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REVIEW ARTICLE

Acid-suppressive drugs and risk of pneumonia: a review

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ABSTRACT

Community-acquired pneumonia is a common diagnosis that can lead to mortality. Acid-suppressive drugs (ASDs) are used for the treatment of acid-related diseases. An acid-suppressive drug may increase the risk of community-acquired pneumonia. This study aimed to overview the association between ASDs and the risk of pneumonia. The online research process was performed to obtain articles related to the current subject using scientific websites and several keywords. Obtained articles were selected according to inclusion criteria. We obtained 16 articles, but we included only six articles according to inclusion criteria. The study concludes that there was a conflict in the results of studies and evidence regarding the role of ASDs in increasing the risk of pneumonia.

Keywords: Association, ASDs, CAP, PPIs, risk.

Introduction

Acid-suppressive drugs (ACDs) are some of the most commonly used drugs for the treatment of acid-related diseases and prevention of gastric mucosal damage; they are either proton pump inhibitors (PPIs) or histamine 2 receptor antagonist (H2RA) [1,2]. PPIs are effective in decreasing the production of gastric acid. The daily dose in most patients is 10–60 mg resulting in relief of symptoms as well as rapid healing of duodenal and gastric ulcers. Most of the patients treated with those drugs have a moderate elevation of gastrin in serum [3–5]. H2RA is a class of drugs that are used to block the effect and action of histamine on the parietal cells in the stomach, this leads to the reduction in the production of acid by these cells; these drugs are used in treating dyspepsia [1]. The usage of PPIs in the long period has been associated with both community-acquired pneumonia and hip fractures [6]. This review was conducted to overview the risk of pneumonia due to acid-suppressive therapy.

Materials and Methods

The online searching process was used to obtain articles related to the current subject by searching through scientific websites, such as PubMed and Google scholar using several keywords such as ASDs, community-acquired pneumonia (CAP), Association, Risk, and Pneumonia. We obtained 16 articles, after exclusion of repeated articles and old articles that were published before 2000, we included six articles which were published between 2004 and 2019.

Discussion

Acid suppressive drugs

ASDs represent the cornerstone in the management process of stress ulcer prophylaxis (SUP) and upper gastrointestinal bleeding in intensive care unit. Several patients require these drugs for SUP and they are admitted to general wards. ASDs are of two classes; H2RA that targets histamine, which is one of the primary acid secretion regulators and the other class is PPIs, which stop the secretion of the acid by inhibiting the proton pump located in the canalicular membrane of the parietal cells [7]. There was evaluation in the therapy of acid-related diseases by H2RAs almost 40 years ago and over the two past decades, they were superseded by more potent PPIs [8] for the treatment of peptic ulcer disease [9] and gastroesophageal reflux disease [10]. Randomized controlled trials [11,12] have clearly revealed that ASDs, especially PPIs improve the quality of life of patients and heal their serious mucosal diseases. PPIs are the only agents that showed reliability in healing uncreative esophagitis and maintain long-term healing [10]. Also, they are effective in the treatment of ulcer prevention

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caused by nonsteroidal anti-inflammatory drugs [13]. The administration of PPIs is either via oral route or intravenously [14]. Generally, these drugs are safe, but the initial concern was due to the complications that range from malabsorption of vitamin to gastric neoplasia [15]. Also, PPIs have shown short-term adverse effects, such as diarrhea, headache, fatigue, dizziness, abdominal pain, and rashes; however, these adverse effects were reported in 5% of the patients administrating PPIs [16].

Acid suppressive drugs and the risk of pneumonia

CAP is a common condition that is associated with substantial morbidity [17]. It was reported in 2006 that 4.2 million ambulatory care visits occurred due to CAP in the United States [18], and 30-day mortality ranged from 3.8% to 8.5% depending on the severity of the disease [19]. Recently, it was suggested that ASDs may increase the risk of community-acquired pneumonia [20], as both H2RA and PPIs increase the susceptibility to infections by increasing gastric pH [21]. The chronic treatment by PPI carries an increased risk of bacterial enteritis as the gastric acidity decrease and this permits the colonization of ingested pathogens and the infection of clostridioides difficile [22]. The long-term usage of PPIs has been associated with community-acquired pneumonia and hip fractures [6]. Pneumonia can be occurred by the action of PPIs, where PPIs induce the reduction of gastric acid and this may lead to the growth of aerobic bacteria in the stomach, which may result in micro-aspiration and colonization in the lung resulting in pneumonia. Moreover, PPIs can interfere with the function of neutrophil and this can increase the risk of bacterial pneumonia [23]. The bacteria can transfer to the lungs through the upper digestive and upper respiratory tracts [8]. In a case–control study [20], it was reaffirmed that PPI usage was associated with increased risk of community-acquired pneumonia, but neither shifts in microbial etiology nor protopathic bias could explain the association. Another study reported that the use of gastric ACDs was associated with an increased risk of community-acquired pneumonia [24]. Another study from Holland suggested a possible association between community-acquired pneumonia and ASD [25]. Some researchers were skeptical about the association between ASDs and pneumonia because causality seemed improbable and results were suspected to be biased [26–28]. In a systematic review and meta-analysis, there were 31 studies identified and it was interpreted that the use of PPIs and H2RA may increase the risk of both hospital-acquired pneumonia and community-acquired pneumonia [29]. There were seven studies [30] reported respiratory infection as a secondary outcome. Another systematic review [17] found that usage of PPIs by outpatients was associated with increased risk of community-acquired pneumonia by 1.5-fold, with the highest risk within the first month after initiation of the therapy. Several studies [31–34] reported no association between the use of PPIs and bacterial infection. Results were conflicted, a meta-analysis failed to show a definite conclusion as a result of these significant heterogeneities [35–39]. Although PPIs have several risks, they became one of the most commonly prescribed drugs globally. It was reported that almost 60% of patients who suffer from dyspepsia are administrating drugs like PPIs without proper indication [40]. In a Saudi study, it was found that 43% of the ASDs prescriptions were written without an appropriate indication [41]. Another Saudi study [42] reported that ASDs were the most commonly prescribed drugs without proper indication. A study from the USA reported that 54% of patients over one year in a single county hospital who discharged were given ASDs without proper indication [43]. Other studies from Ireland and Europe demonstrated that 57% and 51% of patients were improperly given PPIs, respectively [44].

Conclusion

ASDs are effective therapy, which has many beneficial effects for the humankind. However, there are debates on the role of ASDs in increasing the risk of community-acquired pneumonia as there are conflicting results about their role in increasing the risk of community-acquired pneumonia.

List of Abbreviations

CAP	Community-acquired pneumonia
PPI	Proton pump inhibitors
SUP	Stress ulcer prophylaxis

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Consent for publication

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