P-416
IMPACT OF CICLOSPORINE A WITHDRAWAL ON SYMPATHETIC NERVE ACTIVITY AND BLOOD PRESSURE IN RENAL TRANSPLANT RECIPIENTS
Barbara M. Svenneby, Markus Kosch, Ulf M.W. Gerhardt, Helge Hohage, Karl H. Rahn, Martin Hausberg, Med Dept D, University of Muenster, Muenster, Germany, Germany.

Objective: It has been suggested that the increase in blood pressure observed in transplant patients treated with ciclosporine A is mediated by sympathoexcitation induced by CICLOSPORINE A. However, the chronic effects of CICLOSPORINE A on sympathetic outflow in renal transplant patients (RTX) has not been investigated. Therefore, we studied sympathetic nerve activity and blood pressure before and 6 months after withdrawal of CICLOSPORINE A in RTX.

Design and Methods: 18 RTX with histologically proven allograft nephropathy (age 49 ± 2 yr, 72 ± 9 months after transplantation, data are mean ± SEM) were included in the prospectives study and randomized to either withdrawal (n = 11) or continuation (n = 7) of CICLOSPORINE A treatment (average trough levels 72 ± 9 ng/ml and 6.0 ng/ml for ciclosporine and tacrolimus, respectively). Both groups received myocphenolate mofetil (MMF) and prednisolone as additional immunosuppressants. At entry and 6 months later, blood pressure, muscle sympathetic nerve activity (MSNA, microneurography at the peroneal nerve) and plasma catecholamines were measured.

Results: MAP decreased significantly in the CICLOSPORINE A-withdrawal group (96 ± 3 vs. 108 ± 4 mmHg 6 vs. 0 months, p < 0.05) but not in the CICLOSPORINE A continuation group (101 ± 3 vs. 104 ± 6 mmHg, n.s.). However, sympathetic nerve activity - as measured by MSNA and Norepinephrine plasma levels - did not change significantly in either group (MSNA: 51 ± 4 vs. 49 ± 4 bursts/min and 45 ± 5 vs. 45 ± 5 bursts/min in the CICLOSPORINE A withdrawal and CICLOSPORINE A-continuation group, respectively; n.s.). Serum creatinine concentrations were stable in both groups.

Conclusions: CICLOSPORINE A withdrawal in renal transplant patients receiving relatively low doses of CICLOSPORINE A results in a substantial decrease in blood pressure. However, this reduction in blood pressure was not attributable to decreases in sympathetic nerve activity suggesting either that CICLOSPORINE A treatment does not cause chronic sympathoexcitation in RTX or that the CICLOSPORINE A induced sympathoexcitation is not reversible within 6 months.

Key Words: Sympathetic Nerve Activity, Calcineurin Inhibitors, Renal Transplantation

P-418
ACUTE EFFECTS OF DEVICE-GUIDED BREATHING ON CARDIOVASCULAR PARAMETERS AND BAROREFLEX SENSITIVITY IN NORMAL SUBJECTS
Gianfranco Parati, Fabio Givona, Ongaro Guido, Maronati Alberto, Castiglioni Paolo, Gavish Benjamin, Di Rienzo Marco, Mancia Giuseppe. Internal Medicine, University of Milano-Bicocca, Milano, Italy; Cardiology - 2, S.Luca Hospital, Istituto Auxologico Italiano, Milano, Italy; Bioengineering, LaRC, Fondaz. Don Gnocchi, Milano, Italy.

Repeatedly performed slow breathing (SLB) exercise has been reported to reduce blood pressure (BP) in hypertension. Among the possible mechanisms responsible for such an effect, an increased baroreflex sensitivity has been suggested to play a role. Aim of our study was to explore whether acute performance of SLB obtained with a device-guided breathing exercise (RESPeRATE, InterCure) has any influence on BP, pulse interval (PI, 1/HR) and spontaneous sensitivity of baroreflex control of HR (BRS) in normal subjects.

In supine normal volunteers (n = 15): age 39.9 ± 8.4 yrs, 10 males, finger BP, PI, respiratory rate (RR), ETCO2 and SaO2 were continuously recorded for 3 periods of 15 min each: baseline (BAS), SLB, and resumption of spontaneous breathing (SB). Beat-by-beat systolic (SBP) PI and PI values were averaged during each period. SD was used as an index of variability of SBP and PI. BRS was quantified as the LF and HF coefficient (squared ratio of the spectral powers of PI and SBP at 0.1 and 0.3 Hz, respectively) and by the slope of +PI/+SBP and -PI/-SBP sequences.

RR was 12.5 breath/min during BAS and SB and fell to 5.2 breath/min during SLB (p < 0.01). ETCO2 and SaO2 did not change throughout the study. BAS SBP and PI were 124.3 ± 13.5 mm Hg and 0.95 ± 0.134 sec, respectively, with no change during SLB or SB. PI SD was 0.064 ± 0.026 sec in BAS and increased to 0.074 ± 0.028 and 0.082 ± 0.030 sec during SLB and SB respectively (p < 0.01). SBP SD showed a tendency to increase in parallel (NS). The corresponding values of +PI/+SBP slope were 13.0 ± 7.8, 15.0 ± 6.7 and 16.3 ± 6.4 msec/mm Hg (p < 0.05 vs BAS). +HF and +PI/+SBP slope also showed a tendency to increase vs BAS. The number of +PI/+SBP and -PI/-SBP sequences was 7.7 ± 6.6 and 8.4 ± 5.7, respectively, during BAS, increased to 23.2 ± 16.9 and 32.3 ± 16.0 during SLB (p < 0.01) and returned to 10.2 ± 6.9 and 12.4 ± 5.2 during SB (NS vs BAS).

P-417
EXCESSIVE SYMPATHETIC HYPERACTIVITY IN HYPERTENSION SECONDARY TO NEUROVASCULAR COMPRESSION OF THE MEDULLA Oblongata

It is well known that hypertension secondary to renal artery stenosis, and adrenal lesions such as pheochromocytoma is associated with a level of sympathetic hyperactivity, which is less in magnitude than that seen in essential hypertension (EHT). Hypertension has also been reported to occur secondary to neurovascular compression of the ventrolateral medulla (VLM) a site rich in central sympathetic neurones. This study was designed to quantify the magnitude of central sympathetic output in hypertensive patients with neurovascular compression. Twenty-five treated hypertensive subjects who had previously undertaken MR imaging of the brainstem were examined. Using the technique of peroneal microneurography we independently measured central sympathetic output in terms of the mean frequency of single units with defined vasoconstrictor properties (s-MSNA). Twelve subjects had VLM compression (EHT-C) and thirteen did not (EHT). The two groups were matched for age, body mass index (BMI) and mean arterial pressure (mBP). The observed sympathetic activity in both groups was greater than that obtained in matched normal subjects in our laboratory (51 ± 3.4 imp/100 beats). The magnitude of central sympathetic discharge (s-MSNA), expressed in impulses per 100 cardiac beats (imp/100b) was significantly greater in EHT-C than in EHT (P = 0.02; unpaired t test). Data are shown in Table as mean ± SEM. In conclusion, those subjects with neurovascular compression of the VLM had a greater central sympathetic output than those without. This study has shown for the first time that one suggested cause of secondary hypertension is associated with a central sympathetic hyperactivity that is greater, rather than lesser in magnitude than that seen in essential hypertension.

Key Words: Hypertension, Medulla Oblongata, Sympathetic Nervous System