Antibiotic prophylaxis is commonly used to decrease the rate of infections in head and neck surgery. The aim of this paper is to present the available evidence regarding the application of antibiotic prophylaxis in surgical procedures of the head and neck region in healthy patients. A systemic literature review based on Medline and Embase databases was performed. All reviews and meta-analyses based on RCTs in English from 2000 to 2013 were included. Eight out of 532 studies fulfilled all requirements. Within those, only seven different operative procedures were analyzed. Evidence exists for the beneficial use of prophylactic antibiotics for tympanostomy, orthognathic surgery, and operative tooth extractions. Unfortunately, little high-level evidence exists regarding the use of prophylactic antibiotics in head and neck surgery. In numerous cases, no clear benefit of antibiotic prophylaxis has been shown, particularly considering their potential adverse side effects. Antibiotics are often given unnecessarily and are administered too late and for too long. Furthermore, little research has been performed on the large number of routine cases in the above-mentioned areas of specialization within the last few years, although questions arising with respect to the treatment of high-risk patients or of specific infections are discussed on a broad base.