The short-term effect of surgical and pharmacological intervention in obesity caused by MC4R deficiency: a single centre experience

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Introduction

Melanocortin-4-receptor (MC4R) deficiency is the commonest of the rare monogenic forms of obesity. Bariatric surgery (BS) is the most efficacious treatment modality in the more "common" polygenic obesity. Effect of surgical and drug treatment in obesity due to MC4R deficiency is not well-established.

Aim

We aimed to explore the effects of BS and drug treatment among the confirmed cases of obesity due to MC4R deficiency and compare the short term weight loss was control group who were tested negative for MC4R mutations.

Methods

Based on a strong family history and phenotypic characteristics, genetic screening for MC4R mutation(s) was conducted in 27 morbidly obese ICLDC patients. Data on pharmacotherapy and surgical treatment, including treatment dates, and duration was retrieved from electronic patient records. Weight loss percentage at a median of 6 months post-intervention was compared between age- and sex-matched MC4R-deficient and wild-type controls.

Results

Of the 27 patients, 8 were confirmed to have MC4R mutations. Three specific mutations were identified: Val103Ile, Ile170Val and Thr162Ile (most common). Six MC4R deficient patients and eight MC4R normal patients underwent sleeve gastrectomy. Weight loss at median 6 months post bariatric surgery was not significantly different between MC4R deficient and MC4R normal patients (P=0.65). However the weight loss post BS in MC4R deficient patients showed variation depending on the type of mutation [17.99(6.1 –22.54) %]. Homozygous Thr162Ile did not benefit from BS in terms of weight loss compared to their age and sex matched controls. Heterozygous Thr162Ile andIle170Val benefited similarly from BS compared to the controls. Response to Liraglutide treatment was comparable in MC4R Thr162Ile heterozygous patient and controls.

Conclusion

Observations from our study suggest that efficacy of surgical and medical intervention in MC4R deficient patients my depend on the mutation type and zygosity. Thr162Ile homozygous

individuals might require multiple surgery or continued pharmacological intervention to maintain weight loss over longer period of time.

Table 1: Comparison of weight loss following surgical and pharmacological interventions between MCR4 deficient and age and sex- matched MC4R normal individuals.

Type of intervention	Age	Sex	Mutation	Zygosity	Weight loss %	
					MC4R deficient	MC4R Wild type
Sleeve gastrectomy	33.5/32.2	F	Thr162Ile	Heterozygous	19.05	15.24
	23/18	M	Ile170Val	Homozygous	22.54	29.9
	18/17.8	M	Thr162Ile	Homozygous	8.08	35.27
	14/18	F	Thr162Ile	Homozygous	6.91	23.75
	24.5/18	F	Thr162Ile	Heterozygous	20.81	23.75
Liraglutide	22.9/18.2	F	Thr162Ile	Heterozygous	4.89	5.61
Orlistat	20.5/19.5	M	Ile170Val	Homozygous	-0.91	10.29
	12/14.5	M	Thr162Ile	Homozygous	-4.62	-4.1