



Review

Perioperative use of angiotensin-converting-enzyme inhibitors and angiotensin receptor antagonists



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ARTICLE INFO

Article history:

Received 1 February 2017

Received in revised form 18 April 2017

Accepted 21 April 2017

Keywords:

Angiotensin-converting enzyme inhibitors

Perioperative care/therapy

Angiotensin receptor antagonists

ABSTRACT

Study objective: Clinical repercussions of perioperative treatment with ACEIs/ARBs.

Design: Systematic review according to PRISMA statement.

Setting: Perioperative period.

Patients: 29 studies 11 cases/cases series, 12 observational studies and 6 randomized studies.

Measurements: Arterial blood pressure differences, refractory hypotension, other comorbidities.

Main results: The studies show different results regarding the topics measured. They are divided in the results regarding blood pressure, long term morbidities and effects in neuraxial anesthesia.

Conclusions: Withholding ACEI/ARBs on the morning prior to surgery could be recommended as a potentially effective measure, with a low level of evidence, in order to reduce the appearance of hypotension in the perioperative period of non-cardiac surgery.

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1. Introduction

Angiotensin-converting-enzyme inhibitors (ACEI), which were introduced in clinical practice in 1980 and angiotensin II receptors

antagonists; previously known as angiotensin II receptors blockers (ARBs), are two of the most commonly used drugs for the control of blood pressure over the last two decades [1]. These two groups have 4 positive attributes: they generate cardiovascular protection and lead to a decreased incidence of ischemic events and their complications; their early implementation is associated with increased survival rates after myocardial infarction and with a better heart function; on the other hand, they are effective in the treatment of both cardiac dysfunction and hypertension; and finally, they seem to delay the progression of diabetic nephropathy [2].

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They act by blocking the shift from angiotensin I to angiotensin II (generating higher levels of bradykinin) in the case of ACEI and by increasing angiotensin levels (without increasing bradykinin) in the case of ARBs, and this last group is more selective with regard to the suppression of the effects of angiotensin II³. These mechanisms make it possible to achieve a good control of blood pressure.

During anesthesia (either general or epidural), when the sympathetic tone is inhibited, the maintenance of arterial pressure will rely more predominantly on the renin-angiotensin axis or the vasopressin axis. If two of these systems are inhibited and one of these drugs is administered, the hypotension may adopt a more aggressive form of presentation [3]. This fact could account for the appearance of cases of refractory hypotension related to the administration of these drugs during anesthesia [4,5], and it might justify the recommendation to withhold them prior to its induction.

However, joint reviews and the consensus from experts offer disparate recommendations with regard to their management in the context of anesthesia, whereas some reviews [6,7] set out certain doubts regarding their use during the perioperative period. On the other hand, the guidelines for the management of perioperative drugs offer varied opinions [8–15].

In view of this uncertainty, we decided to carry out a systematic review of the studies published on the perioperative management of ACEI/ARBs both in the case of general anesthesia and neuraxial (spinal and epidural) anesthesia and its repercussions, and both in acute forms of presentation and in the long term.

2. Methods

According to PRISMA [16] guidelines during the year 2015 we carried out a search in the databases of PubMed and Index Medicus, with a period that included studies from 1990 to 2015. The selection only included works published in Spanish, French, German and English, and it included randomized essays, observational studies and, due to the low number of available references, cases or case series. The search criteria were: “spinal anesthesia OR general anesthesia OR epidural anesthesia AND angiotensin converting enzyme inhibitor”, “spinal anesthesia OR general anesthesia OR epidural anesthesia AND angiotensin receptor blockers”.

All the articles which focused on the management of these drugs in the perioperative period were included. The study did not include editorial articles, narrative reviews, experimental works or abstracts from conferences.

The search was standardized and it was carried out by two independent reviewers who read the titles, then the abstracts, and then the entire article. All the works were reviewed, and those which were potentially relevant were collected for a more detailed reading by the authors. The reference lists from the relevant articles and the reviews on the subject were examined to identify additional articles. All articles identified after the comprehensive reading were classified according to the Jadad scale [17] (for randomized studies) and the Newcastle-Ottawa scale [18] (for observational studies) by the two reviewers. In case of differences of opinion with regard to the classification, the procedure was repeated by both reviewers and a third reviewer was included in case that an agreement could not be reached, until all discrepancies were corrected.

3. Results

After performing the search we screened 54 articles. Twenty two of them were excluded due to several reasons as being reviews, experimental studies or not being related with the discontinuation of the therapy (Fig. 1).

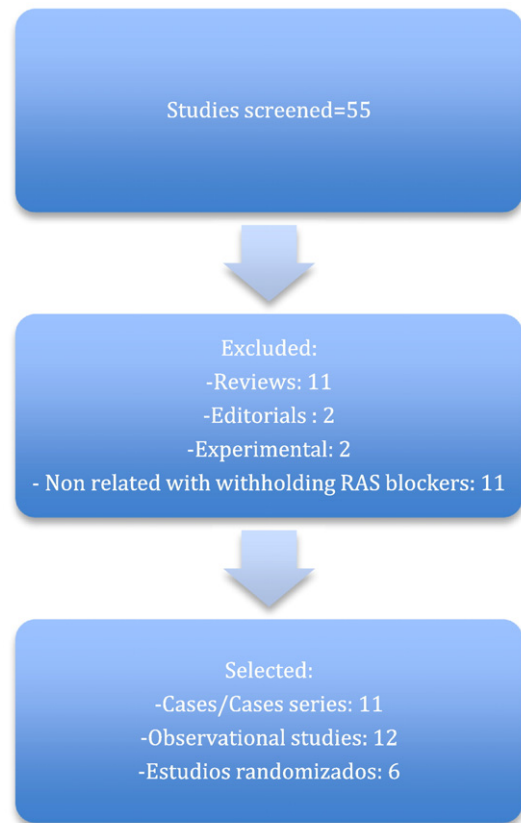


Fig. 1. Selected studies.

3.1. Clinical trials performed in general anesthesia regarding early low pressure

3.1.1. Studies with bigger hypotension in non-withhold group during general anesthesia

In 1990, in a randomized double-blind pilot study [19], captopril was administered in two doses (25 or 50 mg) before inducing general anesthesia in 40 patients (ASA 1 and 2 gynecological surgery). The study observed that patients treated with ACEI showed a higher decrease in blood pressure than those who received a placebo during the 5 min after induction (after minute 2 for systolic blood pressure—SBP—and after minute 3 for diastolic blood pressure—DBP), and that the differences are not due to chance ($p < 0.05$). A standardized pattern of anesthesia was used. The authors report that there were no differences regarding the basal characteristics of the patients.

Four years later, Coriat [20] carried out a randomized work on 56 patients who underwent peripheral vascular surgery with a standardized anesthetic pattern and similar basal characteristics (except for a higher number of diabetic and coronary patients who underwent operation in the group without treatment), and observed that in the group in which ACEI are withheld before the intervention (12 or 24 h), there is a lower number of cases of hypotension (defined as $SAP < 90$ mm Hg requiring vasoactive support) than in the group which maintains the medication until surgery: 100% of the patients who maintain enalapril undergo an episode of hypotension ($n = 11$), compared with 18% of patients if the drug is withheld. Also, 60% ($n = 19$) of the patients undergo hypotension if captopril is maintained, compared with 21% of those in which the drug is withheld ($p > 0.05$) during induction. Lower pressure levels are observed in the group which maintains ACEI and significantly higher levels are observed during post-induction in the group of enalapril users ($p < 0.05$). The dose of vasoactive agents is the same for both groups. No statistically significant differences were observed regarding the number

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