Letter to the Editor-in-Chief

Role of H.E.L.P.-apheresis in the treatment of sudden sensorineural hearing loss in a group of 230 patients

Ruolo della H.E.L.P.-aferesi nel trattamento dell'ipoacusia sensorineurale improvvisa in un gruppo di 230 pazienti

G. BIANCHIN, G. RUSSI[1], N. ROMANO[1], P. FIORAVANTI

Otorhinolaryngology Unit, "Santa Maria Nuova" Hospital, Reggio Emilia, Italy; [1] Transfusion Medicine Unit, "Santa Maria Nuova" Hospital, Reggio Emilia, Italy

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Dear Editor-in-Chief,

It is a matter of fact that the aetiology of SSHL is still unknown, even though many published works tend to establish a correlation between microcirculation disease and SSHL [1-5]. It is also well known that endothelial dysfunction, high levels of haemostatic factors and disturbed blood flow are the fundamentals of thromboembolic diseases and can impair the microcirculation of the cochlea [6-8]. All these features are strongly affected by plasmapheresis, in particular by H.E.L.P.-apheresis, which is a specific apheretic therapy that acutely decreases LDL cholesterol, Lp(a), fibrinogen and other pro-inflammatory markers like CRP, up to 60% in only 2 hours [9]. After a single H.E.L.P. session, flow-mediated vasodilatation improved, significantly [10]. H.E.L.P. also has an acute beneficial effect on endothelial dysfunction and circulating adhesion molecules in patients suffering from SSHL [11]. Furthermore H.E.L.P.-apheresis can effectively lower plasma and whole blood viscosity, improve erythrocyte elasticity and reduce aggregability [12]. Since 2007 our staff is active with apheresis in the treatment of SSHL, thanks to the existing cooperation with the Transfusion Medicine Unit. Our first results were published on "The Laryngoscope" in April 2010 [13]. This was a prospective, randomized, controlled, superiority study (difference ≥ 30%), the first conducted in Italy in this field, approved by the Hospital Ethics Committee, in which a total of 132 patients were admitted to the trial and randomly allocated to two different arms; 60 were given standard treatment (ST) and 72 were treated with a single H.E.L.P.-apheresis followed by the standard treatment (H.E.L.P.-ST). ST consists in an infusion of 10% glycerol (500 ml), once a day, for 10 days, and intramuscular administration of dexamethasone 8 mg once a day, for 10 days.

The inclusion criteria were patients with a value of LDL–cholesterol > 120 mg/dl and/or fibrinogen > 320 mg/dl and with an acute, one-sided, SSHL that occurred not later than 20 days before the beginning of treatment. (All the patients included in the study had a hearing symmetry before the onset of SSHL). In our first study, we considered only pure-tone threshold recovery as the main outcome. Patients submitted to H.E.L.P.-ST had a recovery rate much higher than those submitted to ST (75% *vs.* 25% at 24 hours; 76.4% *vs.* 23.6% at 10 days).

Table I. Baseline characteristics.

Standard treatment			H.E.L.P. apheresis + standard treatment		
	Mean	SD		Mean	SD
No. of patients	115		No. of patients	115	
RH ear affected	69		RH ear affected	47	
LH ear affected	46		LH ear affected	68	
Average age	59.6	34-79	Average age	53.2	32-82
Average before treatment	12 (days)		Average before treatment	11 (days)	
Total cholesterol	232	± 32	Total cholesterol	242	± 37
LDL cholesterol	149	± 28	LDL cholesterol	158	± 33
HDL cholesterol	59	± 18	HDL cholesterol	61	± 20
Fibrinogen	356	± 85	Fibrinogen	345	± 94

Table II. Recovery 24 hours (post) after H.E.L.P. apheresis plus standard treatment or standard treatment.

	H.E.L.P.-ST group (post) (n = 115)	ST group (post) (n = 115)	p*
Patients with improvement	77 (66.9%)	45 (39.1%)	0.00
Patients with no change	38 (33.1%)	70 (60.9%)	

** Chi-square test*

Table III. Recovery 10 days (last) after H.E.L.P. apheresis plus standard treatment or standard treatment.

