A Randomized, Single-blind, Parallel group Pilot Study on the Use of NARL-Sonic Treatment to Induce Fat Mobilization and Visceral Fat Reduction

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Abstract

Objective: To assess the possible beneficial effect of NARL (NorAdrenaline ReLease)-sonic treatment to induce fat mobilization and visceral fat reduction, and to determine its safety.

Method: 20 healthy subjects with central obesity were recruited. They were randomized to group 1 received NARL sonic treatment for a total of 16 weeks while group 2 received sham treatment for the first 8 weeks, followed by active treatment for the subsequent 8 weeks. Anthropometric parameters and ultrasound examination of the abdomen to measure the thickness of subcutaneous fat (SUB), pre-peritoneal fat (PRE) and mesenteric fat (MES) were performed at week 0, 8 and 16.

Results: At baseline, group 1 was less obese with lower BMI (26.7 vs 29.7 kg/m2, p=0.03) and lower WC (91 vs 99cm, p=0.031). The subcutaneous fat thickness (SUB), pre-peritoneal fat thickness (PRE) and were not significantly different between both groups at baseline, though mesenteric fat thickness (MES) was lower in group 1. At week 8, body weight (BW) of group1 showed significant drop compared with baseline (67.6 vs 66.7kg p=0.02) while WC showed no statistically significant change. Both BW and WC in group 2 were not significantly different from baseline. There were significant decrease in MES at both week 8 (0.93 vs 0.76 cm, p=0.001) and week 16 (0.93 vs 0.75 cm, p=0.003) in group 1, while there was only significant drop in MES in group 2 (1.10 vs 1.0cm, p =0.041) at week 16. There was significant increase in SUB at week 16 in group 1 (2.6 vs 3.2cm, p=0.005), while there was no change in SUB at week 16 in group 2.

Conclusion: There was significant change in BW and WC in first 8 week of NARL treatment, accompanied by decrease in mesenteric fat and increase in subcutaneous fat, which suggested possible redistribution of fat.

Introduction

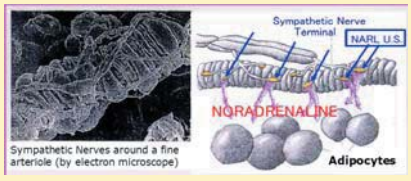
It is believed that visceral adiposity plays an important role in the pathogenesis of insulin resistance and the clustering of metabolic abnormalities seen in the metabolic syndrome. Measurement of mesenteric fat thickness provides an accurate assessment of visceral adiposity, which correlates strongly with visceral fat area measured by MRI, and has stronger association with metabolic indices.

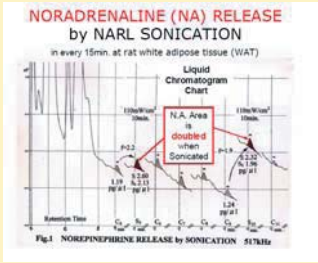
Visceral adipocytes and subcutaneous adipoctyes differ in their lipolytic responses, as outlined below:

	Omental Adipocytes	Mesenteric Adipocytes	Subcutaneous Adipocytes
Lipolytic response to noradrenaline	↑	↑	→
β_3 adrenoceptor action	↑	↑	→
α_2 adrenoceptor action	↓	↓	→

Harmelen et al, Int J Obesity 1997; 21: 972-9

Apart from exercise, there are limited strategies to selectively mobilize visceral fat. Noradrenaline Release (NARL)-US is a specialized ultra-sound technique used at frequency 517 kHz, with intensity weak at around 110~5 mW/cm^2. It can stimulate local release of noradrenaline from sympathetic nerve terminals, independent from central control. In experimental studies, noradrenaline concentration around site of sonication has been noted to increase within 10mins of sonication, and raised free fatty acids (FFA) levels noted, presumably from lipolysis of fat to glycerol and FFA. FFA generated and can be utilized by gentle exercise (50-60kcal) to avoid re-accumulation as fat





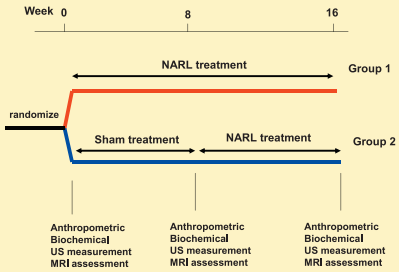
In a preliminary study of 24 healthy subjects (19F, 5 M), mean age 36.6 (22-58), mean BMI 22.2 (18.3-29.9), use of NARL-US was associated with mean % weight loss of 2.5% during study period, with mean ↓ 9.0% in subcutaneous fat area (P<0.001) and ↓11.7% in visceral fat area on CT (P=0.01).

