UHN Canada's Hospital

Current Review of Pharmacological Interventions Publications

Main Takeaways Messages

When non-pharmacological interventions or verbal de-escalation are not a viable de-escalation option or are not working, light sedation should always be considered before heavy sedation.

- Light sedation should be administered using a "low and slow" dosage method.
- Light sedation medications suggested by the present research include valproic acid and benzodiazepines.

Literature Reviews

1. Au, R. T., Hotham, E., & Suppiah, V. (2023). Guidelines and treatment for illicit drug related presentations in emergency departments: A scoping review. Australasian Psychiatry, 10398562231191671.

The article provided an overview of existing guidelines and treatment approaches for managing emergency department (EDs) presentations related to illicit drug use. Within the article, illicit drug use was defined as the use of psychoactive pharmaceutical substances for non-medical purposes. Researchers identified 12 studies from Australia, the USA and the UK from a literature search and reported currently employed pharmacological and non-pharmacological treatment methods and common behavioral symptoms observed among patients admitted to EDs. The article found that agitation, aggression and psychosis were the most reported behavioral symptoms upon patient presentation. Regarding treatment methods, physical restraint use, ventilatory support, routine supportive care and bedside consultations were the most reported non-pharmacological interventions. Use of benzodiazepines and antipsychotics were reported as the most used pharmacological agents to treat agitated and aggressive behaviors among patients. Additionally, the article compared current hospital agitation management practices with each country's respective treatment guidelines. All guidelines recommended the use of benzodiazepines despite the preferred initial approach of verbal de-escalation when managing agitated patients. Additionally, restraint use was frequently reported a non-pharmacological intervention despite guidelines that warn of their use because of the potential risk to patients and hospital staff.

2. Casey, M., Elder, N., Fenn, A., Niznik, J., Khoujah, D., Ding, M., ... & Liu, S. (2023). 369 Geriatric Emergency Department Guidelines 2.0: Systematic Review on the Comparative Safety of Sedating Medications Used in the Treatment of Older Adults With Acute Agitation. Annals of Emergency Medicine, 82(4), S163

The article provided a review of sedating medications used to manage acute agitation among

older adults in out-of-hospital or ED settings. The authors acknowledged that currently used sedating medications are associated with numerous side effects and can pose further complications such as respiratory depression and/or prolonged delirium. 8 online databases were reviewed for articles relevant to acute agitation, geriatrics and sedation and were included in the study if they examined the use of first- or second-generation antipsychotics in patients 65 years or older and explored adverse side effects associated with medication use. 8 studies met exclusion criteria, totaling 194 participants across studies. Common sedative medications identified in the study included haloperidol, droperidol, ketamine, midazolam and olanzapine. Additionally, adverse events were observed in 11% of subjects in the studies explored, a rate that was increased to 29% when patients received a combination of sedative medications to manage their agitation.

3. C Prabhu, S., Geetha, H. S., Arun Kumar, S., Singh, G., & Gogtay, M. (2023). Phenobarbital versus Lorazepam for the Management of Alcohol Withdrawal Syndrome (AWS) in Hospitalized Patients-A Retrospective Cohort Study. J Community Med Public Health, 7(311), 2577-2228.

The article compared the efficacy of Phenobarbital (PB) and Benzodiazepines (BDZ), specifically lorazepam, as primary pharmacological methods for the treatment of symptoms of alcohol withdrawal syndrome (AWS) across various hospital departments. Potential symptoms characterized by AWS include mild to moderate irritability, tremors, hypertension, confusion and agitation. Additionally, the article mentions the importance of appropriate pharmacotherapy methods to prevent secondary complications associated with AWS. Contributory factors to effective pharmacotherapy cited in the article include fast onset action, wide therapeutic window, minor liver metabolism and negligible abuse potential. The study discussed a review of patients who were admitted to the ED as a result of symptoms of AWS and received PB or lorazepam based on physician preference and institutional protocol (which used current guidelines on PB usage and lorazepam usage). Researchers gathered data on patient length of stay, rate of patient admission to the ICU, whether patients needed further sedation after first medication administration, method and rate of dosage and adjunctive pharmacotherapies used in conjunction to PB or lorazepam. Results from the study stated that admission rate to the ICU was lower in the PB group than the lorazepam group. Additionally, lower intubation results were reported in PB group and the requirement of adjunctive dexmedetomidine was needed in fewer patients in the PB group than the lorazepam group. Ultimately, authors of the article suggest that BDZ class of pharmacological management methods should not be the preferred option to treat AWS.

