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Meta-analyses

A meta-analysis of the effect of angiotensin receptor blockers and calcium channel blockers on blood pressure, glycemia and the HOMA-IR index in non-diabetic patients

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ABSTRACT

Objective. This study compared the efficacy of angiotensin receptor blockers (ARBs) and calcium channel blockers (CCBs) in the effect of insulin resistance (IR) as assessed using the homeostasis model assessment of insulin resistance (HOMA-IR) in non-diabetic patients.

Methods. The MEDLINE, EMBASE, and Cochrane Library databases were searched to identify studies published before December 2012 that investigated the use of ARBs and CCBs to determine the effect on the HOMA-IR index in non-diabetics. Parameters on IR and blood pressure were collected. Review Manager 5.2 and Stata 12.0 were used to perform the meta-analysis. Fixed and random effects models were applied to various aspects of the meta-analysis, which assessed the therapeutic effects of the two types of drug using the HOMA-IR index in non-diabetic patients.

Results. The meta-analysis included five clinical trials. Patient comparisons before and after treatment with ARBs and CCBs revealed that ARBs reduced the HOMA-IR index (weighted mean difference (WMD) −0.65, 95% confidence interval (CI) −0.93 to −0.38) and fasting plasma insulin (FPI) (WMD −2.01, 95% CI −3.27 to −0.74) significantly more than CCBs. No significant differences in the therapeutic effects of these two types of drug on blood pressure were observed.

Conclusion. Given that there are no significant differences in the therapeutic effects of ARBs and CCBs on blood pressure, as ARBs are superior to CCBs in their effect on the HOMA-IR index in non-diabetics, they might be a better choice in hypertension patients without diabetes.

Abbreviations: IR, insulin resistance; ARB, angiotensin receptor blocker; PPAR-γ, peroxisome proliferator activated receptors-gamma; ACEI, angiotensin converting enzyme inhibitors; CCB, calcium channel blocker; HOMA-IR, homeostasis model assessment of insulin resistance; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; FPG, fasting plasma glucose; FPI, fasting plasma insulin; SBP, systolic blood pressure; DBP, diastolic blood pressure; ADA, American Diabetes Association; SD, standard deviation; SEM, standard error of the mean; WMD, weighted mean difference; RCTs, randomized controlled trials; RAS, renin–angiotensin system; AT1, Ang II inhibits the angiotensin II receptor 1.

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1. Introduction

With societal changes, as the proportion of individuals residing in urban areas has increased and individual lifestyles have changed, obesity, hyperlipidemia, and diabetes have become global public health problems that have replaced hunger, infection, and other traditional concerns in many regions of the world [1].Insulin resistance (IR) plays an important role in type 2 diabetes [2] and is defined as a condition in which the target organs of insulin exhibit decreased sensitivity to insulin; in other words, in patients with IR, normal doses of insulin produce lower-than-normal biological effects. In recent years, endocrine specialists have conducted studies to assess whether various common antidiabetic drugs, such as metformin [3] and thiazolidinediones [4,5], exhibit promising effects for the treatment of IR in diabetics. However, there is a lack of data from large-scale clinical trials and evidence-based medicine on the pharmaceutical choices for the treatment of non-diabetic patients with IR.

Angiotensin receptor blockers (ARBs) were initially used as antihypertensive drugs. Subsequent studies suggested that ARBs also have specific cardiorenal protective effects and alleviate IR [6]. ARBs that have traditionally been associated with improved IR are telmisartan and irbersartan, because in addition to blocking the AT-II receptor they activate the peroxisome proliferator activated receptors-gamma (PPAR-γ) system [7]. However, a recent study [8] suggested that the effect of telmisartan (activates PPAR-γ) on insulin sensitivity is similar to that of valsartan (does not activate PPAR-γ), and PPAR-γ-mediated stimuli play only a small role in the telmisartan-induced improvement in insulin sensitivity. In several randomized controlled studies, including VALUE [9], CASE-J [10], ARBs/angiotensin converting enzyme inhibitors (ACEIs) appeared to prevent new-onset diabetes mellitus better than treatment with calcium channel blockers (CCBs), which are probably neutral in this role. However, it is still unclear whether the administration of ARBs provides greater metabolic benefits for non-diabetics in terms of the homeostasis model assessment of insulin resistance (HOMA-IR) index than the administration of CCBs.

In recent years, the HOMA-IR index has become widely accepted as a means to detect and rate the severity of IR [11]. However, there are insufficient data from evidence-based medicine on the efficacy of ARBs in terms of their effect on the HOMA-IR index. This investigation focused on the HOMA-IR index in non-diabetic patients, including patients with normal blood glucose, impaired fasting glucose (IFG), or impaired glucose tolerance (IGT). The main outcome measures were the HOMA-IR index, fasting plasma glucose (FPG) and fasting plasma insulin (FPI), and the secondary outcome measures included systolic blood pressure (SBP) and diastolic blood pressure (DBP). To compare the effects of ARBs and CCBs on their ability to improve the HOMA-IR index in non-diabetics and their effects on blood pressure, we conducted a comprehensive meta-analysis of all published clinical trials that met the inclusion criteria for this investigation.

2. Methods

2.1. Study Selection

This investigation required studies to meet the following inclusion criteria: (1) enrolled patients with normal blood sugar levels, IFG, or IGT, with IFG or IGT defined using the American Diabetes Association (ADA) guideline [12]; (2) long-term administration of an ARB or CCB, with an observation period ≥ 8 weeks; (3) the HOMA index was used to assess IR; and (4) a parallel or crossover design, with a drug washout period of at least 2 weeks if a crossover design was used.

This investigation rejected studies using the following exclusion criteria: (1) the patients met the ADA guideline criteria for diabetes [12]; (2) the ARB or CCB was combined with an ACEI; and (3) patients with liver or kidney disease or cancer.

2.2. Data Sources and Searches

This study searched the MEDLINE, EMBASE, and Cochrane Library medical databases to retrieve relevant studies. The searches were performed in English, and each search retrieved studies that were published between establishment of the database and December 2012.

To ensure the comprehensive, accurate retrieval of studies, a comprehensive search strategy was established. Specifically, the MEDLINE and Cochrane Library databases were searched using the method described in the Cochrane Policy Manual for optimizing the sensitivity and precision of the search process [13], whereas EMBASE was searched using a sensitivity–specificity filter optimized by the McMaster/Hedges team [14]. The following search was used: [angiotensin receptor antagonists or angiotensin II type 1 receptor blockers or angiotensin receptor blockers] and [calcium channel blockers] and [homeostasis model assessment or HOMA or index of insulin sensitivity or insulin resistance or insulin sensitivity]. After completing the electronic query of the aforementioned databases, we also searched relevant professional journals manually.

2.3. Data Extraction and Quality Assessment

Two investigators (Y.Y. and Y.X.) independently selected studies from the retrieved literature based on the inclusion criteria and extracted the data and analytical results of these studies. If these two investigators had different opinions regarding the quality of a study, a third investigator (R.W.) examined the disputed study and discussed it with the two aforementioned reviewers. Data were included for consideration only if discussions allowed the three authors to achieve consensus regarding the data.

If necessary, the glucose and insulin concentrations were recalculated to the international system of units. Values for HOMA-IR index were based on values provided by the authors of the included studies. The HOMA-IR index is calculated using the formula: (fasting insulin × fasting glucose)/22.5 or the more recently updated computer model [11].

We evaluated treatment-related changes based on changes between the pre-treatment and post-treatment mean values