

Ferdinando Maggioni  
Silvia Ruffatti  
Filippo Dainese  
Federico Mainardi  
Giorgio Zanchin

## Weight variations in the prophylactic therapy of primary headaches: 6-month follow-up

Published online: 20 July 2005

F. Maggioni (✉) • S. Ruffatti • F. Dainese  
G. Zanchin  
Headache Centre,  
Department of Neurosciences,  
University of Padua,  
Via Giustiniani 3, I-35128 Padua, Italy  
Tel.: +39-049-8213600  
Fax: +39-049-8751770  
e-mail: [ferdinando.maggioni@unipd.it](mailto:ferdinando.maggioni@unipd.it)

F. Mainardi  
Headache Centre,  
Neurologic Division,  
Hospital of Venice, Venice, Italy

**Abstract** We conducted a study on 367 patients (86% female, 14% male; mean age  $37\pm 15$  years) suffering from migraine with and without aura and chronic tension-type headache to evaluate the incidence of weight gain, an undesirable side effect observed during prophylactic therapy in primary headaches. Patients treated with amitriptyline (20 and 40 mg), pizotifen (1 mg), propranolol (80–160 mg), atenolol (50–100 mg), verapamil (160–240 mg), valproate (600 mg) and gabapentin (900–1200 mg) were evaluated after a period of 3 and 6 months. In particular, 89 patients were assessed (78% female, 22% male) at 6 months, of whom 10 were in treatment with amitriptyline 20 mg, 19 with amitriptyline 40 mg, 7 with pizotifen (1 mg), 13 with propranolol (80–160 mg), 4 with verapamil (160 mg), 10 with valproate (600 mg), 15 with atenolol (50 mg) and 11 with gabapentin (900–1200 mg). The control group consisted of 97 patients with migraine (79% female, 21% male; mean age  $35\pm 16$

years) without indication for prophylactic therapy. Weight variations  $\geq 1$  kg were considered. After 6 months of therapy, the percentage of patients with weight gain was 86% with pizotifen (6/7; mean weight increase  $4.4\pm 2.5$  kg), 60% with amitriptyline 20 mg (6/10;  $3.1\pm 1.6$ ), 47% with amitriptyline 40 mg (9/19;  $5.4\pm 2.7$ ), 25% with valproate 600 mg (2/8,  $3.0\pm 2.8$  kg), 25% with verapamil (1/4, 2.5 kg), 20% with atenolol (3/15,  $1.7\pm 0.6$  kg), 9% with gabapentin (1/11, 1.5 kg) and 8% with propranolol (1/13; 6 kg). We conclude that propranolol, gabapentin, atenolol, verapamil and valproate affect body weight in a modest percentage of patients at 6 months. A greater mean weight gain at 6 months was found in patients treated with pizotifen, amitriptyline, and, in one patient out of 13, with propranolol.

**Key words** Weight gain • Migraine • Primary headaches • Prophylactic therapy

### Introduction

Drugs used for prophylactic therapy of primary headaches can cause undesirable effects with long-term treatment;

weight gain is often observed in clinical practice, which in some cases can become a relevant problem. In the medical literature, data on this side effect lack studies specifically assessing this parameter and thus are only partial and not always concordant [1–5].

## Materials and methods

Previously, we conducted a study on 367 patients (86% female, 16% male; mean age  $37 \pm 15$  years) suffering from migraine without aura (MO), migraine with aura (MA) and chronic tension-type headache (CTTH), classified according to IHS criteria [6], to monitor weight variations during prophylactic therapy in relation to dose and type of drug, age, sex, initial body mass index (BMI) and therapeutic efficacy [7].

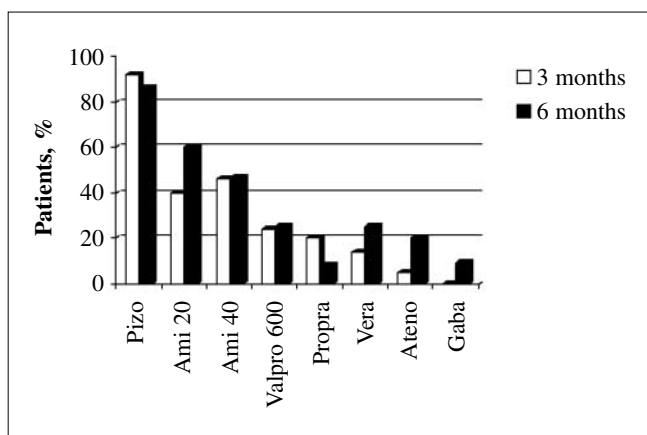
The patients were selected on the basis of indications for prophylactic therapy, BMI (between 18.5 and 30), and absence of metabolic, endocrine and psychiatric diseases, or other conditions or pathologies that could modify body weight. The control group consisted of 97 (79% female, 21% male; mean age  $35 \pm 16$  years) patients with migraine without indication for prophylactic therapy.

For 89 patients the study was extended to 6 months in monotherapy with the following drugs: amitriptyline (20 and 40 mg), pizotifen (1 mg), propranolol (80–160 mg), atenolol (50–100 mg), verapamil (160–240 mg), valproate (600 mg) and gabapentin (900–1200 mg). Weight variations  $\geq 1$  kg were considered.

