

Circulating levels of Eotaxin-1, -2, and -3 chemokines in morbid obesity and 1 year follow up after bariatric surgery

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Background: Chemokines as one of the important mediators in immune cell infiltration have been hypothesized to be involved in macrophage infiltration into adipose tissue in obesity and might therefore play an important role in the development of obesity-related disorders like type 2 diabetes. Eotaxins (eosinophil chemotactic proteins) namely Eotaxin1 (CCL11), Eotaxin2 (CCL24), and Eotaxin3 (CCL26) belong to CC chemokine family, in addition to their important role in asthma, recent reports showed their association to obesity. However, the role of these chemokines is poorly understood.

Aim: Our aim was to study any possible kinetic change and association between circulatory level of Eotaxins (Eotaxin1, Eotaxin2, and Eotaxin3), obesity and type 2 diabetes before and after Laparoscopic Sleeve Gastrectomy (LSG).

Method: 38 morbidly obese participants (16 diabetic and 22 non-diabetic) with a BMI \geq 40 kg/m² underwent LSG, while 32 normal weight subjects (18 diabetic and 14 non-diabetic) with a BMI \leq 25 kg/m² were recruited as controls. We compared the basal levels of circulatory Eotaxins (pg/mL) in morbid obese participants before LSG to the basal levels in normal weight subjects. The correlation between levels of these chemokines and other clinical and biochemical parameters was also studied. Some of the morbidly obese participants were further examined at the time points of 7, 15, 30, 60, 90,180 and 360 days postoperatively.

Fig 1: At baseline, levels of Eotaxin1 was significantly (*p < 0.0001) higher in normal weight diabetic subjects (n=18, 120.1 ± 8.78) compared to other groups, including morbid obese-diabetics (n=16, 70.63 ± 6.17), morbid obese non-diabetics (n=22, 65.47±6.23) and normal weight non-diabetics (n=14, 66.52±5.17). Eotaxin2 levels showed no significant difference between all study groups. However, Eotaxin3 was significantly higher (**p < 0.0003) in morbid obese participants (diabetics; 48.42±4.80, and non-diabetics; 48.93±4.06) compared to normal weight participants (diabetics; 27.47±3.94 and nondiabetics; 20.42 ± 1.93).

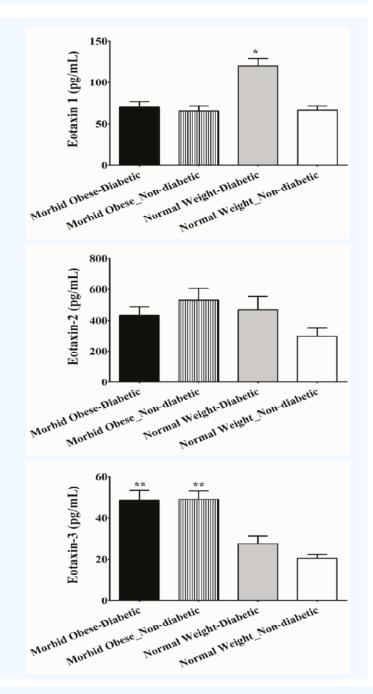
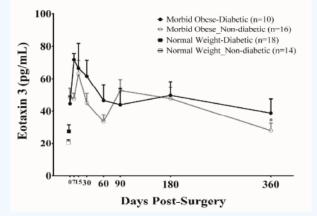
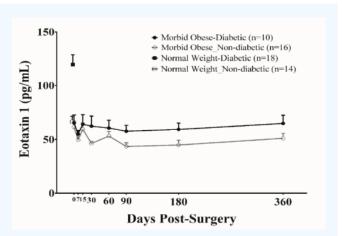
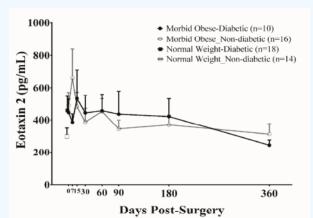


Fig 2: After one year of LSG, the level of Eotaxin3 was significantly (p < 0.02) reduced in morbid obese non-diabetic (29.42 ± 5.71) , reaching a level that is comparable to normal weight participants. A similar pattern of reduction, but no significance was observed in the level of Eoatxin3 (37.94 ± 10.87) in morbid obese diabetic participants after one year of LSG.