4. Khodabux, N., Hamid, M., Perry, R., Cawley-Nash, B., Savvopoulou, I., Gumber, R., & Barrett, M. (2023). Retrospective Analysis of a Single Centre Experience of the Pharmacological Management of Patients With Intellectual Disability & Challenging Behaviour Across Three Audit Cycles. BJPsych Open, 9(S1), S165-S165.

The abstract provides an audit of pharmacological management approaches of patients with intellectual disability (ID) and challenging behavior (CB) at a large acute mental health trust in Leicester, UK. Researchers collected data from three audit cycles (2013, 2014 and 2021) on target behaviors, use of sedative medications, changes in risk assessment and physician adherence to treatment guidelines. Results from the study reported a decrease in multiple medication use to manage CB, data on the amount of participants receiving singular drug therapy increased from 19% to 34% and the number of patients on multiple medication to manage CB also declined over audit years. Additionally, the study reported an increase in documented successful management interventions from 48% to 86%. The study states that adherence to standards and treatment policy varied during audit years. A major limitation of the study is the longitudinal space between the first two audit cycles, which were conducted in 2013 and 2014 and the final audit cycle which was conducted in 2021. In addition, due to variation in treatment policy over audit years, as a result

impacting the validity of the results of the study.

5. Westafer, L. (2023). Which Sedatives Are Best for Managing Severe Agitation in the Emergency Department? ACEP Now.

This is an online article that details specific information about how to navigate agitation in patients in emergency department with sedatives. The article discusses the American College of Emergency Physicians' (ACEP) new clinical policy and highlights that current practices are often based on local traditions rather than evidence-based medicine. The policy recommends a combination of droperidol and midazolam for effective sedation, emphasizing the importance of speed in aggressive situations for safety. It also acknowledges the effectiveness of ketamine for rapid sedation when immediate safety is a concern, despite its potential for negative side effects. The goes into detail about other drugs as well, noting that midazolam is another key component for rapid sedation and that the traditional "5 and 2" combination of haloperidol and lorazepam, while effective, is slower. The article concludes by pointing out the lack of data for specific populations like older adults, pediatric patients, and those in prehospital settings.

6. [Expert consensus on management of pain, agitation and related issues in adult patients with critical respiratory diseases]. (2023). Zhonghua Jie He He Hu Xi Za Zhi = Zhonghua Jiehe He Huxi Zazhi = Chinese Journal of Tuberculosis and Respiratory Diseases, 46(12).

This publication serves as a guideline, developed by the Chinese Thoracic Society and Critical Care Medicine Group of the Chinese Association of Chest Physicians, addresses the complexities of analgesia, sedation, and rehabilitation for critically ill patients with respiratory diseases, emphasizing the need to help with discomfort caused by the disease itself, procedures, and the continuously stressful ICU environment. Pulmonary and critical care experts discussed 19 issues and provided 20 evidence-based recommendations detailed throughout the publication. The guidelines prioritize pain assessment and management before sedation and advocate for non-pharmacological interventions for delirium and sleep disruption. Notably, the recommendations emphasize a disease-specific approach to sedation, with deep sedation recommended for early ARDS and severe asthma, while maintaining spontaneous breathing with lower sedation is advised for COPD patients, highlighting an approach that reaches beyond general sedation protocols across respiratory diseases. The document stresses the importance of adjusting analgesic and sedative dosages based on individual disease characteristics and the specific analog-sedation protocol, particularly addressing the complicated pharmacokinetic alterations in patients.

7. Hupé, C., Larue, C., & Contandriopoulos, D. (2024). Defining chemical restraint: A preliminary step towards measurement and quality assessment. Aggression and Violent Behavior, 77, 101926.

This publication presents a scoping review that is also part of a larger research project about quality evaluation, focused on defining chemical restraint in healthcare and forensic institutions internationally. The authors aimed to explore the international understanding of chemical restraint and formulate its operational definition to support the development of care standards. The study involved a keyword-based literature review across health and social science databases, as well as grey literature. Data was then extracted to identify key components of chemical restraint. The findings highlight the varying interpretations of what chemical restraint does and the intent behind it. Also, the findings highlight whether chemical constraint constitutes coercion, treatment, or just an alternative to physical restraint. The proposed integrative operational definition considers the structure of chemical restraint (medications with sedative properties, routes of administration), the process (administration with or without consent, by force), and the intentions/outcomes (controlling behaviour, ensuring safety, avoiding physical restraint or seclusion). A key emphasis of this definition is the recognition of both control and protection

intentions behind the use of medications that sedate others, alongside the understanding that therapeutic intention, while possibly present, is not the central aspect of chemical restraint. The authors argue that this definition could promote more accurate reporting and allow for reduction efforts of this coercive measure.