	H.E.L.P.-ST group (post) (n = 115) n (%)	ST group (post) (n = 115) n (%)	p*
Patients with improvement	81 (70.4%)	47 (40.9%)	0.00
Patients with no change	34 (29.6%)	68 (59.1%)	

** Chi-square test*

Thanks to these encouraging data, we decided to enlarge our experience with plasmapheresis. Following the same study design and the same clinical hypothesis of the previous work, we started a new study, which is the linear evolution of the work previously published on "The Laryngoscope" in April 2010.

We substantially increased the number of treated patients, reaching a total of 230 patients enrolled. 115 were given ST and 115 were treated with H.E.L.P.-apheresis followed by 10 days of ST (H.E.L.P.-ST). Table I shows the baseline characteristics of patients.

From a clinical point of view, the new evaluation has been enriched with further investigations. We also considered speech perception improvement at 24 hours and at 10 days beyond pure-tone recovery, and we also made a very preliminary evaluation on tinnitus score (THI). The THI was carried out at admission, and at 24 hours and 10 days after the end of treatment establish the behaviour of the perception of tinnitus from patients.

For all these reasons, we can state that our new contribution is an extension of the previous one. The increase in the number of treated patients had no effect on the percentage of pure-tone recovery. Also, the percentage of superiority of apheresis plus standard treatment group (H.E.L.P.-ST) is close to 30% as seen in Tables II and III.

The results of SSHL are difficult to analyze; some variables are particularly important, while others influence the results. A correlation between recoveries and the frequencies observed must not be ignored. In the H.E.L.P.-ST group, we observed recovery in 66.9% of patients at 24 hours and

Table IV. Recovery of patients according to different frequencies at follow-up 24 hours after treatment (post) and 10 days after treatment (last). Paired T-test p = 0.001.

Tonal Threshold		250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz
H.E.L.P.+ST Group 115 pz (post)	Patients with improvement	69 (60%)	77 (66.9%)	76 (66.1%)	56 (48.7%)	62 (53.9%)
	Patients with no change	46 (40%)	38 (33.1%)	39 (33.9%)	59 (51.3%)	53 (46.1%)
ST Group 115 pz (post)	Patients with improvement	45 (39.1%)	45 (39.1%)	42 (36.5%)	35 (30.4%)	45 (35.6%)
	Patients with no change	70 (60.9%)	70 (60.9%)	73 (63.5%)	80 (69.6%)	74 (64.3%)
H.E.L.P.+ST Group 115 pz (last)	Patients with improvement	75 (65.2%)	81 (70.4%)	76 (66.1%)	63 (54.8%)	68 (59.1%)
	Patients with no change	40 (34.8%)	34 (29.6%)	39 (33.9%)	52 (45.2%)	47 (40.8%)
ST Group 115 pz (last)	Patients with improvement	44 (38.3%)	47 (40.9%)	43 (37.4%)	39 (33.9%)	43 (37.4%)
	Patients with no change	71 (61.7%)	68 (59.1%)	72 (62.6%)	76 (66.1%)	72 (62.6%)

H.E.L.P. + ST Group: H.E.L.P. apheresis + Standard Treatment Group; ST Group: Standard Treatment Group.

Table V. Mean tonal thresholds recovery in decibel of patients 24 hours after treatment (post) and 10 days after treatment (last).

Mean pure-tone recovery (post)	250 Hz		500 Hz		1000 Hz		2000 Hz		4000 Hz	
H.E.L.P. + ST Group	11.2	$p^* < 0.05$	12.7	$p^* < 0.05$	11.2	$p^* < 0.05$	7.0	NS	8.6	NS
ST Group	6.9		8.1		6.2		4.1		5.4	
Mean pure-tone recovery (last)	**250 Hz**		**500 Hz**		**1000 Hz**		**2000 Hz**		**4000 Hz**	
H.E.L.P. + ST Group	13	$p^* < 0.05$	15.1	$p^* < 0.05$	12.7	$p^* < 0.05$	8.3	NS	11	$p^* < 0.05$
ST Group	7		9.3		7.3		5.3		5.8	

** t-test; H.E.L.P. + ST Group: H.E.L.P. apheresis + Standard Treatment Group; ST Group: Standard Treatment Group.*

Table VI. Mean recovery of speech perception 24 h (post) and 10 days (last) after H.E.L.P. apheresis plus standard treatment or standard treatment (dB).

