Aspirin Prophylaxis for Migraine with Aura: An Observational Case Series

Wendy E. Turk^a Anouk Uiterwijk^a Raphaël Pasmans^a Vera Meys^a Cenk Ayata^b
Peter J. Koehler^a

^aDepartment of Neurology, Zuyderland MC Heerlen, Heerlen, The Netherlands; ^bStroke Service and Neuroscience Intensive Care Unit, Neurovascular Research Unit, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA, USA

Dear Sir,

Migraine with aura is an independent risk factor for ischemic stroke [1]. Data indirectly suggest that migraine aura may indeed be triggered by transient ischemic events [2–6], and that aspirin may play a role, particularly in case of new onset or frequent migraine auras. Aspirin has been suggested in migraine prophylaxis [7–9]; although none of the studies found a statistically significant effect [10–14], these studies did not make a clear distinction between migraine with or without aura either. Ongoing debate prompted us to conduct a retrospective case study to observe the effect of aspirin prophylaxis on aura and headache in patients suffering from migraine with aura.

Starting in 2010, all migraine with aura patients older than 30 years of age with frequent auras (>2 per month) were started on prophylactic aspirin (80 mg daily) at our outpatient clinic, and data were collected retrospectively from patient files. In case of missing data, patients were contacted by telephone. The following data were collected: age, gender, aura frequency and type of aura, presence of and type of headache, and length of follow-up. Vascular risk factors such as history of smoking, hypertension, diabetes mellitus, cerebrovascular accident, myocardial infarction, and use of oral

contraceptives were also collected. Statistical analysis was carried out using Student paired *t* test.

Forty-nine patients, fulfilling the ICHD-II criteria for migraine with aura, were treated with aspirin prophylaxis 80 mg once daily. An MRI-scan of the brain was done in 25/49 patients, which did not reveal any relevant abnormalities. Two patients were lost to follow-up, since they discontinued aspirin within 2 weeks due to side effects. Five other patients were lost to follow-up due to the inability to contact them. No side effects were reported in the remaining patients. Patient characteristics at inclusion are presented in Table 1 (*n* = 42). The majority of patients were women, and the mean age was 57 years. The mean aura frequency was 10.2/month. The auras were visual, with additional sensory or hemiplegic phenomena in five patients. The 2 patients with hemiplegic migraine did not have a family history of hemiplegic migraine. Both were negative for FHM1, FHM2 was not tested. A total of 12 patients did not suffer from headache following auras, whereas 22 had migraine headache, and 10 reported another type of headache. The mean follow-up of the 42 included patients was 10.2 months. The frequency of migraine aura decreased in 39/42 cases

(93%), with complete disappearance of auras in 20 patients (48%; Table 2). Many of these 20 patients reported disappearance of the auras soon after starting aspirin treatment. Three patients did not experience any benefit and endured the same aura frequency. These were women aged 45, 51, and 56 years with highly frequent auras (16, 20, and 31 per month). At follow-up, the mean aura frequency had decreased from 10.2 to 2.3 times per month (*p* < 0.001). Although we did not check the number of headache days at follow-up, most of the 30 patients, who had headache following their aura, experienced a reduction.

In this retrospective observational case study, we found a remarkable suppression of aura frequency by aspirin prophylaxis in migraine with aura patients. We did not find any indication of secondary migraine auras. Brain-MR scans were done in 25/49 patients and auras were distinct in all cases. The majority of patients had suffered from migraine in the past. One of us (P.J.K.) participated in a study of late-onset migraine (>40 year), in which no relevant abnormalities were found despite intensive work-up (including scans, laboratory tests, and carotid studies) [15].

Although we do not know the precise mechanisms underlying this effect, it may involve the prevention of mild and tran-

Table 1. Patient characteristics

Number of patients	42
Gender	32 women, 10 men
Age, years, mean (range)	57 (34–70)
Length of follow-up, mean (range)	10.2 months (20 days to 64 months)
Type of aura	
Visual	42 patients
Sensory	3 patients
Hemiplegic	2 patients
Mean aura frequency	10.2 times per month
Headache absent	12 patients
Headache present	30 patients
Migraine headache	22 patients
Other types of headache	10 patients
Presence of any vascular risk factor (smoking, DM, HT, CVA, MI, use of oral contraceptive)	29 patients

DM, diabetes mellitus; HT, hypertension; CVA, cerebrovascular accident; MI, myocardial infarction.

Table 2. Frequency of auras per month before (left column) and after taking aspirin (*n* = 42)

6	2	4	1
31	3	31	31
31	0	20	20
20	2	4	0
15	0.25	8	1
4	0	8	0.33
2	0	4	0.5
60	0	12	0
4	0	24	4
16	0.33	8	0
4	0	16	2
4	0	15	1
16	16	25	1
4	0	2	1
12	4	8	2
4	0	4	0
4	0.25	12	0
8	0	4	0
20	2	5	0
3	0	8	0
4	0	10	1

sient hypoxic-ischemic events (e.g., microembolism) as a trigger for cortical spreading depression, the electrophysiological basis of migraine aura, or reduction of platelet serotonin release, and plasma serotonin concentrations. We believe that in previous studies, the aspirin effect was not observed because migraine with or without aura were not distinguished. Moreover, we included only patients over 30 years of age, who had highly frequent auras. The effect of regression to the mean

cannot be ruled out, although we had a reasonable median follow-up of 10.2 months and it is unlikely that the results are entirely explained by this phenomenon. Moreover, many of the 20 patients with complete disappearance of the auras reported that the auras disappeared soon after starting aspirin treatment, suggesting a temporal association. Nevertheless, although this observational series resulted in a remarkable reduction in aura frequency, a prospective randomized con-

trolled trial for migraine aura is necessary to confirm the effect and modify the practice. We suggest that, until then, aspirin may be tried in patients in whom other prophylactic drugs are contraindicated or not tolerated.

Disclosure Statement

The authors have no conflicts of interest to disclose. There was no financial support for this work.

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