A systematic review of compliance to oral nutritional supplements

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CRD summary
This review found that compliance to oral nutritional supplements was generally good especially with high-density options. While the broad conclusions on levels of compliance are probably reliable the results on how other factors might influence compliance may not be reliable.

Authors' objectives
To examine patient compliance with oral nutritional supplements and whether it varied according to healthcare setting, supplement characteristics or patient characteristics.

Searching
Nine electronic databases were searched (including PubMed, The Cochrane Library and CINAHL), conference proceedings were checked and experts were contacted to identify eligible publications. Search terms were reported. The last search date was October 2009.

Study selection
Any study type was eligible provided the participants were adults who received multi-nutrient oral nutritional supplements and compliance with the prescription was reported or could be calculated (healthy volunteers and the overweight were excluded). Any comparator was eligible. Oral nutritional supplement intervention was required to have been prescribed and contain more than two macronutrients plus micronutrients. Details of excluded nutritional interventions were given in the paper. Interventions were excluded if they included other components (such as counselling).

The included studies ranged from randomised controlled trials (RCTs) to surveys. Most studies involved participants in community settings. Most of the oral nutritional supplements used were ready-made multi-nutrient liquids with energy densities ranging from 1.0 to 4.0 kcal/mL. Supplementation ranged from four to 365 days. Prescribed nutritional intake varied between 237 and 1,080 kcal per day. Where comparators were used, these included routine care, other nutritional supplements, placebo and dietary advice. Participants were mostly elderly (mean age 74 years) and had a range of chronic and acute conditions. Mean body mass index (BMI) was 22.8.

Studies were assessed for inclusion by one researcher and decisions were checked by a second.

Assessment of study quality
RCTs were assessed using the Jadad criteria of randomisation, blinding and drop-outs by one researcher and checked by a second.

Data extraction
The main outcome measure extracted was mean compliance to the nutritional prescription (usually a mean percentage with standard deviation). Where this was not reported, the researchers calculated it based on prescription and intake values or number of supplement portions consumed. Compliance figures for the longest period of supplementation were used.

Researchers extracted mode of compliance assessment in each study, any methods to improve compliance, energy intake and patient characteristics. Studies were classified according to setting (definitions in paper): community, hospital and multiple settings.

The authors did not report how many researchers extracted data.

Methods of synthesis
Average compliance was calculated across studies. Mean compliance and standard deviation (SD) were reported. Where possible, mean compliance values from each study were pooled in a meta-analysis and reported as mean compliance and...
standard error of mean (SEM). Heterogeneity was assessed using $I^2$. Where means were reported without measures of dispersion, these were pooled with and without weighing by sample size. Correlations between compliance and factors including study type and setting, energy density, type of supplement and patient characteristics were evaluated by calculating the relevant correlation coefficient ($r^2$) and its p value.

**Results of the review**

Fifty papers reporting on 46 studies (2,282 patients on supplements) were included: 32 RCTs (1,590 patients on supplements) and 14 non-randomised studies (five surveys and nine non-comparative studies). RCTs scored variably on the Jadad scale and only four papers scored 5.

**Compliance overall**: Pooled mean compliance with oral nutritional supplementation was 78.2% (SD 15) across 52 studies (range 37% to 100%). In a meta-analysis overall compliance was 71.6% (SEM 5%; 10 studies, 357 patients). Energy intake was higher in patients who received supplements than in controls (by 375 kcal/day, SEM 72; eight RCTs).

**Compliance according to setting**: Mean compliance was significantly greater in community setting studies (80.9%; 33 studies) compared with hospital setting studies (67.2%; 10 studies) but when an analysis weighted by sample size was used this difference became non-significant. Compliance was not significantly different between randomised and non-randomised studies.

**Compliance with prescription**: The correlation between prescribed and consumed nutritional supplementation energy was high ($r^2=0.833$, p=0.0001; 41 studies) but there was no association between amount of supplementation prescribed and percentage compliance with the prescription.

**Oral nutritional supplementation related factors**: Compliance was not affected by duration of the intervention. Participants complied significantly more with higher energy density supplements ($r^2=0.093$, p=0.05; 41 studies). Studies that used a variety of flavours of supplement (18 studies) reported significantly higher compliance than those studies that offered variety of supplement types (six studies), (81% versus 63%, p=0.027). Giving instructions on when to take the supplements did not appear to alter compliance.

There were no significant differences in compliance between patient groups (disease groupings) or based on BMI but younger patients tended to be associated with lower compliance levels ($r^2=0.148$, p=0.01; 44 studies).

**Authors’ conclusions**

Compliance to oral nutritional supplements was generally good especially with high-density options.

**CRD commentary**

This review addressed a broad question with broadly defined inclusion criteria. The search was comprehensive and did not appear to impose publication or language restrictions. The review processes were generally carried out by one researcher and checked by a second to minimise error or bias. Only the RCTs were assessed for quality and their quality was very variable. The quality of the non-randomised studies was uncertain. Compliance was generally assessed by combining results across studies rather than making comparisons within studies. As the authors noted, such assessments are observational and not randomised and may be subject to error and bias. Use of correlations to assess associations between compliance and other factors did not provide information on the size or clinical significance of the association and so such results may be unreliable.

There were some concerns over study quality and analysis methods but the size of this review suggests that the main conclusions relating to compliance are probably reliable but results on associations between compliance and other factors may not be.

Two of the four authors were employed by supplement companies.

**Implications of the review for practice and research**

**Practice**: The authors recommended that prescriptions should be monitored and adjusted either by reducing to avoid wastage or increasing for greater intake.
Research: The authors recommended that further research should focus on efforts to increase compliance and intake including the role of patient and carer attitudes, the role of education and the role of the healthcare professional.

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