Morbid Obese Subjects			Body Weight	BMI	Abd. Cir.	Waist/Hip ratio	hsCRP	TNFα	Fasting Glu	Fasting Ins	Fasting cpep	HbA1c	Leptin	Adiponectin
	Eotaxin1	r	.219	.135	.158	.233	314	.303	.095	.061	126	.014	.005	164
		p	.187	.419	.344	.160	.055	.065	.572	.715	.450	.934	.977	.324
	Eotaxin2	r	.060	.023	.145	063	331*	.020	257	169	224	296	166	.081
		p	.721	.893	.384	.705	.042	.906	.119	.309	.176	.072	.319	.629
	Eotaxin3	r	.255	.146	.244	.086	172	.208	173	143	.005	193	.092	160
		p	.122	.382	.140	.607	.302	.210	.299	.391	.978	.245	.582	.338
Weight Subjects			Body Weight	BMI	Abd. Cir.	Waist/Hip ratio	hsCRP	TNFα	Fasting Glu	Fasting Ins	Fasting cpep	HbA1c	Leptin	Adiponectin
	Eotaxin1	r	-0.02	0.01	0.31	0.19	0.10	.56**	.591**	.249	013	.63**	-0.03	-0.27
		p	0.93	0.94	0.09	0.27	0.59	<0.0008	<0.0004	.170	.943	< 0.0001	0.88	0.14
	Eotaxin2	r	.367*	0.22	-0.03	0.16	-0.02	0.23	0.23	.084	.051	0.05	0.14	0.02
		p	0.04	0.23	0.87	0.39	0.93	0.21	0.20	.648	.780	0.79	0.45	0.92
	Eotaxin3	r	0.11	0.10	-0.07	0.07	0.08	0.19	0.13	.108	.062	0.14	0.19	-0.06
		p	0.56	0.58	0.69	0.69	0.65	0.29	0.47	.556	.736	0.45	0.30	0.76
			Body Weight	BMI	Abd. Cir.	Waist/Hip ratio	hsCRP	TNFα	Fasting Glu	Fasting Ins	_	HbA1c	Leptin	Adiponectin
		r	Weight		Cir.	ratio			Glu	Ins	срер		^	
	Eotaxin1		Weight629**	56**	Cir.	ratio 0.09	50**	-0.01	Glu -0.07	Ins 539**	cpep621**	0.12	43**	0.05
Diabetic Subjects		r p	Weight		Cir.	ratio			Glu	Ins	срер	0.12 0.50	^	0.05 0.77
Diabetic Subjects		p	Weight629** <0.0001	56** <0.0006	Cir50** <0.002	0.09 0.61	50** <0.002	-0.01 0.96	Glu -0.07 0.70	Ins 539** .001	cpep 621** .000	0.12	43** <0.01	0.05
Diabetic Subjects	Eotaxin2	p r	Weight 629** <0.0001 0.03	56** <0.0006 -0.01	Cir50** <0.002 -0.02	0.09 0.61 -0.04	50** <0.002 -0.23	-0.01 0.96 0.03	Glu -0.07 0.70 -0.06	Ins 539** .001 .054	cpep621** .000 .039	0.12 0.50 -0.25	43** <0.01 -0.04	0.05 0.77 0.08
Diabetic Subjects		p r p	Weight 629** <0.0001 0.03 0.88	56** <0.0006 -0.01 0.98	Cir50** <0.002 -0.02 0.92	ratio 0.09 0.61 -0.04 0.82	50** <0.002 -0.23 0.19	-0.01 0.96 0.03 0.88	Glu -0.07 0.70 -0.06 0.73	Ins 539** .001 .054 .763	cpep621** .000 .039 .825	0.12 0.50 -0.25 0.16	43** <0.01 -0.04 0.82	0.05 0.77 0.08 0.65
