**Supplementary Materials**

Supplementary Table 1:Search Output in Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R)<1946-present>. Search conducted in June 2017.

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| --- | --- | --- |
| **No.** | **Searches** | **Results** |
| 1 | ((Diet\* or vitamin\* or mineral\*) adj3 supplement\*).mp. | 83243 |
| 2 | (Supplement\* or vitamin\*).ti,kf. | 158484 |
| 3 | nutraceutical\*.mp. | 4258 |
| 4 | (nonpharmacologic\* or "non pharmacologic" or "non pharmacological").mp. | 13762 |
| 5 | vitamins.sh. | 29055 |
| 6 | ("vitamin A" or retinol).mp. | 40450 |
| 7 | ("vitamin B1" or thiamine or "vitamin B2" or riboflavin or "vitamin B3" or niacin\* or "vitamin B6" or pyridoxine or "vitamin B12" or cobalamin or "vitamin B complex" or "B vitamins").mp. | 82986 |
| 8 | ("vitamin C" or "ascorbic acid").mp. | 58948 |
| 9 | ("vitamin D" or cholecalciferol).mp. | 64213 |
| 10 | ("vitamin E" or tocopherol).mp. | 45422 |
| 11 | trace elements.sh. | 15124 |
| 12 | calcium.mp. | 551574 |
| 13 | iron.mp. | 192652 |
| 14 | magnesium.mp. | 100466 |
| 15 | phosphate\*.mp. | 297032 |
| 16 | selenium.mp. | 31449 |
| 17 | zinc.mp. | 130587 |
| 18 | ("coenzyme Q10" or CoQ10 or Ubiquinone).mp. | 12131 |
| 19 | dh.fs. | 46025 |
| 20 | or/1-19 | 1519474 |
| 21 | Headache\*.mp. | 83562 |
| 22 | (Migrain\* or megrim or migraineur\* or Migraineuse\*).mp. | 36006 |
| 23 | (cephalalgia\* or cephalgia\* or cephalodynia\* or hemicrania\*).mp. | 1898 |
| 24 | ((head or cranial) adj3 (pain\* or ach\*)).mp. | 2476 |
| 25 | (sick adj1 headache).mp. | 16 |
| 26 | "Alice in Wonderland Syndrome".mp. | 104 |
| 27 | or/21-26 | 104055 |
| 28 | exp Randomized Controlled Trials as Topic/ | 115994 |
| 29 | exp randomized controlled trial/ | 465453 |
| 30 | Random Allocation/ | 93030 |
| 31 | Double Blind Method/ | 147722 |
| 32 | Single Blind Method/ | 24726 |
| 33 | clinical trial/ | 522102 |
| 34 | clinical trial, phase i.pt. | 18808 |
| 35 | clinical trial, phase ii.pt. | 30304 |
| 36 | clinical trial, phase iii.pt. | 13899 |
| 37 | clinical trial, phase iv.pt. | 1492 |
| 38 | controlled clinical trial.pt. | 94192 |
| 39 | randomized controlled trial.pt. | 465276 |
| 40 | pragmatic clinical trial.pt. | 585 |
| 41 | multicenter study.pt. | 229401 |
| 42 | exp Clinical Trials as topic/ | 314687 |
| 43 | or/28-42 | 1235752 |
| 44 | trial\*.ti. | 244271 |
| 45 | (clinical adj trial\*).ti,ab. | 301361 |
| 46 | (blind\*3 or mask\*3).ti,ab. | 307657 |
| 47 | PLACEBOS/ | 35011 |
| 48 | placebo\*.ti,ab. | 196251 |
| 49 | "control group".ti,ab. | 337104 |
| 50 | sham.ti,ab. | 73215 |
| 51 | dummy.ti,ab. | 4765 |
| 52 | RCT.ti. | 1042 |
| 53 | RCTs.ti. | 362 |
| 54 | random\*.ti,ab. | 953986 |
| 55 | or/44-54 | 1704997 |
| 56 | 43 or 55 | 2282294 |
| 57 | Comment/ | 692702 |
| 58 | Editorial/ | 441377 |
| 59 | News/ | 183422 |
| 60 | (letter not (letter and randomized controlled trial)).pt. | 969190 |
| 61 | historical article/ | 348077 |
| 62 | or/57-61 | 2080138 |
| 63 | 56 not 62 | 2212324 |
| 64 | 20 and 27 | 4225 |
| 65 | 63 and 64 | 1281 |
| 66 | 65 not (exp animals/ not humans/) | 1271 |

