

Heparin-induced extracorporeal LDL-precipitation (H.E.L.P.) improves the recovery of hearing in patients suffering from sudden idiopathic hearing loss

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SUMMARY

The pathogenesis of SHL is not elucidated as yet. Insufficient perfusion of the cochlea due to an increased blood viscosity, microthrombosis or an altered vasomotion are being assumed. Hypercholesterolaemia, hyperfibrinogenaemia, and an increased platelet aggregation are frequently observed in patients with sudden sensorineural hearing loss. The aim of this study was to investigate, whether drastic lowering of plasma cholesterol and fibrinogen by a selective extracorporeal apheresis has a beneficial effect on hearing recovery in these patients. Seven patients suffering from SHL were treated with an extracorporeal procedure removing fibrinogen

and cholesterol from plasma. Six of the seven patients immediately showed an improvement of their auditory thresholds following a single H.E.L.P. - treatment.

Our study shows for the first time that acute and drastic removal of plasma fibrinogen and low density lipoproteins is an effective clinical tool in the treatment of patients with SHL.

Key words: sudden hearing loss, cholesterol, fibrinogen, H.E.L.P., LDL

INTRODUCTION

There is an increasing incidence of sudden hearing loss (SHL) in Western countries. At present, 20 out of 100.000 subjects are being affected per year. The pathogenesis has not been elucidated as yet ¹. Numerous divergent concepts are applied in the treatment of SHL, reaching from psychotherapy to surgical closure of suspected perilymphatic fistulas, but the beneficial effect for the recovery of hearing is uncertain ². However it is likely that different pathomechanisms as inflammation, autoimmune processes or viral infections can lead to SHL. In the majority of cases, the disorder may be due to an impaired perfusion of the cochlea. Blood viscosity, microthrombosis, free radical induced damage of endothelium, and an endothelial dysfunction with impaired vasomotion as main factors affecting the microcirculation are discussed ^{3,4}. Hypercholesterolaemia, hyperfibrinogenaemia, and an increased platelet aggregation are frequently observed in SHL - patients ^{5,6}. High plasma fibrinogen levels increases erythrocyte-aggregation, blood viscosity and the risk of microthrombosis in the cochlea. High blood cholesterol levels are thought to influence the nitric oxide release from the endothelium disturbing the vasomotion ⁷, which may be of particular importance as the cochlea is supplied by a small end-arteria without the possibility of shunting.

In this study, we raised the question, whether drastic lowering of plasma cholesterol and fibrinogen has an impact on hearing recovery after sudden sensorineural hearing loss. Therefore we have treated SHL - patients with an extracorporeal procedure (H.E.L.P. - apheresis) removing fibrinogen and cholesterol from the plasma and followed the impact on their auditory thresholds.

PATIENTS AND METHODS

Seven patients suffering from sudden sensorineural hearing loss or from an acute episode of chronic progredient hearing loss were included in the study. Retrocochlear damage was excluded by standard audiological testing and brainstem audiometry. Middle ear hearing loss was ruled out by tympanometry and ear microscopy. Morbus Menière, toxic sensorineural hearing loss due to otitis media

and noise induced hearing loss were also excluded. Patient data are summarized in table no. 1.

table 1

patient no.	sex / age (years)	hearing loss threshold	frequency	Start of H.E.L.P. after		cholesterol (F ₁)	LDL - C (F ₁)	HDL - C (F ₁)	Lp (a) (F ₂)	fibrinogen (F ₃)
				pretreatment*	hearing loss					
1	m / 55	54 dB	0.12 - 3 kHz	yes	10 days	216 (124)	161 (79)	40 (33)	<5 (<5)	248 (128)
2	f / 68	27 dB	0.12 - 10kHz	no	4 days	277 (140)	180 (71)	75 (62)	19 (6)	465 (133)
3	f / 63	103 dB	0.12 - 10kHz	yes	11 days	356 (87)	202 (38)	46 (39)	<5 (<5)	245 (122)
4	f / 76	52 dB	0.12 - 10kHz	no	7 days	232 (103)	155 (43)	64 (59)	<5 (<5)	323 (98)
5	m / 54	22 dB	1 - 10 kHz	no	1 day	205 (88)	143 (39)	33 (30)	6 (<5)	303 (117)
6	m / 61	24 dB	0.12 - 2 kHz	no	3 days	267 (99)	192 (44)	55 (45)	<5 (<5)	316 (97)
7	m / 32	35 dB	1 - 6 kHz	no	4 days	197 (107)	128 (56)	50 (41)	34 (18)	221 (110)

Laboratory values are expressed in mg/dl, the plasma concentrations after H.E.L.P.-apheresis are given in brackets. Factors for conversion to S.I. units: F₁ = 0.0256(nmol L⁻¹), F₂ = 10(g L⁻¹), F₃ = 29.4(μmol L⁻¹).

