Withdrawal treatment vs prophylactic treatment

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Author & Year: Hagen et al, 2009[348] **Study design:** RCT **Setting:** Multicentre trial; out-patient clinics of five University hospitals in Norway **Duration of follow-up:** 4 years	**Patient group:** Patients with suspected medication overuse headache (MOH) **Inclusion criteria:** Age 18-70 years; MOH defined as headache≥15 days/month for at least 3 months combined with intake of ergots, triptans, opioids and/or combination medication (simple analgesics combined with caffeine) for ≥10 days per month, or of simple analgesics ≥15 days for a minimum of 3 months. **Exclusion criteria:** Contraindications for all types of prophylactic drugs; no improvement of headache at previous trials to stop overused medication for at least 3 weeks; history of hemicrania continua, chronic paroxysmal hemicranias or cluster headache; patient used analgesics frequently for other complaints than headache; pregnant, breastfeeding or not using effective contraception. **All patients** **N:** 64 (randomised); 61 (fulfilled inclusion criteria). **Group 1 Withdrawal** **N:** 22 (randomised); 20 (completed 1 month visit); 19 (completed 3 month visit); 18 (completed 5 month visit; 14 (completed 12 month visit)	**Group 1** **Withdrawal of medication** Advised to abruptly withdraw overused medication. If required: • allowed to use rescue medication up to 2 days per week. • offered sick leave for up to 2 weeks, offered inpatient detoxification if failed to complete the out-patient detoxification programme. • offered to start preventive treatment after three months. **Group 2** **Prophylactic treatment** Preventive treatment was started on day one. Medications used according to primary	**Change in days with acute headache medication use per month** *(mean change score, SD)*	**At 3 months:** **Group 1:** -19.1, 8.97* (n=20) **Group 2:** -13.2, 10.89*(n=17) **Group 3:** -6.9, 10.17*(n=19) **At 5 months:** **Group 1:** -18.5, 9.08*(n=20) **Group 2:** -11.6, 10.21*(n=17) **Group 3:** -6.1, 9.65*(n=19) **At 12 months:** **Group 1:** -16.1, 10.68*(n=20) **Group 2:** -14.2, 4.77* (n=17)	**Funding:** NR **Limitations:** Open label trial. Method of allocation concealment was unclear. **Additional outcomes:** Change from baseline in: Headache hours; Headache index (headache days/month x mean daily headache hours x mean daily headache severity); Sick leave days per month; and Anxiety and depression measured by HADS. **Notes:** Rescue medications for group 1 included: 10-25mg of amitryptiline (for lack of sleep), 50 mg of diclofenac or 500mg of
			Responder rate *without medication overuse and with ≥50% reduction in monthly headache days compared with baseline*	**At 5 months:** **Group 2:** 41%, (7/17) **Group 3:** 5%, (1/18) 2v3, p value: 0.010 **At 12 months:** **Group 1:** 25%, (4/14) **Group 2:** 53%, (9/16) 1v2, p value: 0.081	
			Change in patient reported headache days per month from baseline *(mean change*	**At 3 months:** **Group 1:** -4.2 , 4.38*(n=20) **Group 2:** -7.2 , 8.85*(n=17) **Group 3:** -1.6, 7.16* (n=19) **At 5 months:**	

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	Age (mean): 42.1 years **Drop outs:** 8 (at 12 month follow up) **No. of headache days per month (mean):** 24.1 **No. of days with analgesics/month (mean):** 22.9 **<u>Group 2 Prophylactic treatment</u>** **N:** 19(randomised); 17 (completed 1 month visit); 17 (completed 3 month visit); 17 (completed 5 month visit; 16 (completed 12 month visit) **Age (mean):** 41.6 years **Drop outs:** 3 (at 12 month follow up) **No. of headache days per month (mean):** 25.2 **No. of days with analgesics/month (mean):** 23.5 **<u>Group 3 Control group</u>** **N:** 20 (randomised); 19 (completed 1 month visit); 18 (completed 3 month visit); 18 (completed 5 month visit) **Age (mean):** 38.7 years **Drop outs:** 2 (at 5 month follow up) **No. of headache days per month (mean):** 26.8 **No. of days with analgesics/month (mean):** 23.7	diagnosis were: angiotensin II blockers β-blockers, valproate, tricyclic antidepressants (for migraine + TTH only), valproate, tricyclic antidepressants and gabapentin (for TTH only). **<u>Group 3 Control group</u>** No direct advice to stop using analgesics or start any preventive treatment. All patients used a headache diary during baseline period and after randomisation. Baseline period was for at least 3 months prior to randomisation.	*score, SD)*	**Group 1:** -4.8, 7.37* (n=20) **Group 2:** -7.3, 9.04*(n=17) **Group 3:** -2.1, 6.22* (n=19) **<u>At 12 months:</u>** **Group 1:** -5.1, 10.90* (n=20) **Group 2:** -10.3, 8.75* (n=17)	naproxen orally, and/or 20mg metoclopramide. Control group finished the study period after 5 months observation and were then offered treatment considered optimal for them (withdrawal or prophylactic). *calculated at NCGC
			Mental health component (MCS-12) mean, SD at 12 months	**Group 1:** 14.6, 18.27*(n=20) **Group 2:** 13.9, 23.14*(n=17)	
			Physical health component (PCS-12) *mean, SD at 12 months*	**Group 1:** 6.5, 19.23*(n=20) **Group 2:** 20.2, 27.33*(n=17)	

Abbreviations: NR=not reported, NA=not applicable, M/F=male/female, N=total number of patients randomised, SD=Standard deviation, SE=Standard error, ITT=Intention to treat analysis, MOH=Medication overuse headache, TTH=Tension type headache, HADS=hospital anxiety and depression scale.