Supplementary Table 2:Reasons for the risk of bias judgment decisions

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| --- | --- | --- | --- | --- | --- | --- |
| **Trial** | **Sequence generation** | **Allocation concealment** | **Blinding of participants and personnel** | **Blinding of outcome assessment** | **Incomplete outcome data** | **Selective reporting** |
|
| **Khorvash et al. 201621** | U- No reporting on sequence generation | U- No reporting on allocation concealment | L- "It was a randomized, double blinded, placebo-controlled clinical trial." "For the placebo group the capsules were made the same in appearance." | U- "It was a randomized, double blinded, placebo-controlled clinical trial." "For the placebo group the capsules were made the same in appearance." | L- "All the participants finished the study and no one excluded neither voluntarily left the study." | L- Study protocol to inform judgment not found. However, all listed outcomes in the methods section are reported on |
| **Menon et al. 201622** | L- "A blocked random allocation sequence was generated using n Query Advisor (Statistical Solutions, Cork, Ireland)." | U- "Patients and everyone involved in this trial were blinded to randomisation and group allocation." | L- "Patients and everyone involved in this trial were blinded to randomisation and group allocation." | L- "Patients and everyone involved in this trial were blinded to randomisation and group allocation." | U- Similar proportions of patients were excluded from data analyses for the same reasons and it is unlikely whether the reasons may be related to the outcomes | L- All listed outcomes in the methods section (and according to the trial protocol registration information: MSC/09/05/HREC) are reported on |
| **Mottaghi et al. 201523** | U- "The present study was randomized, double-blind clinical trial, and controlled with placebo." | U- "Thirty-nine patients in intervention group and 38 patients in the control group were located with simple randomization method." | U- "The present study was randomized, double-blind clinical trial, and controlled with placebo." | U- "The present study was randomized, double-blind clinical trial, and controlled with placebo." | U- Of the 39 and 38 patients randomised to the intervention and control arms respectively, 33 and 32 patients completed the study and were included in analyses. No reason was reported as per why the patients did not complete the study and/or not included in the analyses | L- All listed outcomes in the methods section (and according to the study registration information: IRCT2012122911763N4) are reported on |
| **Sadeghi et al. 201524** | L- "Patients were randomly assigned to consume pyridoxine supplement (n = 33) or placebo (n = 33) for 12 weeks using envelopes containing numbers from a table of random numbers." | L- "Patients were randomly assigned to consume pyridoxine supplement (n = 33) or placebo (n = 33) for 12 weeks using envelopes containing numbers from a table of random numbers." | L- "Patients and investigators were not aware of allocated groups. Placebo capsules were similar in shape, color, and taste to pyridoxine capsule, which was produced in the School of Pharmacy, Isfahan University of Medical Sciences." | L- "Patients and investigators were not aware of allocated groups." | H- 10 and 2 patients excluded from the intervention and control groups respectively due to different reasons only one of which (and number of patients) was the same in both groups. | L- All listed outcomes in the methods section (and according to the study registration information: IRCT2013060411763N9) are reported on |
| **Gaul et al. 201525** | L- "Randomization was done by computer and randomization lists were prepared. Randomization was done by blocks of four per center. A blockwise randomization was used." | U- "The investigator sequentially allocated the random numbers to patients, starting from the lowest number. The sequential order was verified by fax sent to a blinded person at the sponsor and from entries in the screening logs." | L- "Both investigator and patient were blinded to the treatments." | L- "Both investigator and patient were blinded to the treatments." | L- A small number excluded from analyses. However, reasons for exclusion are the same in the two groups with almost the same numbers excluded. | L- All listed outcomes in the methods section (and according to the study protocol registration information: DRKS00004565) are reported on |
| **Menon et al. 201226** | L- "A blocked random allocation sequence was generated using Microsoft Excel (Microsoft, Redmond, Washington, USA)." | U- "The participants and everyone involved in this trial were blinded to randomization and group allocation." | L- "The participants and everyone involved in this trial were blinded to randomization and group allocation. Both the vitamin and the placebo tablets were produced by Blackmores and were identical in appearance." | L- "The participants and everyone involved in this trial were blinded to randomization and group allocation." | U- The same number of patients received intervention in the study arms. However, dissimilar numbers discontinued medication/finished the study although analysis was based on a modified intention-to-treat principle | L- Study protocol to inform judgment not found. However, all listed outcomes in the methods section are reported on |