* pretreatment for 10 days with prednisolone (250mg reduced by 25 mg daily) and 500 ml dextrane intravenously

Audiometric testing consisted of pure tone audiometry (according to ISO standard) and the measurement of distortion products of otoacoustic emissions (ILO 92 Otodynamics, London). Audiometric measurements were performed immediately before and after H.E.L.P - apheresis, the next day and after 1 week. In order to quantify the hearing loss (dB HL), an average pure tone threshold was calculated in the frequency range affected. The improvement of the hearing loss was also expressed in percentage.

A single H.E.L.P.-apheresis was performed in all SHL - patients to remove low density lipoproteins, fibrinogen, and lipoprotein (a) from plasma. The procedure was described in detail elsewhere⁸. The apparatus used, a Plasmatec Secura[®], was provided by B. Braun (Melsungen, Germany). A total of 3 L of plasma was treated. Blood samples were obtained directly before and after the H.E.L.P.-apheresis for laboratory measurements.

Clinical chemistry and coagulation tests were measured with standard procedures. Plasma viscosity was determined in a capillary tube plasma viscometer (Fresenius, Germany) and erythrocyte aggregation was measured using the Myrenne Erythrocyte Aggregometer (Myrenne, Roetgen, Germany).

RESULTS AND CONCLUSIONS

In six of the seven patients we observed a fast improvement of the auditory thresholds within 24 hours after H.E.L.P.-apheresis (table no. 2). Already during the

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table 2

patient no.	hearing loss (dB) before / after H.E.L.P.				hearing improvement 7 days after H.E.L.P.	
	0 h	1 h	24 h	7 d	dB	%
1	54	48	31	31	23	43
2	27	32	10	10	17	63
3	103	99	77	76	26	25
4	52	59	63	52	0	0
5	29	13	7	7	22	76
6	24	27	5	5	19	79
7	35	28	21	8	27	77

apheresis all of them reported a relief of the pressure in the ear. In four of the seven patients, the auditory thresholds returned to normal values. Even 11 days after the onset of the hearing loss, an improvement was observed within 24 hours. Low, high, and pancochlear frequency loss of hearing responded similar to the H.E.L.P.-apheresis. This beneficial effect was not related to the extent of hypercholesterolaemia or hyperfibrinogenaemia. Follow up of the patients for one month revealed a persistent improvement of the auditory thresholds.

The mean plasma LDL-cholesterol and fibrinogen levels before treatment were 250 ± 52 mg/dl and 344 ± 85 mg/dl respectively. LDL-cholesterol and fibrinogen were drastically lowered by the H.E.L.P.-apheresis to levels of 110 ± 19 mg/dl and 115 ± 17 mg/dl respectively. The removal of this plasma factors was associated with a significant decrease in plasma viscosity (1.25 ± 0.1 mPa/s to 1.0 ± 0.03 mPa/s) and erythrocyte aggregation (28 ± 3 arbitrary units to 8 ± 3 arbitrary units).

In this study, we show for the first time that in SHL - patients an acute and drastic decrease of plasma-LDL and fibrinogen with a single extracorporeal H.E.L.P. - apheresis was almost immediately followed by an improvement of auditory thresholds. The H.E.L.P. treatment was excellently tolerated, no adverse effects were observed.

The mechanisms responsible for the beneficial effect of H.E.L.P.-apheresis in SHL - patients are not clear. One explanation could be the improvement of microcirculation by the impact of H.E.L.P.-apheresis on hemorheological factors ⁹. Another factor could be the effect of lowering plasma cholesterol on the endothelial dysfunction. Recently it has been described that elevated plasma cholesterol concentrations can suppress the release of nitric oxide from the vascular endothelium in vivo, thus impairing the capability of arteries to autoregulate as an answer to local mediators ⁷. As the supplying vessel of the cochlea is a functional endartery, autoregulation is essential to maintain perfusion ³. Therefore, it can be speculated that the drastic reduction of plasma cholesterol may have a positive impact on the vasomotion of endarteries, thus improving the perfusion and function of the cochlea.

Six of our patients treated with H.E.L.P.-apheresis showed a distinct improvement of the hearing threshold. The immediate hearing improvement within less than 24 hours is extraordinary. The close time-connection of hearing improvement and the H.E.L.P.-apheresis is a strong argument that the extracorporeal removal of plasma low density lipoproteins and fibrinogen is a clinically useful tool to treat SHL. We have now started a study to identify the possible mechanisms after H.E.L.P.-apheresis, which may be responsible for this beneficial effect on the auditory thresholds.

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