Title: EFFECTS OF CATECHOLAMINES AND BLOOD TRANSFUSION ON CELLULAR IMMUNE FUNCTION FOLLOWING TRAUMA

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Introduction : Immune dysfunction has been reported after severe trauma [1]. Hormonal response to stress [2] and blood transfusion [3] have been shown to impair cellular immune function. This study was designed to assess the role of catecholamine plasma levels and transfusion on the changes in T cell subsets following trauma.

Patients and Methods : With institutional approval and informed consent, 15 ICU patients (mean age 33.6±14.3 years) with severe blunt trauma were studied. Injury severity score was 32±8, Eight patients received transfusion (8.4±6.0 units of homologous blood). None received ß-adrenergic agonist agents. Mean stay in ICU was 4±1 weeks. TISS index was calculated weekly. Blood samples were collected on Day 2 and every week thereafter. Epinephrine (E.) plasma levels (pg/ml) were analyzed by HPLC. Absolute numbers of lymphocytes (L), T cells CD2, and the following T cell subsets: mature T cells CD3, helper cells CD4, suppressor/cytotoxic cells CD8, inducer of helper cells 4B4 (CD29), inducer of suppressor cells 2H4 (CD45R), cells bearing IL2 receptors CD25, activated T cells CD26 were measured with a flow cytometric immunofluorescence method using monoclonal antibodies. Results were given as mean±SEM. Statistical analysis was by Student's t test ($p<0.05$ significant).

Results : Immunological effects of E. plasma levels and transfusion on T cell subsets are shown on Table I.

Table I: T cell subsets, E. plasma levels, and blood transfusion

* p<0.05 ** p<0.01 *** p<0.001 - not significant

	Controls	High E.		Normal E.	Transfusion		No transf.
L	2.44±0.45	1.51±0.80	*	2.27±1.20	0.95±0.46	*	2.18±1.44
CD4	0.95±0.16	0.55±0.36	*	0.84±0.44	0.34±0.30	-	0.53±0.23
CD8	0.48±0.08	0.35±0.21	-	0.40±0.24	0.17±0.10	*	0.43±0.32
4B4	0.43±0.19	0.34±0.30	-	0.32±0.28	0.11±0.11	-	0.24±0.21
2H4	0.42±0.21	0.23±0.17	-	0.23±0.15	0.12±0.10	-	0.17±0.14
CD26	0.42±0.10	0.43±0.29	**	0.84±0.79	0.19±0.15	*	0.49±0.29
E.		1302±940	***	132±77	399.2±147.5	-	295.4±90.7
TISS		23.9±3.0	-	21.3±3.0	33.7±2.2	-	36.3±2.2

Discussion : The results indicate that T cell subsets are normal in injured patients with normal E. plasma levels, except for a decrease in 2H4 and a rise in CD 26 cells suggesting activation of the immune system. All T cell subsets were markely decreased in patients with high E. plasma levels, suggesting a redistribution of lymphocytes to the tissues at the expense of the blood. Patients who received blood transfusion showed a significant decrease in L, CD8 and CD26 cells, but not in CD4 and in inducer cells (4B4 and 2H4), which supports the hypothesis of a drop in cytotoxic cells. Future evaluations should focus on the direct identification of cytotoxic cells and on their involvement in the immune dysfunction following trauma and surgery.

References : 1. MILLER S.E. et al., Surg.ClinsNAm., 1982;62:167-81. 2. CRARY B. et al., J.Immunol., 1983;3:1178-81; 3. COLLINS J.A. et al., WorldJ.Surg., 1987;11:75-81.

A227

TITLE: INFUSION OF PROPOFOL VERSUS INFUSION OF MIDAZOLAM FOR SEDATION IN THE ICU FOLLOWING CORONARY ARTERY SURGERY

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INTRODUCTION: A midazolam (M) infusion is currently being used to provide sedation in the cardiac ICU to promote a smooth post-operative recovery but may result in a prolonged emergence. Similarly, a propofol (P) infusion may provide adequate sedation but allow faster emergence. However, P may cause cardiovascular depression. We compared the sedative and hemodynamic effects of both drugs in this setting.

