Comparative evaluation of therapeutic interventions during hemorrhagic shock

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MEETING ABSTRACTS

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P1
Effects of thyroid hormones on major cardiovascular risk in acute coronary syndromes
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Introduction In this study we aimed to investigate the relationship between thyroid hormone abnormalities and major cardiovascular events and sudden cardiac death at 3 and 6 months after discharge in patients who were admitted to the Emergency Department with acute coronary syndrome.

Methods The study group included 110 patients without known thyroid dysfunction who were referred to the Emergency Department with acute coronary syndrome. FT3, FT4 and TSH levels were measured in all patients on admission. Patients were divided into STEMI, NSTEMI and UAP groups. Patient records were checked at 3 and 6 months of discharge in terms of sudden cardiac death and major cardiovascular events. The relationship between thyroid hormone levels and acute cardiac death and major cardiovascular disorders at 3 and 6 months of discharge was evaluated.

Results The mean TSH, FT3 and FT4 levels of the study group versus control group were as follows: TSH levels of study group 1.87 ± 1.73 μIU/ml, FT3 3.2 ± 1.34 pg/ml, FT4 1.45 ± 0.64 ng/dl. Abnormalities in the thyroid hormone function tests were noted in 26 patients (23.6%). Of these seven patients (6.3%) had subclinical hypothyroidism, two patients (1.8%) had euthyroid sick syndrome and 10 patients (9%) had high serum FT4 levels despite normal FT3 and TSH values.

Conclusions We noted subclinical hypothyroidism, less frequently euthyroid sick syndrome and hyperthyroidism. No relationship was noted between thyroid hormone levels and sudden cardiac death and major cardiovascular disorders at 3 and 6 months follow-up. However, studies including larger patient groups are needed to clarify if there is a relationship between thyroid hormone levels on admission and sudden death and major cardiovascular events in patients with acute coronary syndrome.

References

P2
Effect of reperfusion therapy on QTd and QTcd in patients with acute STEMI
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Introduction Acute ischemia alters action potentials and affects myocardial repolarization. Dispersion of repolarization is arrhythmogenic. QT dispersion has been suggested to give information about the heterogeneity of myocardial repolarization.

Methods Our study included 60 patients presented with acute STEMI, the study populations were divided into two groups: Group I: 30 patients who underwent primary PCI. Group II: 15 patients who received streptokinase. Group III: 15 patients who did not receive reperfusion therapy. QTd and QTcd were measured and compared in the three groups on admission, after 24 hours and after 5 days.

Results QTd and QTcd were significantly higher in patients with anterior compared with inferior MI (79.16 ± 25.67 ms vs. 62 ± 18.17 ms, P = 0.004 regarding QTd and 91.95 ± 28.76 ms vs. 68.33 ± 23.52 ms, P < 0.001 regarding QTcd). After 24 hours, QTd and QTcd were significantly longer in Group I than Groups II and III (34.33 ± 13.56 ms vs. 48 ± 18.2 ms vs. 66 ± 24.43 ms respectively, P < 0.05 as regards QTd and 39.33 ± 11.72 ms vs. 55 ± 23.84 ms vs. 74.60 ± 26.7 ms respectively, P < 0.05 as regards QTcd). On the 5th day reduction in QTd and QTcd was statistically significantly lower in Group I than Groups II and III (23 ± 9.52 ms vs. 45.33 ± 15.97 ms vs. 58.66 ± 23.25 ms respectively, P < 0.05 for QTd and 26 ± 11.63 ms vs. 52.66 ± 21.2 ms vs. 60.66 ± 23.25 ms respectively, P < 0.05 for QTd). QT and QTc on admission were higher in patients who developed ventricular arrhythmias than patients who did not (90 ± 11.55 ms vs. 70 ± 24.54 ms, P = 0.05 regarding QTd and 110 ± 8.61 ms vs. 80.53 ± 28.78 ms with P = 0.028 regarding QTc). Patients with early peaking of enzymes had more reduction in QTd and QTcd early after reperfusion (43.2 ± 11.44 vs. 60.5 ± 13.16, P < 0.001 regarding QTd and 49.60 ± 15.93 vs. 68.5 ± 17.55, P < 0.001 regarding QTcd).

Conclusions QTd is higher in patients with acute MI (AMI) who developed ventricular arrhythmias. So QTd and QTcd on admission may be a helpful parameter that can detect patients with AMI who are at risk for development of ventricular arrhythmias. Reperfusion therapy with primary PCI or thrombolytic agents reduces QTd and QTcd in patients with AMI; however QTd and QTcd are shorter with primary PCI compared with thrombolytic therapy.

