Role of Metformin in the treatment of Hypothalamic obesity

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Background:

- A syndrome of rapid, unrelenting weight gain is often observed in patients with structural lesions of the hypothalamus.eg-Craniopharyngioma (Figure-1)
- Disruption of homeostatic functioning of the hypothalamic centres results in hyperphagia, autonomic imbalance, reduction of energy expenditure, and hyperinsulinemia[1].
- Hypothalamic obesity syndrome (HOS) is often refractory to standard dietary and lifestyle Interventions[2].
- Metformin induces anorectic effects via an increase in the central sensitivity to leptin.This provides a rationale for novel therapeutic approaches associating leptin and metformin in the treatment of HOS[3].

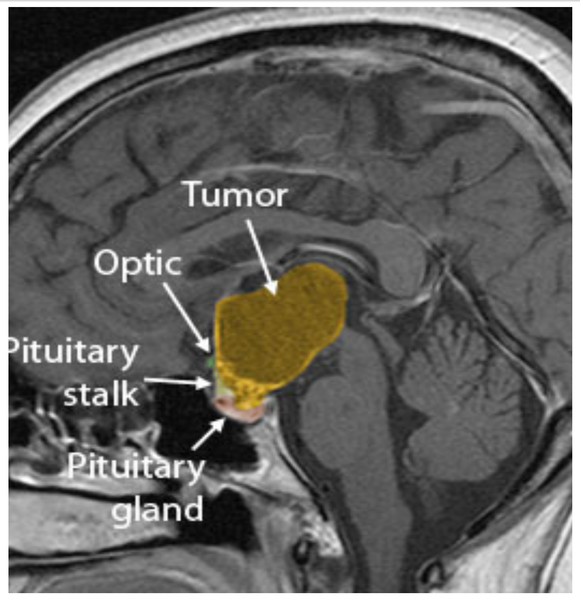


Fig 1-Showing large cystic craniopharyngioma

Objective:

Describe changes of BMI in HOS patients with perichismatic tumours treated with metformin.

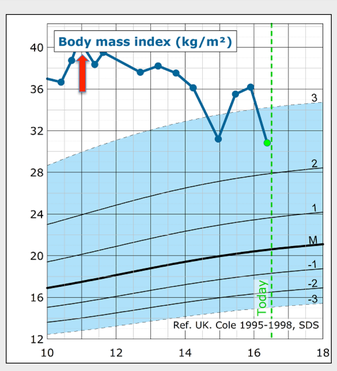
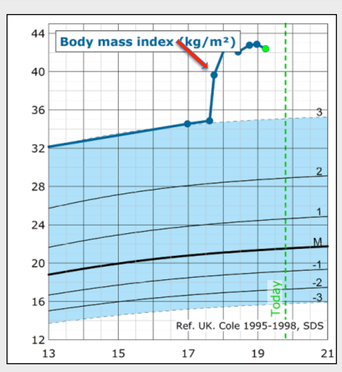
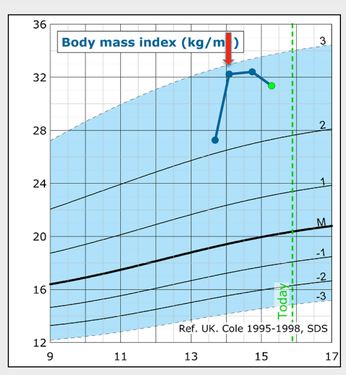
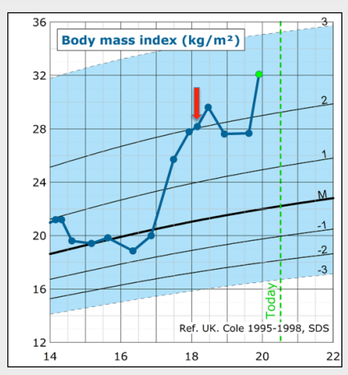
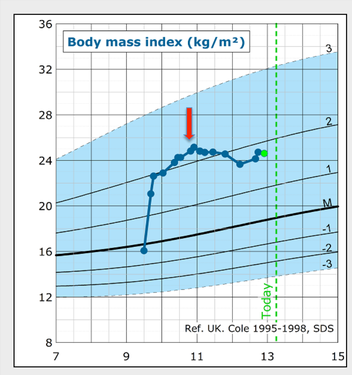
Method:

The medical records of patients with HOS due to perichiasmatic tumours at a single centre, treated with metformin were examined to establish the age at diagnosis of the primary tumour, the body mass index (BMI) at diagnosis, at commencement of metformin and at the most recent assessment. BMI was converted to BMI standard deviation score (SDS) using WHO ref data 2006-2007.

Results:

There were 5 patients (4 females), median age of 10.7 years at diagnosis of the hypothalamic lesion (range 5.7-13.8). The median period of follow up following commencement of metformin was 1.8 years (range 1.3-5.4). Patient characteristics, BMI-SDS at diagnosis, ages at commencement of treatment with metformin and at the most recent assessment are shown below (Table-1).

Table 1- Patient characteristics and metformin treatment outcome

Patient characteristics/Sex		Patient 1/F	Patient 2/F	Patient 3/F	Patient 4/M	Patient 5/F
Hypothalamic disorder		NF1 / Pilomyxoid astrocytoma	Hamartoma	Hamartoma	Cranio-pharyngioma	Cranio-pharyngioma
Primary treatment		Cranial irradiation	Partial resection	Resection	Partial Resection + Cranial irradiation	Resection
BMI-SDS (Age in yrs)	At diagnosis	+0.96 (5.7)	+3.06 (10.7)	+2.19 (13.8)	+1.69 (12.5)	-0.29 (9.5)
	Commencement of metformin	+3.2 (11.0)	+3.55 (17.8)	+2.91 (14.0)	+2.02 (18.1)	+2.22 (10.9)
	Most recent assessment	+2.52 (16.4)	+3.78 (19.2)	+2.68 (15.3)	+2.57 (19.9)	+1.78 (12.9)
BMI-SDS growth chart (Red arrow indicates time of commencement of metformin)						

Conclusion:

- Metformin stabilised BMI SDS in these patients with HOS, but caution is advised because of the size of the population and possible selection bias.
- A randomised control trial should now be considered to rigorously examine the effectiveness of metformin in the management of this most challenging problem of HOS.

References:

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3) Metabolism: Clinical & Experimental, 03 2011, vol./is. 60/3(327-34), 0026-0495;1532- 8600 (2011 Mar)