METHODS: After written informed consent and institutional approval, thirty coronary artery surgery patients with good LV function were assigned to one of two treatment groups in an open randomised fashion.

Following a lorazepam 60 mcg/kg oral premedication, a continuous Sufentanil infusion (1.25-5 mcg/(kg.h)) was used as the standard anesthetic technique. The S infusion (0.625 mcg/(kg.h)) was continued in the ICU for 4 hours to provide analgesia.

As soon as initial hemodynamic stability was achieved in the ICU, sedation was commenced with either a bolus dose of P 1 mg/kg or M 70 mcg/kg, which was immediately followed by a continuous infusion of P 4 mg/(kg.h) or M 75 mcg/(kg.h) respectively. Deep sedation (assessed as asleep with only sluggish response to glabellar tap or loud auditory stimulus) was maintained and assessed hourly; then if necessary, stepwise adjustment of the infusion rate was used to maintain the desired level of sedation. The adjustment step for the infusion rate of P was 1 mg/(kg.h) with a range of 2-6 mg/(kg.h) and for M 25 mcg/(kg.h) with a range of 25-150 mcg/(kg.h). An abrupt lightening of sedation was treated by a single stepwise increase of infusion rate, augmented by a bolus dose of P 0.5 mg/kg or M 35 mcg/kg as appropriate. Sedation was continued until the patient was fully rewarmed and hemodynamic parameters were considered satisfactory and stable. The quality of sedation (good-adequate-poor) was evaluated as well as the number of augmentory bolus doses required and adjustments of the infusion rate. Times from stopping the sedative drug to patient cooperation, weaning and extubation were compared.

The initial hemodynamic measurements were at 15 min intervals, thereafter hourly, and included HR, ABPs, ABPd, CVPm, PAPs, PAPd, CI, SVR, PVR, LVSWI and RVSWI. Filling pressures were kept within normal preset levels. Hemodynamic data were analysed for statistical significance using ANOVA for repeated measurements, followed by the Student-Newman-Keuls procedure for multiple comparisons.

RESULTS: Demographic data were comparable in both groups.

		P(n=15)	M(n=15)
Inf Rate (mg/(kg.h)-mcg/(kg.h))	MEAN	2.71	92
Duration Inf (h.min)	MEAN	9.28	9.45
Sufentanil dose (mcg/kg)	MEAN	15.54	18.01x
	MEDIAN	15.50	17.70x
N of adjustm inf rate	MEAN	3.27(1-5)	5.27*(3-8)
N of boluses + adjustm inf rate	MEAN	2.27(1-4)	4.67*(1-8)
Stop sedation to coop (min)	MEAN	11(3-35)	72°(20-300)
	MEDIAN	10	45°
Stop sed to weaning (min)	MEAN	52(10-125)	195°(75-555)
	MEDIAN	40	150°
Stop sed to extubation (min)	MEAN	250(15-525)	391+(270-660)
	MEDIAN	268	335+

(x=two-sided unpaired Student's t-test: P=0.028; *=two-sided unpaired Student's t-test: P<0.001; °=Mann-Whitney rank sum test: P<0.001; +=Mann-Whitney rank sum test: P=0.014).

Following both bolus injections there was a fall in the ABPm which was only significant with P (80 ± 11 mmHg --> 67 ± 10 mmHg) and remained so throughout the study. Despite this fall in ABPm, HR did not change significantly. Both P and M caused a reduction in SVR, almost reaching significance in the P group. There was no significant change in HR, CI or LVSWI in either group.

DISCUSSION: The quality of sedation was assessed as good in both groups, but required significantly more additional bolus doses and infusion rate adjustments in the M group. Measured hemodynamic parameters were stable throughout the infusion period, apart from a moderate but acceptable decrease in ABPm in the P group, which was considered to be mainly due te the fall in SVR. Post infusion patient cooperation was significantly faster in the P group as well as weaning off the ventilator and extubation.