P3
Biochemical studies of some diagnostic enzymes in myocardial infarction
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Introduction Myocardial infarction (MI) is a key component of the burden of cardiovascular disease (CVD). The main causal and treatable risk factors for MI include hypertension, hypercholesterolemia or dyslipidemia, diabetes mellitus, and smoking. Acute MI results in cellular necrosis with release of constituent proteins into the circulation. Measurement of specific enzymes has become an important clinical tool for the diagnosis and management of MI. The aim of this study was to demonstrate the role of arginase and adenosine deaminase (ADA) in patients suffering from MI, and in a group of patients with chronic renal failure (CRF) with cardiovascular diseases (CVD).
tended to accumulate in the plasma and to cause negative effects on haemostasis, more recent products (for example, HES 130/0.4) are characterised by improved pharmacological properties. The present study was designed to compare the efficacy and safety of 10% HES 130/0.4 and 10% HES 200/0.5.

**Methods** In this post-hoc analysis of a prospective, randomised, double-blind, multicenter therapeutic equivalence trial, 76 patients undergoing elective on-pump cardiac surgery received perioperative volume replacement using either 10% HES 130/0.4 (n = 37) or 10% HES 200/0.5 (n = 39) up to a maximum dose of 20 ml/kg.

**Results** Equivalent volumes of investigational medications were infused until 24 hours after the first administration (1,577 ± 1,540 ml; treatment difference 37 [-150; 223] ml; P < 0.0001 for equivalence). Whereas standard laboratory tests of coagulation were comparable between groups, von Willebrand factor activity on the first postoperative morning tended to be higher following treatment with 10% HES 130/0.4 compared with 10% HES 200/0.5 (P = 0.025), with this difference being statistically significant in the per-protocol analysis (P = 0.02). Treatment groups were comparable concerning other safety parameters and the incidence of adverse drug reactions. In particular, renal function was well preserved in both groups.

**Conclusions** 10% HES 130/0.4 was equally effective and safe as compared with 10% HES 200/0.5 for volume therapy in patients undergoing cardiovascular surgery. Postoperative coagulation and renal function, as measured by standard laboratory tests, were similar among groups.

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**P88**

**Nicorandil versus nitroglycerin: a pilot study**

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**Introduction** Continuous exposure to nitrates is associated with tachyphylaxis. This study compares the effects and tolerance during intravenous treatment with nitroglycerin and nicorandil over a 48-hour period.

**Methods** Twenty patients with congestive heart failure and pulmonary capillary wedge pressure (PCWP) ≥18 mmHg were randomly assigned to nicorandil or nitroglycerin intravenous infusions. Doses were titrated to obtain a reduction of PCWP of at least 30% at 6 hours and then maintained for 48 hours.

**Results** There was no statistical difference between the groups in terms of age, sex, and NYHA grade. The pretreatment PCWP for nicorandil was 25.7 mmHg, decreasing to 18.4 mmHg at 6 hours. The values for nicorandil were 25.4 mmHg and 17.3 mmHg, respectively. There was no statistical difference between the two groups (P = 0.79 pretreatment and 0.23 at 6 hours). The mean PCWP values for 24 hours were 19.7 and 17.4, respectively, which was statistically significant (P = 0.036). Similarly, the values for 48 hours were 20.6 and 17.9, which was significant (P = 0.026) (see Table 1).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nicorandil</th>
<th>Nitroglycerin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>10 (8/2)</td>
<td>10 (7/3)</td>
</tr>
<tr>
<td>Age</td>
<td>49.9</td>
<td>51.4</td>
</tr>
<tr>
<td>Pretreatment</td>
<td>25.7</td>
<td>25.4</td>
</tr>
<tr>
<td>6 hours</td>
<td>18.4</td>
<td>17.3</td>
</tr>
<tr>
<td>24 hours</td>
<td>19.7</td>
<td>17.4</td>
</tr>
<tr>
<td>48 hours</td>
<td>20.6</td>
<td>17.9</td>
</tr>
</tbody>
</table>

**Conclusions** Intravenous nicorandil administration gives similar reductions in PCWP compared with nitroglycerin with significantly less haemodynamic tolerance over a 48-hour period compared with nitroglycerin. This might represent a clinical advantage of nicorandil in the short-term treatment of patients with congestive heart failure.

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**P89**

**Dopamine versus norepinephrine in septic shock: a meta-analysis**

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**Introduction** The aim of this meta-analysis is to compare the changes in hemodynamic parameters among patients with septic shock who have received either of the two agents in their management and try to deduce the superiority of one over the other.

