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Side Effect of Antipsychotic Drugs on the Gastrointestinal Tract: A Review of the Literature

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Abstract

The antipsychotic preparations which are widely used in medical practice possess an extensive range of the negative side effects including operating on organs of system of digestion. In the offered review influence of antipsychotics on a digestive tract is considered.

Keywords: Antipsychotic Preparations, Side Effect, Digestive Tract

Introduction

Currently, psychotropic drugs are among the most popular pharmacological agents [1-3]. However, these medications have a wide range of side effects that have an undesirable negative impact on many tissues, organs and systems of the patient's body [4, 5]. One of the targets of this negative effect of AP is the digestive system [6-8]. This review of the literature is devoted to the effect of AP on the gastrointestinal tract [9, 10].

Dyspeptic Disorders

Side effects of AP associated with their effect on the digestive system are often manifested in the form of dyspeptic disorders (nausea, vomiting, diarrhea, decreased appetite), which is typical for the following drugs: chlorpromazine, chlorprotixen, thioridazine, flufenazine, thioproperazine, haloperidol, trifluperidol, sultoprid and risperidone [11]. Poor nutrition and a passive lifestyle increase gastrointestinal disorders.

Dysfunction of the Salivary Glands

Usually the effect of AP on the digestive organs is due to their M-cholinolytic activity. These adverse reactions are typical for many traditional AP and some atypical drugs (clozapine, olanzapine) [12]. Thus, the blockade of M-cholinoreceptors inhibits the function of the salivary glands, which leads to the development of xerostomia (dry mouth) [12-16]. It causes discomfort in patients, but is rarely a reason for refusing treatment, since its severity significantly decreases soon after the start of APT [13]. Dry mouth does not require special treatment, but frequent mouthwashes and fluid intake are advisable to relieve the condition.

Oddly enough, clozapine causes dry mouth only in rare cases [13-18]. Unlike most AP, on the contrary, it causes hypersalivation, which is observed in about a third of patients [13]. Hypersalivation may occur much less frequently during treatment with olanzapine. The mechanism of its development is not exactly established. It is believed that hypersalivation may be associated with an increase in the secretory function of the salivary glands, as well as with a violation of swallowing due to dysfunction of the upper digestive tract.

The severity of hypersalivation is dose-dependent, and tolerance to this effect develops over time [13]. Hypersalivation increases during sleep, which is fraught with the danger of saliva aspiration and the development of aspiration pneumonia. This complication is especially common in patients with excessive sedation and prolonged physical fixation [1]. According to my data, hypersalivation is observed in 29.7% of patients with malignant neuroleptic syndrome.

Hypersalivation is one of the reasons for patients ' violation of the therapy regime due to subjective discomfort and stigma [19].

To reduce the severity of hypersalivation, drugs with different mechanisms of action are used [20-23]. This, first of all, M-holinoblokatory mainly local use: ipratropium bromide aerosol, atropine eye drops taken orally, hyoscine (transdermal patch), pirenzepine [24]. Second, the corrector of extrapyramidal symptoms (trihexyphenidyl, biperiden) [25]. Third, antidepressants with anticholinergic effects (amitriptyline) [26, 27]. Fourth, drugs that reduce the activity of the adrenergic system (clonidine, guanfacine) [28]. Fifth, terazosin, which may be more effective than cholinolytics [29, 30]. Finally, we recommend additional administration of certain AP that selectively block D2 - and D3-dopamine receptors and do not affect other mediator systems (sulpiride, amisulpiride) [31].

There are also reports on the effectiveness of botulinum toxin, which inhibits parasympathetic innervation of the salivary glands [11]. This complication can be avoided by slowly increasing the dose of the AP used, starting with very small doses.

Dysfunction of the salivary glands, caused by the side effect of AP, is one of the reasons for the appearance of dental problems in the long term (caries, stomatitis, including mycotic etiology) [11-13]. Symptoms of stomatitis can spread to the pharynx and esophagus. However, such consequences are associated not only with the side effects of AP, but also with the lack of hygienic measures in mentally ill patients.

Dysphagia

Dysphagia is a serious complication of APT, defined as disorders of swallowing and / or passing solid and liquid food through the esophagus into the stomach [32-40]. Dysphagia is caused by many AP regardless of their chemical nature and type [35]. According to the literature, the frequency of this complication of APT is from 9 to 42% [32].

This pathology receives little attention from both the patients themselves and the medical staff [14-35]. However, it is a deadly disease due to the threat of aspiration with the subsequent development of aspiration pneumonia, mechanical asphyxia due to the closure of the respiratory tract by food masses, exhaustion and dehydration [41-43].

There is evidence that the death of adults with organic mental illness is 43 times more likely to occur from asphyxia than in the General population [32]. According to our research, asphyxia as a cause of death occurs in 2.8-10.0% of patients with schizophrenia [44].

Thus, dysphagia plays a significant role in excess mortality of mentally ill patients compared to the General population [32-35].

In addition, other consequences of dysphagia include physical discomfort, anxiety about eating or drinking, and social isolation [38].

Dysphagia is divided by its mechanism into oropharyngeal and esophageal [38]. In the first case, the patient experiences difficulties when initiating swallowing or when passing food from the oropharynx to the upper esophagus. In patients with esophageal dysphagia, the passage of food through the esophagus is difficult [32-38]. AP can cause both types of dysphagia or aggravate the manifestations of an existing pathology.

The pathogenesis of dysphagia is diverse. Violations can capture different phases of swallowing [35].

1) As a manifestation of extrapyramidal syndrome caused by the side effect of AP, dysphagia develops due to a decrease in oropharyngeal reflexes and bradykinesia of the muscles of the oral cavity and pharynx [33-35]. According to my data, in malignant neuroleptic syndrome, dysphagia occurs in 21.6% of cases [1].