8. White, G., Adessky, N., Chen, F. W., Regazzoni, A., Tourian, L., Chagnon, M., ... & Perreault, M. (2023). Valproic Acid For Agitation In The Intensive Care Unit: a Retrospective Analysis Of Psychiatric Consults.

The article presents a comprehensive analysis of the use of valproic acid as a treatment for agitation in intensive care unit (ICU) settings. The article cites international critical care's recommended guidelines towards the use of light sedation as a prevention method of agitation-related harm in ICU settings. It was suggested that according to recent guidelines, physicians should move away from using benzodiazepines and antipsychotics due to potential safety issues associated with their use. As a potentially alternative to the use of traditional antipsychotics, the study suggests the use of valproic acid (VPA), an anticonvulsant and mood stabilizer commonly used to treat bipolar disorder and epilepsy. Researchers in the study collected data on details regarding cause of ICU admission and cause of agitation in ICU and details regarding VPA use, including route of administration, total daily dosage, use of co-medications, RASS score and resultant agitation-related events. The study included 78 patients in the VPA treatment group and 97 in the control group. Participants in the study were all subject to psychiatric evaluation. The results of the VPA group displayed a progressive increase in agitation-free patients from day 1 of treatment (6.5%) to day 7 (39.5%). Additionally, the use of co-medication for agitation decreased from 58% at day 1 to 45% at day 7. Thus, the researchers stated that VPA could be used as a potential alternative to traditional antipsychotics due to it's absence of severe side effects like those seen in traditional antipsychotics use and it's proven results towards agitation management as seen in the study's results.

9. Wild, A., Kumar, P., Howells, F., Emara, H., & Williams, P. (2023). Comparison of Management (Non-Pharmalogical Approaches and Rapid Tranquilisation) of Older Adults (≫ 65 Years) With Dementia Between the Dementia Ward, Acute Medical Unit and the Geriatric Ward in a Rural Health Board. BJPsych Open, 9(S1), S187-S187.

The abstract examined protocol adherence for managing distress in older adults in geriatric wards and acute medical units. Practices regarding the use of managing distress using non-pharmacological approaches and rapid tranquilization were examined. Focus groups, case notes and drug charts were collected from informal discussion with nurses and junior doctors regarding their opinions on managing distressing behaviors in patients with dementia using de-escalation techniques. Results from the study support the fact that while HCWs in acute hospital wards are faced with stressful environments due to lack of staffing and high patient load, non-pharmacological de-escalation approaches were still prioritized when managing agitated patients.

10. Wilson, J., White, N., Croft, M., Ahmed, S., Illsley, L., & Hughes, P. (2023). Antipsychotic Prescribing for Behavioural and Psychological Symptoms of Dementia: An Audit of Prescribing Practices in the Harrogate Community Mental Health Team for Older Adults. BJPsych Open, 9(S1), S187-S188.

The abstract reviewed the use of antipsychotic prescription use among a mental health team in Harrogate, UK. The study explored compliance with NICE guidelines (guidelines for evidence-based recommendations for health and care in England) and improvements to the prescribing and monitoring process. Researchers collected electronic data from 24 patients related to patient records which were compared with standards from NICE guidelines developed in 2018. Results from the study state that while all 24 patients were receiving antipsychotics for severe distress and 88% of patients were assessed for source of distress before treatment began, only 42% of patients had a non-pharmacological intervention before anti-psych treatment started. For patients that did not receive non-pharmacological intervention, patient files listed reasons related to urgency of treatment or reasons were not explicitly documented/not explained well. Additionally, only 63% of files provided evidence of a discussion of the risks of treatment with the patient and less than 22% of patients had physical health monitoring at one year of treatment. The abstract provides an insight into numerous shortcomings in non-pharmacological treatment use and documentation in patient records in healthcare settings. While non-pharmacological methods are outlined as primary de-escalation methods according to NICE guidelines, the mental health team failed to employ such strategies. Researchers also suggested the implementation of checklists before antipsychotic prescription use that identifies risks and benefits, initial monitoring and suggested non-pharmacological treatment methods.