| **Tarighat Esfanjani et al. 201227** | U- "In this clinical trial, 133 migrainous patients were randomly assigned into three intervention groups." | H- "In this clinical trial, 133 migrainous patients were randomly assigned into three intervention groups. The present study was a single-blind clinical trial in which subjects were assigned into one out of four groups". | U- "The present study was a single-blind clinical trial in which subjects were assigned into one out of four groups" | H- "The present study was a single-blind clinical trial in which subjects were assigned into one out of four groups" | L- "From 139 volunteered subjects who met the inclusion criteria and entered the study, six patients were withdrawn from the study because of gastrointestinal discomfort (four due to magnesium supplements and two due to Mg–L-carnitine uses)." | L- Study protocol to inform judgment not found. However, all listed outcomes in the methods section are reported on |
| **Bruijn et al. 201028** | U- "A 40-week, randomised, double-blind, cross-over design was used to examine the effect of riboflavin compared with placebo in young children with migraine. The hospital pharmacists guarded the randomisation key." | U- "Treatment allocation was concealed from the participants and investigators for the duration of the study. The hospital pharmacists guarded the randomisation key." | L- "Treatment allocation was concealed from the participants and investigators for the duration of the study. To ensure the double-blind design, carotene 100 mg was used as placebo. Both carotene and riboflavin give an orange discolouration of the urine." | L- "Treatment allocation was concealed from the participants and investigators for the duration of the study." | L- Although 4 patients were discontinued from one of the randomised arms and none from the other arm, the reasons for discontinuation are unrelated to treatment and/or outcome.  Comparable number of participants excluded from analysis in the study groups post randomization and due to the same reasons. | L- Study protocol to inform judgment not found. However, all listed outcomes in the methods section are reported on |
| **Lea et al. 200929** | L- "A blocked random allocation sequence was generated using Microsoft Excel (Microsoft, USA)." | L- "Specialized staff who were not involved in the study allocated labelled treatment containers with the participants unique sequence  number." | L- "Patients and primary investigators were blinded to the randomization and group allocation. The vitamin and placebo tablets, produced by Blackmores, were indistinguishable." | L- "Patients and primary investigators were blinded to the randomization and group allocation." | L- Of the 52 patients randomised to study arms and commenced treatment, "Five patients were lost to follow-up owing to lack of compliance". Similar number of losses were recorded in the study arms. | L- Study protocol to inform judgment not found. However, all listed outcomes in the methods section are reported on |
| **Mahdavi et al. 200930** | U- "This 12 week study is a randomised controlled study with two arms, intervention and control" No reporting on sequence generation and the randomization process is questionable | U- "This 12 week study is a randomised controlled study with two arms, intervention and control" No reporting on sequence generation and the randomization process is questionable | H- "This 12 week study is a randomised controlled study with two arms, intervention and control" No mention of blinding | H- "This 12 week study is a randomised controlled study with two arms, intervention and control" No mention of blinding | H- "18 patients were excluded from the study (14 from Mg and 4 from control) due to not coming for the visits." | L- Study protocol to inform judgment not found. However, all listed outcomes in the methods section are reported on |
| **MacLennan et al. 200831** | L- "The computer generated list of random numbers was created and administered by the hospital Pharmacy Department." | U- "Each family collected their capsules directly from the Pharmacy, and treatment allocation was concealed to the participants and investigators for the duration of the study." | L- "Treatment allocation was concealed to the participants and investigators for the duration of the study." | L- "Treatment allocation was concealed to the participants and investigators for the duration of the study. Only the data monitoring committee could view unblinded data, and they did not have any contact with study participants." | L- "No patients were lost to follow-up or withdrew consent. Data was analyzed for the primary outcome for all 48 patients randomized." | L- All a priori listed outcomes in the study protocol are reported on |
| **Koseoglu 200832** | U- "30 patients were allocated as Mg treatment group and 10 patients as placebo treatment group, by using a simple randomization method." | H- No statement regarding concealment of treatment allocation | U- No statement on blinding except the following: "This double blind, randomized, placebo controlled study was conducted in Erciyes University, Neurology-Headache Outpatient Clinic and Nuclear Medicine Department." | U- No statement on blinding except the following: "This double blind, randomized, placebo controlled study was conducted in Erciyes University, Neurology-Headache Outpatient Clinic and Nuclear Medicine Department." | L- All randomised patients included in outcome analysis | L- No study protocol to inform judgment. However all listed outcomes in the methods section are reported on |
