Beta-2-adrenergic receptor functionality and genotype in patients with liver cirrhosis

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Background

The role of the **sympathetic nervous system (SNS) in causing inflammation** is still not completely understood. This study was designed to investigate the contribution of **polymorphic b2 adrenoceptors (b2AR)** to the pro-inflammatory effects of the SNS patients with liver cirrhosis.

b2AR gene contains three single nucleotide polymorphisms (SNPs) at amino acid positions 16, 27, and 164.

Aim

To study the potential influence of genotype on lymphocytes b2AR functionality in patients with cirrhosis

Method

We studied 52 **cirrhotic patients** with esophageal varices and portal hypertension (hepatic venous pressure gradient (HVPG) 13±4 mmHg, CHILD 7±2 and MELD 11 ± 4 scores) and 26 healthy volunteers as controls.

Mononuclear cells were isolated from the whole blood. Basal and stimulated intracellular cAMP levels (isoproterenol stimulus from 10^{-8} to10^{-3}), and **b2AR allelic variants** (Arg16Gly, rs1042713; Gln27Glu, rs1042714; Thr164Ile, rs1800888) were determined.

Student's t-test was used to compare means, and the χ2 test was used to compare percentages. A two-tailed P value of less than 0.05 was considered significant.

Results

b2AR functionality was significantly **decreased in cirrhosis vs. control** (14±15,5 pmol/ml vs 90±66 pmol/ml at ISO 10^{-5} stimulus, respectively, $p<0.05$). This decreased B2AR functionality was similar in patients: (i) in primary or secondary prophylaxis (15±19 and 14±13 pmol/ml, respectively), and (ii) in responder or nonresponder to propranolol during HVPG (14±16 and 14±15 pmol/ml, respectively).

The prevalence of **different genotypes** did not differ between patients stratified according to any clinical variable. In cirrhotic patients the decreased in b2AR functionality was the same for all the studied allelic variants (naïve v.s SNP, 15±17 vs 13±16 pmol/ml).

		Control (n=26)	Cirrhotic (n=52)	
			Primary prophylaxis (n=22)	Secondary prophylaxis (n=30)
Age (years)		59±13	52±11	55±11
Female, n(%)		13 (50)	3(13)	4(13)
Child-Plug score		-	6,3±1.8	7,2±1.5
MELD		-	10±4.3	12±2.8
Gly16 Arg n(%)	GG	7 (27)	3(16,6)	11 (41)
	GA	0	3 (16,6)	2 (7)
	AA	19 (73)	12 (66,6)	14 (52)
Allele A (*Arg16*)		*0.73*	*0.75*	*0.55*
Gln27Glu	CC	16 (62)	12 (67)	13 (48)
	CG	6 (23)	5 (28)	8 (30)
	GG	4 (15)	1 (6)	6 (22)
Allele G (*Glu27*)		*0.26*	*0.20*	*0.37*
Thr164Ile	CC	21 (81)	17 (94)	26 (96)
	CT	2 (8)	1 (6)	1 (4)
	TT	3 (11)	0	0
Allele T(*Ile154*)		*0.16*	*0. 03*	*0. 02*

TABLE 1: Demographic and genetic data

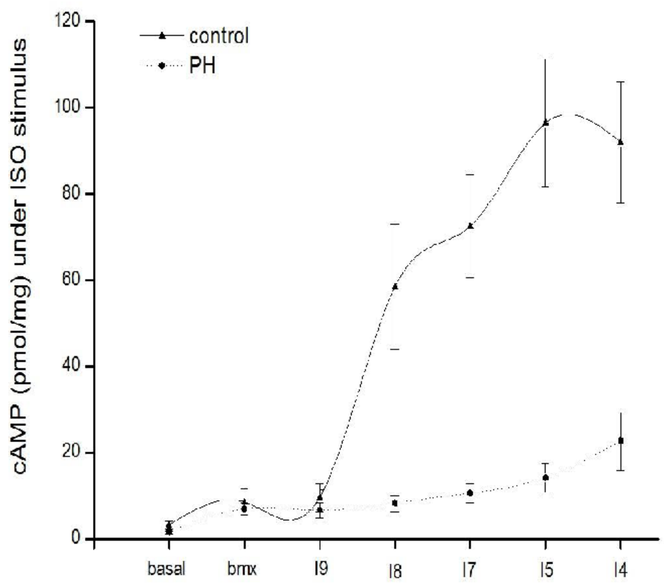

FIGURE 1: Cyclic AMP (cAMP) level under isoproterenol 10-3 to 10-9 (PH: portal hypertension patients, Controls: Healthy volunteers, ISO: isoproterenol).

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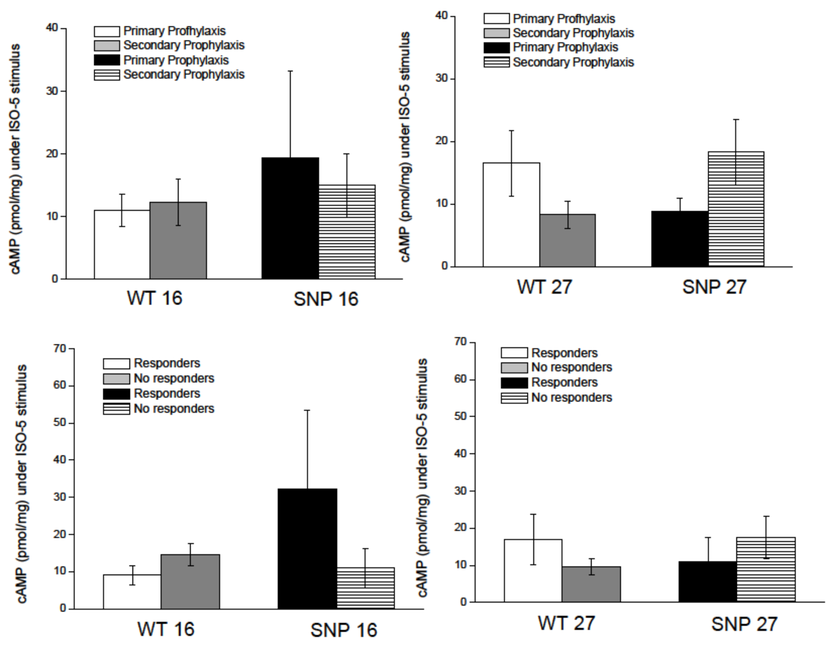

FIGURE 2: Cyclic AMP (cAMP) level under isoproterenol 10-3 to 10-9 (PH: portal hypertension patients, Controls: Healthy volunteers, ISO: isoproterenol).

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Conclusion

In patients with cirrhosis and portal hypertension the functionality of b2AR is significantly decreased. This change is not related to b2AR allelic variants. Although the amount of adrenergic receptor on lymphocytes has been shown to be related to the number of adrenergic receptors on heart tissue, future studies should employ a more direct assessment on liver.