**Methods** A total of 880 articles were identified by a computerized search using MEDLINE, OVID and the Cochrane Central Register of Controlled Trials, of which six randomised controlled studies were included in the study. Observational data, retrospective studies or animal-based studies were excluded. Main outcome measures evaluated were the changes from the baseline in heart rate, mean arterial pressure, oxygen delivery index, oxygen extraction, systemic vascular resistance index (SVRI), cardiac index (CI), central venous pressure, blood lactate levels, urine output, mean pulmonary artery pressure (MPAP), pulmonary capillary wedge pressure, right ventricular ejection fraction (RVEF), arrhythmias and 28-day mortality rates. The statistical analysis was performed using Comprehensive Meta-Analysis software.

**Results** No significant difference was found in mortality between the two groups (RR = 1.067, CI = 0.984 to 1.157, P = 0.115). In the norepinephrine group, heart rate was significantly lower in comparison with baseline (mean change = –16.32 beats/minute, CI = –22.23 to –10.51, P < 0.001) and so also was the occurrence of arrhythmias (RR = 2.34, CI = 1.456 to 3.775, P < 0.001). The SVRI, however, was significantly higher in this group (difference in mean 185 dynes/cm5/m2, CI = 141.214 to 229.05, P < 0.001). Patients who were on dopamine had significantly better RVEFs (mean difference = 2.38%, CI = 1.058 to 3.671, P < 0.001) and a lower lactate level (mean difference = –0.170 mmol/l, CI = –0.331 to –0.009, P = 0.038). Urine output, oxygen delivery, MPAP, and oxygen consumption were not significantly different between the two groups.

**Conclusions** Patients who received dopamine had a better right ventricular ejection fraction, lower lactate levels, lower systemic vascular resistance index and a trend towards a better cardiac index. However, this group was noted to have more arrhythmias and a higher baseline heart rate versus the norepinephrine group. Overall, there was no difference in the 28-day mortality between the two groups. Although there are certain hemodynamic advantages, we were unable to deduce the superiority of one pressor. The results support the current practice of individualizing the choice of an initial vasopressor based on patient profile.

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**P90**

**Comparative evaluation of therapeutic interventions during hemorrhagic shock**

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**Introduction** Resuscitation of patients with hemorrhagic shock (HS) represents a challenge in emergency medicine. The uncontrollable bleeding and subsequent cardiovascular collapse are responsible for 40% of the early mortality rate in trauma.

**Methods** Twelve Large White pigs at 5 months of age, weighing 25 kg, were submitted to a surgical procedure for liver resection or autologous liver transplantation. Ketamine 5+ (5 mg/kg, i.m.) and midazolam (0.5 mg/kg, i.m.) were used as a premedicant. Anesthesia was induced with propofol (3 mg/kg, i.v.) and maintained with 1.5% isoflurano...
end-tidal concentration and volume-controlled ventilation (8 ml/kg) on 40% inspired oxygen fraction. Analgesia and neuromuscular blockade were accomplishments with continuous infusion of fentanyl (0.4 mg/kg/minute) and pancuronium (0.3 mg/kg/hour). The shock was diagnosed when blood loss exceeds 40% of the total blood volume. The HS results in mean arterial pressure reduce (MAP ≤50 mmHg), 50% cardiac output reduction (CO) and central venous saturation (SvO2) decreased to 70 mmHg. The animals underwent hemodynamic, arterial blood gases and venous monitoring, at baseline (t0), impact moment (t1), after treatment (t2), intervals of 15 minutes after shock treatment (t3, t4, t5, t6), and 120 minutes after treatment (t7). Subsequent to shock diagnosis, the animals were randomly divided into GI treated with vasopressin (0.01 IU/kg/minute), norepinephrine (0.3 mg/kg/minute) and Ringer’s lactate solution (aliquots of 20 ml/kg/20 minutes until MAP >60 mmHg). GI was equal to GI but ringer lactate administration was replaced during 20 minutes of whole blood stored during 10 days at half blood loss volume.

**Results** See Table 1. Both groups showed a significant parameter decrease during hemorrhagic shock (t1) compared with t0. After treatment GI showed improvements in all parameters, GI showed improvement until t3. During t4 the animals presented a significant increase in K levels, lactate and decreased SvO2, CO, MAP followed by an increase in SvO2 (89%). The differences between the two groups and moments were statistically significant (P >0.01). GI had a 50% of mortality rate between t4 and t5 related with potassium increase. Subsequent to animal blood treatment, the patients showed an increase in T wave, ventricular fibrillation and death.