| **Sandor et al. 200533** | L- "Medications were randomized in blocks of 10 packages (five placebo, five CoQ10) with a different order for each block, known only to MSE. Patients were allocated in sequence to the randomized phase." | L- "Sealed envelopes with treatment codes were added; only the code of one patient with cutaneous allergy was broken." | U- "The design of this double-blind, randomized, two-parallel group trial. Placebo consisted of the same ingredients as verum-instead CoQ10, they contained Quinolin yellow (E 104) and Ponceau red (E 124), classified as fit for human consumption in the European Union (EU) and Switzerland and without any known effect on migraine." | U- No information on blinding of outcome assessment except for the following: "The design of this double-blind, randomized, two-parallel group trial.” | U- "Six patients dropped out after randomization: three for lack of efficacy (two with placebo), two were lost to follow-up in the verum group after the second month. One patient in the verum group withdrew because of cutaneous allergy after having started the treatment and was therefore not included into statistical analysis." | L- Study protocol to inform judgment not found. However, all listed outcomes in the methods section are reported on |
| **Wang et al. 200334** | L- "The allocation schedule was generated using Proc Plan in the Statistical Analysis System’s (SAS)  Software, version 6.11." | U- Although not explicitly stated, it seems, based on the method reporting, that treatment allocation was concealed not only to the patients but also to all the study staff but the method is not reported | L-"Subjects, the study and site coordinators, and all investigators were not aware of the study drug assignment until after the study statistician had analyzed all study data." | L- "Subjects, the study and site coordinators, and all investigators were not aware of the study drug assignment until after the study statistician had analyzed all study data." | U- "Of those enrolled, 73% completed the study and 27% dropped out (16  randomized to MgO and 16 to placebo," and with similar reasons for dropping out. | L- Study protocol to inform judgment not found. However, all listed outcomes in the methods section are reported on |
| **Schoenen et al. 199835** | U- "The study medications were randomized in 10 blocks of 10 packages, each block comprising five placebo and five active treatments. In each center, patients were allocated in sequence to the randomized phase, starting with the lowest treatment package number." | L-"Sealed envelopes containing the treatment codes were added to treatment material." | L- “This was a double-blind, randomized, two-parallel group trial.” The two interventions studies were identical in appearance and colored urine alike. | U- “This was a double-blind, randomized, two-parallel group trial. The total blinded and randomized treatment period was thus 3 months with monthly control visits.” | U- "Statistical analysis was carried out on an intention-to-treat basis. In the patients' diaries, migraine headaches separated by less than 24 hours were counted as one single attack. Values for patients who dropped out were included according to the last value-carried-forward method." | L- Study protocol to inform judgment not found. However, all listed outcomes in the methods section are reported on |
| **Peikert ET AL. 199636** | U- "The patients were double-blind and randomly assigned to magnesium or placebo in blocks." | H- "The patients were double-blind and randomly assigned to magnesium or placebo in blocks." | U- "The patients were double-blind and randomly assigned to magnesium or placebo in blocks." | H- "The patients were double-blind and randomly assigned to magnesium or placebo in blocks." | U- "The evaluation was done according to the intention-to-treat principle. It includes all patients who submitted an at least 4-week long headache diary and who randomly received the study medication." | L- Study protocol to inform judgment not found. However, all listed outcomes in the methods section are reported on |
| **Pfaffenrath et al. 199637** | U- "The study was a prospective, multinational, multicentre, randomized, double-blind, placebo-controlled phase III clinical trial with two groups in a parallel design" | U- "The study was a prospective, multinational, multicentre, randomized, double-blind, placebo-controlled phase III clinical trial with two groups in a parallel design" | U- "The study was a prospective, multinational, multicentre, randomized, double-blind, placebo-controlled phase III clinical trial with two groups in a parallel design" | U- "The study was a prospective, multinational, multicentre, randomized, double-blind, placebo-controlled phase III clinical trial with two groups in a parallel design" | U- "Four patients (11.4%) of the intervention MAH group and four patients (11.8%) of the placebo group dropped out for different drug-related reasons but only one in the MAH group due to a lack of efficacy in contrast to four under placebo. These eight patients were included within the intention-to-treat analysis as well as in the per-protocol analysis." | L- Study protocol to inform judgment not found. However, all listed outcomes in the methods section are reported on |

