (21.3; 25.7)	28.2 (24.6; 34.3)**

Table 2: Blood gas parameters prior to and immediately after the first ADVOS treatment.
Blood gas parameters of two subgroups (i.e., patients with ARDS and patients with severe metabolic acidosis immediately prior to the ADVOS treatment.
Median (IQ25; IQ75). Non-parametric paired Wilcoxon test. **p < 0.01

The authors conclude:

The ADVOS therapy is a safe and effective procedure for the treatment of multiple organ failure based on principles of the hemodialysis. It was able to remove water-soluble and protein-bound substances and correct severe metabolic and respiratory acidosis in critically ill patients. The wide therapeutic range of the ADVOS therapy is convincing. The number of adverse events were comparable to other studies assessing conventional renal replacement systems in critically ill patients.

We think that

These retrospective results clearly show that:

1. A therapy that offers liver, lung and kidney support together with acid-base-balance correction and CO_2 removal in a single device appears to be very meaningful clinically.
2. The ADVOS treatment is feasible and safe in patients with multiple organ failure.
3. Individual detoxification functions of the ADVOS device contribute to the overall detoxification of the patient.
   - Through the combined removal of CO_2 and bicarbonate production, respiratory and metabolic acidosis were significantly improved.
   - With the improvement of the acid-base balance, the actual functions of the liver, lungs and kidneys could be supported.
   - The improvement achieved by removing toxins and balancing electrolytes and fluids led to a stabilization of the circulatory system combined with a significant reduction in catecholamine requirements.
4. The combined effects of the ADVOS procedure triggered a reduction of the expected mortality.
   - According to the SOFA score of the patients, the expected mortality was > 80%, while the current mortality in the treated patients was significantly lower with rates of 50% after 28 days and 62% after 90 days.

If you have further questions or suggestions - please contact us at marketing@advitos.com.

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