

may not initially be recognized^{7,12}. A recent history of administration or increase in dose of an antipsychotic should raise clinical suspicion of ALD. Additional etiologies including allergic reaction and airway obstruction should be ruled out when considering ALD. If the clinical context and presentation are consistent with ALD (clutching of the throat, worsening stridor, breathiness, slurred speech, dyspnea, dysphagia, and/or dystonias in other parts of the body), the diagnosis of ALD can be made in two different ways. First, if there is immediate response to parenteral anticholinergic therapy. Second, if there is an inability to perform glottic challenges including sniffing or forceful coughing. ALD can be confirmed via laryngoscopy showing abnormal motion of the vocal cords. Vocal cords will either have decreased movement or will have paradoxical motion (adduction with inhalation)¹⁰.

Management

There are two types of medications that effectively treat ALD, anticholinergics and antihistamines. The anticholinergic medications include biperiden, benztropine, trihexyphenidyl, and orphenadrine. Diphenhydramine is the most commonly used antihistaminic agent. The route of administration can be intramuscularly or intravenously and dosing usually consists of biperiden 2mg, benztropine 2mg, or diphenhydramine 25mg to 50mg². The reversal agents should be continued over the next several days as dystonic reactions are likely to recur even if the antipsychotic is discontinued^{2,15}. Multiple cases have shown resolution of symptoms of ALD with administration of anticholinergic or antihistaminic agents^{1,4,5,6,8,9,10,13}. In one case, there appeared to be utility in using benzodiazepines in ALD¹, however there is insufficient evidence to suggest routine use of benzodiazepines in ALD. A major concern with benzodiazepines is the risk of respiratory compromise. A case reported by Lanzaro et al. described the use of clozapine in treating ALD when initial management with anticholinergics and antihistamines were ineffective. The authors attributed the improvement in the dystonia to the antidystonic effect of clozapine²⁴. It should be noted that the patient in this case was also receiving FGAs for treatment of persistent psychosis in addition to the anticholinergic and antihistaminic agents. Therefore, it is likely that substituting the FGAs for an SGA such as clozapine, which has a low potential for causing EPS, may have been key to resolving ALD in this case.

Conclusion

While ALD remains a rare complication of antipsychotic drug administration, the awareness and ability to act quickly is critical in treating this life-threatening event. The incidence of ALD related to SGAs continues to be reported in literature, therefore ALD should remain as a differential diagnosis in all patients being treated with antipsychotics

regardless of the class. Clinicians who are managing patients being treated with antipsychotics and those evaluating patients in acute care settings such as urgent cares and emergency departments should be aware of the presenting signs and symptoms of ALD and the appropriate treatment in order to prevent future deaths from occurring.

As mentioned previously, there are limited available data in the published literature regarding ALD and the cited references and conclusions are based largely on case reports and case series. This represents a limitation of this review article as the conclusions of causality cannot be inferred from uncontrolled observational data. Therefore, it may be difficult to generalize to clinical practice, introduces the possibility of over-interpretation of results, and has the potential for confounding and recall bias within the study samples. However, due to the rare nature of this disease and high likelihood of under recognition, large scale observational studies are challenging and randomized clinical trials may not capture enough events to be statistically significant. Case control studies may provide a better understanding of incidence rates, allow for detection of delayed clinical outcomes and infer causality. Despite the limitations as previously described, the cumulative data thus far provides a narrative review of a unique phenomenon that requires a high degree of diagnostic suspicion that is important to recognize in the appropriate clinical setting due to the available treatments that may be life-saving.

Conflicts of Interest

There are no conflicts of interest or forms of financial support.

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