**Table 1 (abstract P90)**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>CO (l/min)</th>
<th>MAP (mmHg)</th>
<th>SvO2 (%)</th>
<th>PAP (mmHg)</th>
<th>K (mmol/l)</th>
<th>Lactate (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>t0 GI</td>
<td>3.6 ± 0.4</td>
<td>86 ± 10</td>
<td>75 ± 5</td>
<td>18 ± 2</td>
<td>3.5 ± 0.4</td>
<td>19 ± 8</td>
</tr>
<tr>
<td>t1 GI</td>
<td>1.3 ± 0.3</td>
<td>48 ± 10</td>
<td>58 ± 5</td>
<td>8 ± 3</td>
<td>4 ± 0.5</td>
<td>47 ± 8</td>
</tr>
<tr>
<td>t0 GII</td>
<td>4 ± 0.4</td>
<td>84 ± 8</td>
<td>76 ± 3</td>
<td>20 ± 3</td>
<td>4 ± 0.2</td>
<td>20 ± 10</td>
</tr>
<tr>
<td>t1 GII</td>
<td>1.5 ± 0.5</td>
<td>44 ± 5</td>
<td>57 ± 2</td>
<td>10 ± 2</td>
<td>4 ± 0.3</td>
<td>50 ± 10</td>
</tr>
</tbody>
</table>

**Conclusions** It is possible to conclude that whole blood replacement in animals with HS should be slow and steady to avoid the effects of high K administration during a short period. Those therapeutic interventions are indicated to avoid the consequences of HS.

**Reference**

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**P91**

**Effects of vasopressinergic V1 receptor agonists on sublingual microcirculatory blood flow in patients with catecholamine-dependent septic shock**

A Morelli¹, A Donati², C Ertmer³, S Rehberg¹, A Orecchioni¹, A Di Russo¹, G Citterio¹, MR Lombroso², L Botticelli¹, A Valentinii, P Pelaia³, P Pietropaoli¹, M Westphal¹

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**Introduction** Arginine vasopressin (AVP) and terlipressin (TP) are increasingly used to stabilize mean arterial pressure in the setting of septic shock. Whether these vasopressor agents negatively impact on microcirculatory perfusion is still not fully understood. The objective of the present study was, therefore, to elucidate the effects of AVP and TP on microcirculatory perfusion in patients with catecholamine-dependent septic shock.

**Methods** We enrolled 60 fluid-resuscitated septic shock patients requiring norepinephrine (NE) to maintain mean arterial pressure (MAP) between 65 and 75 mmHg. Patients were randomly allocated to be treated with either continuous TP infusion (1 μg/kg/hour), or AVP (0.04 U/minute), or titrated NE (control; each n = 20). In both the TP and AVP groups, NE was titrated to achieve a MAP between 65 and 75 mmHg. Data from right heart catheterization and sidestream dark-field imaging were obtained at baseline and after 6 hours.

**Results** No significant differences were found between groups in terms of MAP, cardiac index, mixed-venous oxygen saturation, arterial lactate, and microvascular flow index of the small vessels (2.1 (1.8; 2.4) vs. 3.0 (2.6; 3.0) for TP, 1.9 (1.7; 2.3) vs. 2.7 (2.0; 3.0) for AVP, 2.3 (2.1; 2.6) vs. 3.0 (2.9; 3.0) for NE). Conversely, AVP and TP significantly reduced NE requirements over time (0.57 (0.29; 1.04) vs. 0.16 (0.03; 0.37) μg/kg/minute for TP and 0.40 (0.20; 1.05) vs. 0.23 (0.03; 0.77) μg/kg/minute for AVP; all P <0.05). However, no differences were found between TP and AVP after 6 hours.

**Conclusions** The results of the present study suggest that vasopressinergic V1 agonists allow a reduction in catecholamine requirements without negative impact on microvascular perfusion as compared with sole NE therapy.

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**P92**

**Vasopressin for the treatment of vasodilatory shock: an ESICM systematic review and a meta-analysis**

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**Introduction** We examine benefits and risks of vasopressin/terlipressin use in patients with vasodilatory shock on mortality and morbidity.

**Methods** We searched the CENTRAL, MEDLINE, Embase, and LILACS (through to August 2010) databases. Randomized and quasi-randomized trials of vasopressin/terlipressin versus placebo or supportive treatment in adult and pediatric patients with vasodilatory shock were included. The primary outcome for this review was short-term all-cause mortality.

**Results** We computed data from 10 randomized trials (n = 1,111). The overall (28-day, 30-day, ICU, hospital and 24-hour) mortality for those treated with vasopressin and terlipressin versus control patients was 237 of 582 (40.7%) versus 226 of 528 (42.8%) (RR, 0.92; 95% CI, 0.81 to 1.00).