Use of α_2-Adrenergic Agonists to Improve Surgical Field Visibility in Endoscopy Sinus Surgery: A Systematic Review of Randomised Controlled Trials

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ABSTRACT

Purpose: We assessed the evidence for the use of α_2-adrenergic agonists (A2AAs) in bleeding control and field quality in endoscopic sinus surgery.

Methods: We systematically reviewed randomized clinical trials (RCTs) assessing A2AAs in endoscopic sinus surgery. Abstracts were reviewed by 2 investigators for eligibility, and selected articles were fully reviewed. Data on study design, population, A2AA drug and control groups, bleeding and surgical field quality outcomes, and adverse effects were extracted and synthesized.

Findings: A total of 13 RCTs that included 896 individuals (7 double-blind trials, 5 single-blind trials, and 1 open-label trial) were selected that assessed the efficacy of clonidine (6 RCTs, 407 patients), dexmedetomidine (6 RCT, 423 patients), or both (1 RCT, 66 patients). Clonidine was compared with placebo (3 RCTs), midazolam (1 RCT), and remifentanil (2 RCTs). Dexmedetomidine was compared with esmolol (2 RCTs), remifentanil (2 RCTs), nitroglycerin and esmolol (1 RCT), and magnesium sulfate (1 RCT). Clonidine and dexmedetomidine were compared in 1 RCT. Clonidine reduced the proportion of individuals with an impaired surgical field by 23% vs placebo (number needed to treat = 4). Clonidine was better than midazolam and remifentanil in 2 trials, and dexmedetomidine was better than magnesium sulfate and esmolol in 2 trials but was not superior to esmolol, remifentanil, or nitroglycerin in 4 trials. Dexmedetomidine produced significantly better differences in bleeding outcomes versus clonidine. Adverse events were infrequent and mainly caused by hypotension or bradycardia.

Implications: RCTs consistently report that A2AAs reduce bleeding and improve surgical field quality during endoscopic sinus surgery. Adverse event reporting was often omitted in RCTs. Well-designed RCTs with appropriate sample sizes are desirable to identify the best A2AAs and confirm their potential effects on clinical outcomes. (*Clin Ther*. 2017;▮:▮▮▮–▮▮▮)

Key words: adrenergic α_2-receptor agonists, clonidine, dexmedetomidine, otorhinolaryngologic surgical procedures, surgical blood loss.

INTRODUCTION

Endoscopic sinus surgery is minimally invasive, fast, and tolerable, but the outcome may depend heavily on the surgical field conditions.[1,2] Excessive bleeding compromises surgical field visibility, makes the identification of anatomical landmarks more difficult, and increases the risk of harming the surrounding structures. Uncontrolled bleeding also significantly increases surgical time.[3,4]

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Several approaches have been tested to reduce intraoperative bleeding, including nonpharmacologic measures, such as the reverse Trendelenburg position, and pharmacologic adjuvants, such as preoperative corticosteroids to reduce inflammation, the injection of adrenaline in the diseased mucosa before surgery, the administration of intravenous or topical tranexamic acid, and repeated packing with Cottonoid soaked in adrenaline during surgery.[5–9] In addition, controlled hypotension during surgery may be induced by using an anesthetic regimen, including opioids and/or hypotensive α_2-adrenergic agonists (A2AAs) (dexmedetomidine or clonidine). A2Aas act mainly on the central nervous system, where the stimulation of α_2-receptors induces peripheral arterial vasodilation.[10,11]

The rationale for using A2Aas to prevent intense bleeding in endoscopic sinus surgery is based on their hypotensive effect, resulting from the stimulation of α_2-adrenergic receptors in the central nervous system. A_2-Adrenergic stimulation induces hypotension as a part of the homeostatic down-regulation response to adrenergic stress but also has a sedative effect, which is desirable for adjunctive anesthesia and has been reported to reduce intraoperative and postoperative analgesic requirements.[10,12] As opposed to opioids and other agents used for hypotensive anesthesia, A2AA-mediated hypotension is not the result of peripheral effects and does not induce substantial tissue vasodilation, thus limiting mucosal bleeding during surgery.

Clonidine is an established cheap drug used for decades in hypertension in various clinical settings.[12] Although its empirical application as an anesthetic adjuvant is relatively extended, little evidence supports its use. Dexmedetomidine, a highly selective A2AA compound, became available in the United States in 1999 but was only introduced in the European market in 2011 with the indication of sedation of nonintubated patients before and/or during surgery.[13]

Interest in the use of A2Aas as adjuvant anesthetics for the reduction of surgical field bleeding in endoscopic sinus surgery has increased after a number of clinical studies have been performed. In addition, significant cost differences exist among A2AA. This information justifies this systematic review of the evidence on the use of A2Aas in endoscopic sinus surgery, whose aim is to summarize the available evidence on the efficacy of A2Aas as anesthetic adjuvants in endoscopic sinus surgery, particularly in bleeding control, surgical field quality, and the duration of surgery and anesthesia and to review possible differences in safety and efficacy between A2Aas.

MATERIALS AND METHODS

Search Strategy

Studies that assessed the efficacy of A2Aas as part of a hypotensive anesthesia regimen in endoscopic sinus surgery between January1980 and October 2017 were searched for in the MEDLINE and Scopus databases. The search used combinations of the following Medical Subject Heading terms: *otorhinolaryngologic surgical procedure, paranasal sinus surgery, endoscopy, functional endoscopic sinus surgery, endoscopic sinus surgery, microsurgery, nasal polyps, surgery, nasal septum, surgery, nasal surgical procedures, paranasal sinuses, preanaesthetic medication, sinusitis, surgery, clonidine, dexmedetomidine, intraoperative bleeding, blood loss, surgical,* and *controlled hypotension*. The language was restricted to English, French, Spanish, Portuguese, and Italian. Only full published reports of randomized clinical trials (RCTs) were considered; data from case reports, abstracts to congresses and letters not reporting RCTs, and duplicate records identified by title, authors, journal citation, and date published were excluded. Additional references were identified through by a search of references.

Eligibility Criteria

Inclusion criteria were articles on RCTs that included adult patients undergoing endoscopic sinus surgery, articles on A2Aas given orally or intravenously before surgery and/or during the surgery, and articles that compared patients with a control group treated with placebo or other drugs with randomized treatment allocation. Other operations and nonendoscopic nasal operations, such as rhinoplasty and septoplasty, were excluded. Articles that did not report outcomes for bleeding control and/or surgical field quality were excluded (Supplemental Table I).

Data Collection

Two reviewers (MAQ-M and YE) independently screened the references identified by the search strategy by title and abstract. To be selected, abstracts had to clearly identify the study design, have an appropriate