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 hyperinsulinemia1.
- Hypothalamic obesity syndrome (HOS) is often refractory to standard dietary and lifestyle interventions2.
- 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 HOS3.

Objective:
Describe changes of BMI in HOS patients with perichiasmatic 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

<table>
<thead>
<tr>
<th>Patient characteristics/Sex</th>
<th>Patient 1/F</th>
<th>Patient 2/F</th>
<th>Patient 3/F</th>
<th>Patient 4/M</th>
<th>Patient 5/F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothalamic disorder</td>
<td>NF1 / Pilomyxoid astrocytoma</td>
<td>Hamartoma</td>
<td>Hamartoma</td>
<td>Craniopharyngioma</td>
<td>Craniopharyngioma</td>
</tr>
<tr>
<td>Primary treatment</td>
<td>Cranial irradiation</td>
<td>Partial resection</td>
<td>Resection</td>
<td>Partial Resection + Cranial irradiation</td>
<td>Resection</td>
</tr>
<tr>
<td>BMI-SDS (Age in yrs)</td>
<td>At diagnosis</td>
<td>+0.96 (5.7)</td>
<td>+3.06 (10.7)</td>
<td>+2.19 (13.8)</td>
<td>+1.69 (12.5)</td>
</tr>
<tr>
<td></td>
<td>Commencement of metformin</td>
<td>+3.2 (11.0)</td>
<td>+3.55 (17.8)</td>
<td>+2.91 (14.0)</td>
<td>+2.02 (18.1)</td>
</tr>
<tr>
<td></td>
<td>Most recent assessment</td>
<td>+2.52 (16.4)</td>
<td>+3.78 (19.2)</td>
<td>+2.68 (15.3)</td>
<td>+2.57 (19.9)</td>
</tr>
</tbody>
</table>

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