2) In tardive dyskinesia, the most common type of dysphagia is observed in the form of Oro-faringo-esophageal dyskinesia, and tongue dyskinesia [35-42]. This also includes esophageal dysphagia caused by asynchronous and erratic movements of the esophagus due to its isolated dyskinesia.

3) Acute laryngeal or esophageal dystonia, whether or not associated with orophacial dystonia, is characterized by a deterioration in esophageal muscle contraction and hypertonicity of its upper sphincter [35].

Risk factors such as xerostomia, poor dental status, old age, neurological diseases, polypragmasia, sedatives, and CNS depression play a certain role in the development of dysphagia. The risk of aspiration and asphyxia increases due to polyphagia and carelessness when eating, which is often observed among mentally ill people.

Diagnosis of neuroleptic dysphagia is documented by endoscopy of the upper parts of the Aero-digestive tract with dynamic tests, contrast x-ray examination of the esophagus, video fluoroscopy and manometry [42].

To facilitate swallowing, patients should be prescribed a sparing diet with a liquid consistency of food [33-38]. In severe forms of the disease, nutrition should be carried out through a nasogastric probe, sometimes it is necessary to impose a gastro-or eyunostomy [32-45]. It is also necessary to conduct maintenance and corrective therapy.
J. Horiguchi and co-authors (1999) described a marked improvement in the condition of a patient with dysphagia caused by neuroleptic language and esophageal dyskinesia after administration of sulpiride.

There have been described cases when the cancellation of trigger AP or even a reduction in its dose was sufficient for the relief of neuroleptic dysphagia [15-35]. The importance of interaction between doctors of various profiles for the diagnosis and treatment of drug-induced dysphagia in mentally ill patients is emphasized.

The most valuable method of preventing this complication of APT is to obtain accurate information about the medications taken by the patient [14].

In addition to esophageal dyskinesia, AP can cause its expansion and hypokinesia, which contributes to the violation of the function of this organ and the development of esophageal dysphagia with all the serious consequences that follow from this, described above [15, 16].

Pathology of the Stomach

There is relatively little literature on stomach pathology associated with AP administration. Reduced gastric secretion and motility caused by AP are described [46, 47]. At the same time, anorexia, nausea, vomiting, pain in the upper part of the abdominal cavity, flatulence after eating, heaviness in the abdomen, early satiation, belching, heartburn, regurgitation are observed [48, 49]. The effect of haloperidol on the stomach was confirmed in the experiment.

C. Rauber-Lüthy and co-authors (2013) report nine cases of gastric pharmacobesoar formation after taking large doses of quetiapine (6-24. 4 g, or ten to 61 tablets per day) [50]. Bezoars were detected during endoscopic examination and successfully removed. At the same time, there was a technical difficulty due to the "gelatinous-sticky-viscous" consistency of the formations.

Ogilvy Syndrome

Weakened intestinal motility is one of the typical side effects of AP, which are mainly high-potency and have pronounced anticholinergic properties [11-52]. These include periciazine, pipotiazine, levomepromazine, alimemazine, metophenazate, chlorprotixen, benperidol, and sultoprid [52-57]. However, especially often intestinal complications are observed in the treatment of clozapine.

Thus, paralytic ileus that occurs during clozapine therapy, especially in elderly patients, is a fairly serious complication, in 25-27% of cases, it is fatal.

This pathological condition is currently being considered within the framework of the so-called Ogilvie syndrome (Ogilvie), which is often observed in APT [58, 59].

The essence of the pathology is the development of paralytic colonic obstruction (acute pseudo-obstruction), characterized by the sudden appearance of pronounced dilatation of the colon in the absence of anatomical obstacles to the promotion of intestinal contents [57, 58].

The most common symptoms are bloating, flatulence, and progressive weight loss, as well as nausea, vomiting, abdominal pain, and constipation [59, 60]. The process is complicated by the appearance of fecal blockage, ischemia of the intestinal wall and the development of hemorrhagic or necrotic-ulcerative ischemic colitis with perforation of ulcers and peritonitis. Although Ogilvy syndrome is completely unknown to most practitioners, its manifestation, such as constipation, is often described as a side effect of APT.

Treatment of Ogilvy syndrome should be comprehensive [58, 59]. Tt is necessary to reduce the dose of the used trigger AP as much as possible, change the drug or even stop APT. You should install a nasogastric probe for periodic active aspiration and insert a gas outlet tube [58-60]. Cleansing enemas, especially siphon enemas, are not very effective and often even harmful because of the danger of perforation of the intestinal wall [61]. It is believed that the most effective conservative treatment for Ogilvy syndrome is colonoscopic decompression of the colon.

Drug therapy contains drugs that help to strengthen the motility of the large intestine [57, 58]. Acetylcholinesterase inhibitors (neostigmine, physostigmine, galactamine, proserine, phosphacol) are effective [62, 63-67]. The effect of the use of erythromycin, which affects the intestinal receptors and stimulates smooth muscle contractions, was revealed [11]. Normalization of the intestinal microflora is extremely important, especially in the presence of clostridial infection, which clinically manifests itself with abundant mucus discharge.

In cases complicated by perforation and the clinical picture of the “acute abdomen”, emergency surgical intervention is shown, which, according To S. O. Trenin and co-authors (2007), occurs in 22% of cases [58].

Conclusion

Thus, the negative side effect of AP extends to some extent to almost all organs of the digestive tract without exception [64]. These undesirable effects of AP are often the main cause of violation of compliance and refusal of patients from APT, or even represent a serious vital danger [6]. Therefore, it is extremely important to further accumulate knowledge on this problem in order to develop a rational clinical strategy aimed at preventing, early diagnosis and effective treatment of digestive pathology associated with AP.

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