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Almost all Antipsychotics Result in Weight gain: A meta-Analysis

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Editorial Note

Antipsychotics (AP) induce weight gain. However, reviews and meta-analyses generally are restricted to second generation antipsychotics (SGA) and do not stratify for duration of AP use.

s It is hypothesized that patients gain more weight if duration of AP use is longer. Method: A meta-analysis was conducted of clinical trials of AP that reported weight change. Outcome measures were body weight change, change in BMI and clinically relevant weight change (7% weight gain or loss).

Duration of AP-use was stratified as follows 6 weeks, 6-16 weeks, 16-38 weeks and 38 weeks. Forest plots stratified by AP as well as by duration of use were generated and results were summarized 307 articles met inclusion criteria.

The majority were AP switch studies. Almost all AP showed a degree of weight gain after prolonged use, except for amisulpride, aripiprazole and ziprasidone, for which prolonged exposure resulted in negligible weight change.

The level of weight gain per AP varied from discrete to severe. Contrary to expectations, switch of AP did not result in weight loss for amisulpride, aripiprazole or ziprasidone. In AP-naive patients, weight gain was much more pronounced for all AP. Given prolonged exposure, virtually all AP are associated with weight gain.

The rational of switching AP to achieve weight reduction may be overrated. In AP-naive patients, weight gain is more pronounced. Addendum: New data will be available, considering association of psychiatric diagnosis and obesity and antipsychotic medication.

Weight gain resulting in overweight and more particularly obesity is a growing problem worldwide. Overweight and particularly obesity predicts cardiovascular risk, metabolic syndrome and diabetes mellitus type 2 as well as an increased risk for cancer.

Controlled and uncontrolled studies reporting the effects of discontinuation, dose reduction, switch to a partial agonist, or switch from polypharmacy to monotherapy on weight were included.

Primary outcome was difference in weight compared to maintenance groups based on controlled studies. Secondary outcome was change in weight from initiation of one of the included interventions until follow-up in a pre-post analysis.

Data Synthesis

In order to include a maximum of studies, we combined end-scores and change scores for primary outcomes. Thereby, we abstain from calculating standardized measures, as the combination of dispersion of end- and change scores cannot be combined in a standardized effect size If change scores as well as end scores were reported, end-scores were preferred.

All results were reported with 95% confidence intervals and 95% prediction intervals Missing measures of dispersion were imputed as recommended by Cochrane Random effects were reported, assuming underlying heterogeneity of effects due to variations in the interventions.

The degree of heterogeneity was quantified using the I2 statistic, which can be interpreted as the percentage of variation observed between the trials attributable to between-trial differences, rather than sampling error (chance).

Heterogeneity was explored by analyses of subgroups and meta-regressions. Results from randomized clinical trials and uncontrolled studies were analyzed and reported separately.

Results from RCTs were pooled with pre-post studies if data for these were available. Weight gain is a major adverse effect of antipsychotic medication, negatively affecting physical and mental well-being. The objective of this study was to explore if dose reduction, discontinuation, switch to a partial agonist, or switch from polypharmacy to monotherapy will lead to weight loss.

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