Hair Analysis for Monitoring Treatment with Triptans in Migraine Patients

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The adoption of triptans has been considered a cornerstone of migraine treatment. These medications, selective agonists at 5-hydroxytryptamine 1B/1D (5-$HT_{1B/1D}$) receptor subtype, are recommended as first-line drugs for the treatment of migraine attack (acute treatment) in patients suffering from moderate-severe migraine. However, regular and frequent use of triptans, like of any other symptomatic analgesic, can cause chronic migraine (that occurs on ≥15 days per month for at least 3 months) and medication-overuse headache (MOH) (The International Classification of Headache Disorders - ICHD-3 beta, 2013). MOH is a chronic headache, which is precisely due to analgesics overuse. It is a serious, disabling and difficult to treat disorder that affects about 30% of patient in specialty care. Only the withdrawal of the overused medication can lead to an improvement (Abrams, 2013). However, relapses are frequent and the monitoring of the treatment is crucial for its success. For this purpose, direct methods, such as dosage of analgesic/antimigraine drugs in blood and urine, are not available in clinical practice. The keratin matrix is increasingly used to monitor adherence to pharmacological treatments and to document objectively the progress of detoxification programs of drug addicts (Kintz et al, 2006). The aim of our study was to test whether it was possible to determine the triptans on the market in Italy (sumatriptan, rizatriptan, zolmitriptan, eletriptan, almotriptan, and frovatriptan) in the hair of patients who used them and whether hair analysis was able to distinguish the occasional use by the overuse of these drugs. According to ICHD-3 beta, overuse is defined as 'regular intake of one or more triptans in any formulations, on 10 or more days per month for >3 months'.

We analysed the hair samples of 110 migraine patients (mean age: 44 ± 11 years; female: 96%) who reported using triptans to treat their migraines. All patients gave their written informed consent to participate in the study. The Ethics Committee of the Province of Modena approved the study. For each patient a detailed pharmacological history relative to the previous three months and a sample of hair (at least 6 mm in diameter and 4 cm in length) were collected. Hair samples were analysed by liquid chromatography-electrospray tandem mass spectrometry (LC-MS/MS).

Eletriptan was the most used triptan (31%) followed by almotriptan (30%) and sumatriptan (25.5%). Patients who overused triptans were 45 (41%). These patients in the previous three months had taken an amount of triptans about four times higher than occasional users. To date, hair samples of patients taking eletriptan, almotriptan, sumatriptan and rizatriptan have been analysed. All these triptans were detectable in the hair of both occasional users and subjects overusing them. Concentrations measured in the hair were always higher in overusing patients than in occasional users. The differences were statistically significant for almotriptan and eletriptan (Student's t test, $p < 0.05$). For these two triptans, among the most lipid-soluble that probably penetrate more easily into the keratin matrix, there was also a significant correlation between the doses taken in the previous three months and their concentrations in the hair. The Spearman correlation coefficient respectively was 0.6733 (P=0.0001), and 0.4959 (P=0.0029) for almotriptan and eletriptan. Our results showed that almotriptan, eletriptan, rizatriptan, sumatriptan and zolmitriptan penetrate into the hair and accumulate in the keratin matrix, where they can be determined. Moreover, by hair analysis it is possible to detect triptans either taken occasionally or in excessive doses. Therefore, hair analysis can be used in clinical practice for monitoring the use of triptans by migraine patients, to document the overuse, and the outcome of the withdrawal treatment.