Mean speech perception recovery (post)		
H.E.L.P.+ST Group	10.3	$p^* < 0.05$
ST Group	6.1	
Mean speech perception recovery (last)		
H.E.L.P.+ST Group	12	$p^* < 0.05$
ST Group	7.3	

** t-test.*

70.4% at 10 days after treatment. Only 33.1% at 24 hours and 29.6% of the patients at 10 days showed no change. In the ST group, recovery was 39.1% at 24 hours and 40.1% at 10 days, while 60.9% at 24 hours and 59.1% at 10 days had no change. Next we examined in detail the recovery of patients for each frequency. Table IV shows recovery of patients according to different frequencies at different follow-up times (24 hours and 10 days) for the two different groups. For the H.E.L.P.-ST group, the improvement was statistically significant at both the first and second follow-ups and for all frequencies. (Paired T – test; $p = 0.001$).

Table V shows the absolute values of the mean pure-tone recovery in decibels according to frequency; higher values were seen for the H.E.L.P.-ST group compared to the ST group for all frequencies. The recovery absolute values vary, in the post follow-up, for the H.E.L.P.-ST group from 12.7 dB at 500 Hz to 8.6 dB at 4000 Hz, compared to 8.1 dB at 500 Hz to 4.1 dB at 2000 Hz in the ST group ($p < 0.05$; $p < 0.05$). In the last follow-up, the trend is similar with a range from 15.1 dB at 500 Hz to 11 dB at 4000 Hz for the H.E.L.P.-ST group, while the ST group showed a range from 9.3 dB at 500 Hz to 5.3 at 2000 Hz ($p < 0.05$; $p < 0.05$). The analysis of the results of the H.E.L.P.-ST group compared to ST group allow for the consideration that H.E.L.P.-apheresis is the element responsible for the difference.

Mean speech perception, measured by the sound level at which patients could recognize 50% of the presented test words, was 10.3 dB after 24 hours in the H.E.L.P.-ST group and 6.1 dB in the ST group ($p < 0.05$). Moreover, 10 days after treatment mean speech perception was significantly better ($p < 0.05$) in the H.E.L.P.-ST group (12 dB) with respect to ST group (7.3 dB; Table VI).

Our preliminary data support the hypothesis that H.E.L.P.-apheresis is also effective in treatment of tinnitus [14]. We collected a small amount of data, but the results obtained from THI seem to be encouraging, with a recovery of two points in the 58% of the patients in the H.E.L.P.-ST group, with respect to ST group where 32% of the patients presented a recovery of two points.

Our intention was to offer a further contribution to our first publication in terms of clinical evidence, including speech perception by measuring and tinnitus score improvement. In our opinion, as already reported by others [15 16], the patient's quality of life seems to be better in those subjects submitted to apheresis, thanks to quicker clinical improvement and good tolerability. Our new data suggest that H.E.L.P.- apheresis is a safe and effective treatment for SSHL. In particular, in a specific group of patients, with alterations in LDL-cholesterol and fibrinogen, H.E.L.P.-apheresis, represents an additional option available for clinical treatment of sudden sensorineural hearing loss.

Best Regards,
G. Bianchin, G. Russi, N. Romano, P. Fioravanti

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Address for correspondence: Giovanni Bianchin, MD, Otorhinolaryngology Unit, "Santa Maria Nuova" Hospital, viale Risorgimento 80, 42123, Reggio Emilia, Italy. Tel.: +39 0522 296124. Fax: +39 0522 295839. E-mail: giovanni.bianchin@asmn.re.it