Diabetic Subjects	Eotaxin2	p r p r	Weight629** <0.0001 0.03 0.88 .56**	56** <0.0006 -0.01 0.98 .61**	Cir50** <0.002 -0.02 0.92 .60**	ratio 0.09 0.61 -0.04 0.82 -0.08	50** <0.002 -0.23 0.19 .57**	-0.01 0.96 0.03 0.88 .469**	Glu -0.07 0.70 -0.06 0.73 0.12	Ins539** .001 .054 .763 .517** .002	cpep621** .000 .039 .825 .568**	0.12 0.50 -0.25 0.16 -0.02 0.93	43** <0.01 -0.04 0.82 .57** <0.0004	0.05 0.77 0.08 0.65 -0.07
Diabetic Subjects	Eotaxin2 Eotaxin3	p r p r	Weight629** <0.0001 0.03 0.88 .56** <0.0005	56** <0.0006 -0.01 0.98 .61** <0.0001	Cir50** <0.002 -0.02 0.92 .60** <0.0001 Abd.	ratio 0.09 0.61 -0.04 0.82 -0.08 0.64 Waist/Hip	50** <0.002 -0.23 0.19 .57** <0.0004	-0.01 0.96 0.03 0.88 .469** <0.004	Glu -0.07 0.70 -0.06 0.73 0.12 0.51 Fasting	Ins539** .001 .054 .763 .517** .002 Fasting	cpep621** .000 .039 .825 .568** .000 Fasting	0.12 0.50 -0.25 0.16 -0.02 0.93	43** <0.01 -0.04 0.82 .57** <0.0004	0.05 0.77 0.08 0.65 -0.07
Diabetic Subjects	Eotaxin2 Eotaxin3 Eotaxin1	p r p r	Weight629** <0.0001 0.03 0.88 .56** <0.0005 Body Weight	56** <0.0006 -0.01 0.98 .61** <0.0001	Cir50** <0.002 -0.02 0.92 .60** <0.0001 Abd. Cir.	ratio 0.09 0.61 -0.04 0.82 -0.08 0.64 Waist/Hip ratio	50** <0.002 -0.23 0.19 .57** <0.0004 hsCRP	-0.01 0.96 0.03 0.88 .469** <0.004 TNFα	Glu -0.07 0.70 -0.06 0.73 0.12 0.51 Fasting Glu	Ins539** .001 .054 .763 .517** .002 Fasting Ins	cpep621** .000 .039 .825 .568** .000 Fasting cpep	0.12 0.50 -0.25 0.16 -0.02 0.93	43** <0.01 -0.04 0.82 .57** <0.0004	0.05 0.77 0.08 0.65 -0.07 0.71
Diabetic Subjects Non- diabetic	Eotaxin2 Eotaxin3 Eotaxin1	p r p r	Weight 629** <0.0001 0.03 0.88 .56** <0.0005 Body Weight .056	56** <0.0006 -0.01 0.98 .61** <0.0001 BMI089	Cir50** <0.002 -0.02 0.92 .60** <0.0001 Abd. Cir043	ratio 0.09 0.61 -0.04 0.82 -0.08 0.64 Waist/Hip ratio .071	50** <0.002 -0.23 0.19 .57** <0.0004 hsCRP304	-0.01 0.96 0.03 0.88 .469*** <0.004 TNFα	Glu -0.07 0.70 -0.06 0.73 0.12 0.51 Fasting Glu .002	Ins539** .001 .054 .763 .517** .002 Fasting Ins053	cpep621** .000 .039 .825 .568** .000 Fasting cpep065	0.12 0.50 -0.25 0.16 -0.02 0.93 HbA1c	43** <0.01 -0.04 0.82 .57** <0.0004 Leptin 088	0.05 0.77 0.08 0.65 -0.07 0.71 Adiponectin