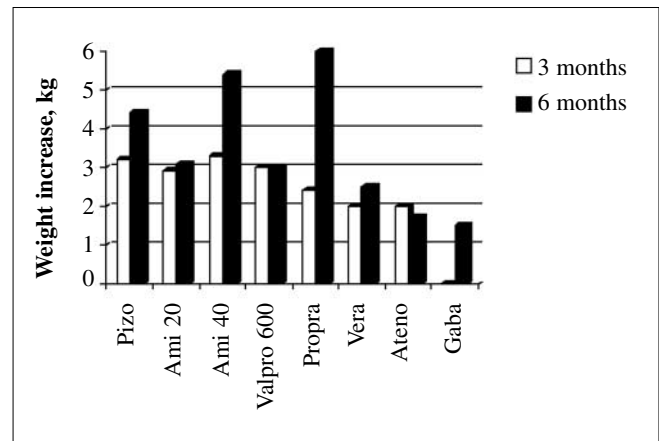
## Results

The evaluation of weight variations after 3 months of therapy revealed a greater percentage of weight gain in the groups treated with flunarizine 10 mg (92%), followed by pizotifen (65%), flunarizine 5 mg (56%) and amitriptyline (40%); these were followed by propranolol, valproate, verapamil and atenolol with percentages between 5 and 20%. No significant differences were observed related to sex, age, initial BMI and therapeutic efficacy [7].

Eighty-nine patients (78% female, 22% male) were treated for 6 months, of whom 10 were in treatment with



**Fig. 1** Percent of patients with weight increase in the different study groups at 3 and 6 months



**Fig. 2** Mean weight increase (kg) in the proportion of patients gaining weight at 3 and 6 months

amitriptyline 20 mg, 19 with amitriptyline 40 mg, 7 with pizotifen (1 mg), 13 with propranolol (80–160 mg), 4 with verapamil (160 mg), 10 with valproate (600 mg), 15 with atenolol and 11 with gabapentin. We do not yet have data on flunarizine at six months.

After 6 months of therapy, the percentage of patients with weight increase was 86% with pizotifen (6/7; mean weight increase  $4.4 \pm 2.5$  kg), 60% with amitriptyline 20 mg (6/10;  $3.1 \pm 1.6$  kg), 47% with amitriptyline 40 mg (9/19;  $5.4 \pm 2.7$  kg), 25% with verapamil (1/4, 2.5 kg), 20% with valproate 600 mg (2/10,  $3.0 \pm 2.8$  kg), 20% with atenolol (3/15,  $1.7 \pm 0.6$  kg), 9% with gabapentin (1/11, 1.5 kg) and 8% with propranolol (1/13; 6 kg) (Figs. 1 and 2). The control group recorded an average weight variation of  $< 1$  kg.

## Discussion

Most of the drugs used in the prophylactic therapy of primary headaches cause weight variations, according to the type of drug involved. In our previous study [7], after just 3 months of therapy, pizotifen, flunarizine and amitriptyline can induce weight gain in a considerable percentage of patients, varying from 90 to 40% depending on the type of drug, while propranolol, gabapentin, atenolol, verapamil and valproate seem to have a lesser impact on body weight.

This study on patients treated for 6 months shows a further weight increase compared to 3 months in the groups taking pizotifen and amitriptyline, a fact that was also observed in one patient among the 13 treated with propranolol. Valproate, verapamil, atenolol and gabapentin do not cause further weight increase during extended treatment (Figs. 1 and 2).

---

**Conclusions**

Verapamil, valproate, atenolol and gabapentin affect body weight in a modest and stable percentage of patients at 3

and 6 months. Pizotifen and amitriptyline cause an additional weight increase at 6 months, to an average of 5.4, 4.4 and 3.1 kg for amitriptyline 40 mg, pizotifen and amitriptyline 20 mg respectively.

---

**References**

1. Centonze V, Magrone D, Vino M et al (1990) Flunarizine in migraine prophylaxis: efficacy and tolerability of 5 mg and 10 mg dose levels. *Cephalalgia* 10:17–24
2. Fava M (2000) Weight gain and antidepressant. *J Clin Psychiatry* 61[Suppl 11]:37–41
3. Freitag FG, Diamond S, Diamond ML et al (2001) Divalproex in the long-term treatment of chronic daily headache. *Headache* 41:271–278
4. Jallon P, Picard F (2001) Bodyweight gain and anticonvulsants: a comparative review. *Drug Saf* 24:969–978
5. Young WB, Rozen TD (2005) Preventive treatment of migraine: effect on weight. *Cephalalgia* 25:1–11
6. Headache Classification Subcommittee of the International Headache Society (2004) *The International Classification of Headache Disorders*, 2nd edn. *Cephalalgia* 24[Suppl 1]:1–160
7. Dainese F, Mainardi F, Maggioni F, Perin C, Ruffati S, Zanchin G (2003) Bodyweight in headache prophylaxis. *Cephalalgia* 23:693–694