Supplementary Table 3:Results for migraine frequency, and days with migraine, from heterogeneous trials

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| --- | --- | --- | --- |
| **Migraine Frequency (per month)** | | | |
| Subgroup | Number of trials | Number analyzed | Effect estimate (95% CI);  I-squared statistic for heterogeneity |
| *Magnesium (Minerals)27, 30, 32, 36* | *4* | *266* | *MD -2.57 (-4.21 to -0.94); I2 = 88%, p<0.0001* |
|  |  |  |  |
| *≥18years24, 27, 30, 32, 33, 35, 36* | *7* | *356* | *MD -2.16 (-3.06 to -1.25); I2 = 79%, p<0.0001* |
|  |  |  |  |
| *Trials with high RoB assessment24, 27, 30, 32, 36* | *5* | *259* | *MD -2.68 (-4.23 to -1.13); I2 = 85%, p<0.0001* |
|  |  |  |  |
| *Non-industry funded trials21, 23, 24, 27, 30, 32, 35, 36* | *8* | *394* | *MD -2.00 (-2.98 to -1.03); I2 = 78%, p<0.0001* |
| **Days with Migraine** | | | |
| Subgroup | Number of trials | Number analyzed | Pooled effect estimate (95% CI);  I-squared statistic for heterogeneity |
| *Magnesium (Minerals)27, 30, 36* | *3* | *226* | *MD -3.00 (-5.02 to -0.98); I2 = 87%, p=0.0005* |
| *Vitamin B235* | *1* | *54* | *MD -3.50 (-4.98 to -2.02)* |
| *Coenzyme Q1033* | *1* | *43* | *MD -0.50 (-2.74 to 1.74)* |
|  |  |  |  |
| *Vitamins33, 35* | *2* | *97* | *MD -2.12 (-5.05 to -0.81); I2 = 79%, p=0.03* |
|  |  |  |  |
| *Trials with unclear RoB assessment25, 33, 35* | *3* | *209* | *MD -1.66 (-3.59 to 0.28); I2 = 78%, p = 0.01* |
| *Trials with high RoB assessment27, 30, 36* | *3* | *226* | *MD -3.00 (-5.02 to -0.98); I2 = 87%, p=0.0005* |

RoB = risk of bias; MD = mean difference; CI = confidence intervals; I2 = I-squared statistic; RoB = Risk of Bias

Supplementary Figure 1:Forest plot for migraine severity

Only one trial on vitamin B2 (RoM 0.00 (-6.64 to 6.64)) – not included in the forest plot

Supplementary Figure 2:Forest plot for days with migraine

Only one trial each on vitamin B2 (MD -3.50 (-4.98 to -2.02)) and coenzyme Q10 (MD -0.50 (-2.74 to 1.74)) – not included in the forest plot