Objectives

1. Assess the possible beneficial effect of NARL-sonic treatment to induce fat mobilization and visceral fat reduction
2. Evaluate the safety and tolerability of applying NARL ultrasound on body surfaces

Methods

Twenty subjects were recruited. All subjects had central obesity with waist circumference: Male ≥90 cm ; Female≥80cm. Written Informed consent was obtained from all subjects.



Results

Table 1 Comparison of baseline parameters

Subject characteristics	Group 1 NARLx 16w N=10	Group 2 NARLx 8w N=10	*P* value
Weight (kg)	67.6 ±9.8	80.7 ±14.5	0.029
BMI (kg/m^2)	26.7 ± 2.0	29.7 ± 3.5	0.03
Waist circumference (cm)	90.7 ± 7.7	99.4 ± 8.9	0.031
Percentage body fat (bioimpedance)	33.1 ± 4.2	36.1 ± 7.1	0.263
Systolic BP (mmHg)	123 ± 13	129 ± 22	0.43
Diastolic BP (mmHg)	75± 11	76 ±26	0.96
Total cholesterol (mmol/l)	4.8 ± 0.9	5.7 ±1.4	0.14
LDL cholesterol (mmol/l)	2.6 ± 0.8	3.3 ± 1.3	0.20
HDL cholesterol (mmol/l)	1.63± 0.5	1.56 ± 0.4	0.76
TG (mmol/l)	1.31 ± 0.6	1.98 ± 1.2	0.13
Fasting glucose (mmol/l)	5.10 ± 0.6	6.01 ± 1.2	0.06
Fasting insulin (pmol/l)	47.4 ± 29.5	65.4 ± 26.5	0.17
US pre-peritoneal fat (cm)	1.52 ± 0.45	1.76 ± 0.36	0.20
US subcutaneous fat (cm)	2.73 ± 0.93	3.01 ± 1.18	0.56
US mesenteric fat (cm)	0.93 ± 0.14	1.11 ± 0.18	0.021
MRI total fat area (cm^2)	47031 ±22469	47732 ±13837	0.93
MRI visceral fat area (cm^2)	13909 ±6002	17017 ±6910	0.30
MRI subcutaneous fat area (cm^2)	33122 ±20905	30714 ±11614	0.75

At baseline, group 1 were less obese with lower BMI, and lower waist circumference. The subcutaneous fat thickness and pre-peritoneal fat thickness was not significantly different between the 2 groups, though group1 also had lower mesenteric fat thickness. Visceral fat area as measured by MRI was not significantly lower in group 1.

The procedure was well-tolerated with no reported adverse effects. At week 8, body weight (BW) of group 1 showed significant drop compared to baseline (67.6kg vs 66.7kg, p=0.020) while there was no significant change in WC. Both BW and WC did not change significantly from baseline.

There was significant decrease in mesenteric fat thickness at both week 8 (0.93 vs 0.76cm, p=0.001) and week 16 (0.93 vs 0.75cm, p=0.003) in group 1. For group 2, there was no significant change in mesenteric fat thickness at week 8 (after sham intervention), while there was only significant drop in mesenteric fat thickness in group 2 at 16 weeks (1.10 vs 1.00 cm, p=0.041). There was significant increase in subcutaneous fat thickness measured by US at week 16 in group 1 (2.6 vs 3.2cm, p=0.005). There was no change in subcutaneous fat thickess in group 2.

There was no significant change in visceral fat area as measured by MRI for either treatment group during the study period. There was no significant change in metabolic parameters during the study period in either treatment group.

Table 2. Correlation coefficients of mesenteric fat thickness with different parameters at baseline

	BW	WC	Insulin	TG	MES	MRI total fat	MRI visceral fat
BW		0.911**	0.49*	0.542*	0.69**	0.56*	0.63 **
WC	0.911**		0.48*	0.40	0.71**	0.64**	0.52*
Insulin	0.49*	0.48*		0.15	0.29	0.29	0.41
TG	0.542*	0.40	0.15		0.38	0.15	0.60**
MES	0.69**	0.71**	0.29	0.38		0.33	0.57**
MRI total fat	0.56*	0.64**	0.29	0.15	0.33		0.42
MRI visceral fat	0.63 **	0.52*	0.41	0.60**	0.57**	0.42	

**p<0.01,*p<0.05

Baseline measurement of mesenteric fat thickness is highly correlated with waist circumference, body weight and MRI Measurement of visceral fat.

Conclusions

There was significant change in BW and WC in first 8 week of NARL treatment. NARL treatment was well-tolerated, and preliminary data suggested possible reduction in visceral fat as measured by mesenteric fat thickness. NARL treatment was associated with decrease in mesenteric fat thickness and increase in subcutaneous fat, suggesting possible redistribution of fat. Further studies on the metabolic profile and adipokines following NARL treatment are warranted.

Acknowledgements

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