Journal of the American Society of Hypertension 12(2) (2018) 80–96

Research Article

Effects of orlistat on blood pressure: a systematic review and meta-analysis of 27 randomized controlled clinical trials

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Manuscript received August 31, 2017 and accepted December 6, 2017

Abstract

Obesity and high blood pressure (BP) are strongly related and weight loss is mightily associated with a significant BP decrease. The aim of the present meta-analysis was to evaluate and quantify the BP decrease associated with orlistat use in randomized controlled trials. The search included PubMed-Medline, Scopus, Web of Science and Google Scholar databases by up to June 05, 2017, to identify randomized controlled trials investigating the impact of orlistat on blood pressure. Quantitative data synthesis was performed using a random-effects model, with weighed mean difference and 95% confidence interval as summary statistics. Meta-regression and leave-one-out sensitivity analyses were performed to assess the modifiers of treatment response. Our meta-analysis included 27 randomized controlled clinical trials which comprehended overall 8150 subjects (4419 in the orlistat group and 3731 in the control one). We observed a statistically significant decreasing effect of orlistat on both systolic BP (−1.15 mmHg [−2.11, −0.19]) and diastolic BP (−1.07 mmHg [−1.69, −0.45]), regardless of its dosage. Significant associations were found between changes in systolic BP and diastolic BP with treatment duration but not with corresponding baseline BP values. In conclusion, Orlistat use contributes weight loss associated decrease in BP in overweight and obese subjects. J Am Soc Hypertens 2018;12(2):80–96.

Keywords: Blood pressure; meta-analysis; orlistat; randomized clinical trials.

Introduction

The prevalence of overweight and obesity worldwide has constantly increased during the last decades, with an estimated doubling from 1980 to recent years.[1] Although it is hard to provide a globally accepted definition of obesity, this concept is generally expressed as a function of body mass index (BMI), waist circumference, or waist/height ratio.[2,3] In 2013–2014, a US national survey estimated the overall prevalence of obesity in American adults to be 37.7%,[4] and previous evaluations report that over one-third of the world's population is overweight or obese.[5] In the US, it has been estimated that obesity is per se

The authors declare no conflicts of interest to disclose.

The authors received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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1933-1711/$ - see front matter
https://doi.org/10.1016/j.jash.2017.12.002

responsible for one of every 10 preventable deaths, most of which are related to cardiovascular disease.[6]

The epidemiological and pathophysiological associations between obesity and high blood pressure (BP) are well acknowledged, the former being a major risk factor for hypertension.[7,8] This observation is now confirmed in young subjects as well.[9] Furthermore, the Anglo-Scandinavian Cardiac Outcome trial suggested that an increased BMI is a determinant of treatment–resistant hypertension.[10]

In line with that, weight loss is associated with a significant BP decrease, especially in mild hypertension.[11] In a long-term trial, the patients who normalized their BMI also experienced a larger improvement in BP and in a number of metabolic and hormonal parameters, including insulin sensitivity, plasma leptin, and activation of the renin-angiotensin-aldosterone system.[12] Some drugs that were regularly used alongside diet as weight loss products, like sibutramine, have been shown to raise BP.[13,14] Orlistat, instead, seems to have a slight decreasing effect on BP.[14]

The last meta-analysis considering the effect of antiobesity drugs on BP focused its attention on hypertensive patients only and not on a specific drugs.[14] On the contrary, we aimed to carry out a meta-analysis of randomized controlled trials to specifically investigate if orlistat use is associated to BP decrease and to assess the magnitude of the decrease in both normotensive and hypertensive subjects.

Materials and Methods

Search Strategy

This study was designed according to the guidelines of the 2009 preferred reporting items for systematic reviews and meta-analysis statement.[15] PubMed-Medline, SCOPUS, Web of Science, and Google Scholar databases were searched using the following search terms in titles and abstracts (also in combination with MESH terms): (orlistat) AND (''blood pressure'' OR hypertension OR antihypertensive OR hypotension OR hypotensive) AND (''randomized controlled trial'' OR randomized). The wild-card term ''*'' was used to increase the sensitivity of the search strategy. No language restriction was used in the literature search. The search was limited to studies in humans. The literature was searched from inception to June 05, 2017.

Study Selection

The following criteria was used to identify eligible studies: (1) randomized controlled trials with either parallel or cross-over design; (2) investigation of the effects of orlistat on BP; (3) treatment duration of at least two months; and (4) providing systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) values in both orlistat and control groups on baseline and end-trial. Exclusion criteria were (1) experimental studies; (2) uncontrolled studies; (3) lack of SBP and/or DBP values on baseline or end-trial; (4) studies where orlistat was added to other pharmacological treatments or dietary supplement supposed to influence body weight and/or BP; and (5) studies enrolling patients specifically enrolled because of endocrine disorders (for instance polycystic ovary syndrome). In case of the latter item, authors of the article(s) were contacted and requested to provide necessary numerical data. Two authors conducted the study selection process, and discrepancies were resolved through discussion by a third author.

Data Extraction

Eligible studies were reviewed, and the following data were abstracted: (1) first author's name; (2) year of publication; (3) country where the study was performed; (4) study design; (5) number of participants in the orlistat and control groups; (6) type and dose of orlistat treatment; (7) treatment duration; (8) age, gender, and BMI of study participants; and (9) data regarding baseline and final SBP and DBP. Two authors performed the data extraction, and disagreements were resolved by a third author.

Quality Assessment

According to the Cochrane instructions, a systematic evaluation of the risk of bias in the studies eligible for the meta-analysis was conducted using the Cochrane criteria.[16] Adequacy of sequence generation, allocation concealment, blinding, addressing of dropouts (incomplete outcome data), selective outcome reporting, and other potential sources of bias were the parameters used for the risk of bias assessment of each study. As per Cochrane recommendations, each study was judged to have a low, high, or unclear risk of bias. Two authors carried out the quality evaluation, and a third author resolved the discrepancies.

Quantitative Data Synthesis

Meta-analysis was conducted using Comprehensive Meta-Analysis V2 software (Biostat, NJ).[17] All values were collated as percent change from baseline in each group. Standard deviations (SDs) of the mean difference were calculated using the following formula: $SD = \text{square root } [(SD_{pretreatment})^2 + (SD_{posttreatment})^2 - (2R \times SD_{pretreatment} \times SD_{posttreatment})]$, assuming a correlation coefficient (R) = 0.5. Conversion of 95% confidence interval (CI) to SD was made according to Cochrane instructions.[16] Where standard error of the mean was only reported, standard deviation (SD) was estimated using the following formula: SD = standard error of the mean × sqrt (n), where n is the number of subjects. Net changes in measurements (change scores) were calculated