Diabetic Subjects Non- diabetic	Eotaxin2 Eotaxin3 Eotaxin1	p r p r p	Weight629** <0.0001 0.03 0.88 .56** <0.0005 Body Weight .056 .745	56** <0.0006 -0.01 0.98 .61** <0.0001 BMI089	Cir50** <0.002 -0.02 0.92 .60** <0.0001 Abd. Cir043 .806	ratio 0.09 0.61 -0.04 0.82 -0.08 0.64 Waist/Hip ratio .071 .682	50** <0.002 -0.23 0.19 .57** <0.0004 hsCRP304 .072	-0.01 0.96 0.03 0.88 .469** <0.004 TNFα .216 .205	Glu -0.07 0.70 -0.06 0.73 0.12 0.51 Fasting Glu .002 .990	Ins539** .001 .054 .763 .517** .002 Fasting Ins053 .758	cpep621** .000 .039 .825 .568** .000 Fasting cpep065 .707	0.12 0.50 -0.25 0.16 -0.02 0.93 HbA1c 204 .232	43** <0.01 -0.04 0.82 .57** <0.0004 Leptin088 .612	0.05 0.77 0.08 0.65 -0.07 0.71 Adiponectin .111 .520
Non- diabetic Subjects	Eotaxin2 Eotaxin3 Eotaxin1	p r p r p	Weight629** <0.0001 0.03 0.88 .56** <0.0005 Body Weight .056 .745 .376*	56** <0.0006 -0.01 0.98 .61** <0.0001 BMI089 .605 .387*	Cir50** <0.002 -0.02 0.92 .60** <0.0001 Abd. Cir043 .806 .337*	ratio 0.09 0.61 -0.04 0.82 -0.08 0.64 Waist/Hip ratio 0.71 0.682 0.190	50** <0.002 -0.23 0.19 .57** <0.0004 hsCRP304 .072 .120	-0.01 0.96 0.03 0.88 .469** <0.004 TNFα .216 .205 .288	Glu -0.07 0.70 -0.06 0.73 0.12 0.51 Fasting Glu .002 .990147	Ins539** .001 .054 .763 .517** .002 Fasting Ins053 .758	cpep621** .000 .039 .825 .568** .000 Fasting cpep065 .707 .202	0.12 0.50 -0.25 0.16 -0.02 0.93 HbA1c -204 .232 205	43** <0.01 -0.04 0.82 .57** <0.0004 Leptin088 .612 .201	0.05 0.77 0.08 0.65 -0.07 0.71 Adiponectin .111 .520 022

Table 1: Spearman correlation analysis of baseline levels of Eotaxin chemokines.

Conclusion: We observed an association between the circulatory levels of Eotaxin chemokines (inverse association of Eotaxin-1 and direct association of Eotaxin-3), with the level of obesity and markers of low grade chronic inflammation before and after LSG.

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References:

- 1. Dalmas, E, Rouault, C, Abdennour, M, Rovere, C, Rizkalla, S, Bar-Hen, A, Nahon, JL, Bouillot, JL, Guerre-Millo, M, Clement, K, Poitou, C: Variations in circulating inflammatory factors are related to changes in calorie and carbohydrate intakes early in the course of surgery-induced weight reduction. *Am. J. Clin. Nutr.* 94:450-458, 2011
- 2. Gentili, A, Zaibi, MS, Alomar, SY, De Vuono, S, Ricci, MA, Alaeddin, A, Siepi, D, Boni, M, Vaudo, G, Trayhurn, P, Lupattelli, G: Circulating Levels of the Adipokines Monocyte Chemotactic Protein-4 (MCP-4), Macrophage Inflammatory Protein-1beta (MIP-1beta), and Eotaxin-3 in Severe Obesity and Following Bariatric Surgery. *Horm. Metab Res.* 48:847-853, 2016