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REVIEW ARTICLE

Approach to agitation in the pediatric emergency department

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Psychomotor agitation, Child, Adolescent, Emergency Medical Services.

Abstract

Psychomotor agitation and self/hetero-aggressiveness in children and adolescents can represent a challenge in the pediatric emergency department (ED), they are a frequent occurrence that account for up to 5% of emergency assessments in the United States. Agitation is a highly nonspecific sign, which may result from organic and/or psychiatric conditions, and requires, in its management, the adequacy of ED spaces, training of the professionals involved and an increase in mental health resources in the EDs. The initial diagnostic evaluation should lead to the most appropriate therapeutic choice, although in many situations it is necessary to intervene before finishing the diagnostic exploration. This intervention must firstly contemplate environmental and non-pharmacological measures. When necessary, pharmacological restraint can be carried out, physical restraint being discouraged at these ages. There is little literature on the correct approach to these occurrences, and there is no guideline, so that more than half of the ER professionals feel inadequately prepared in their management. This work aims to bring together the evidence and consensus available in the literature to create practical support for the approach of the agitated patient in pediatric emergency care, with a focus on non-pharmacological and pharmacological approaches, it is based on a literature review, using multiple databases of articles in English, Portuguese and Spanish. The National Institute for Health and Care Excellence (NICE) guidelines were also analyzed although they apply to aggressive and violent behavior and not psychomotor agitation, understanding the difference, but looking for overlapping and applicable elements.

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INTRODUCTION

In recent years, there has been a relative increase in visits to pediatric emergency units for matters related to mental health, which account for up to 5% of pediatric visits in emergency units in the United States and appear to be a growing phenomenon.[1-3] Some authors have indicated that the increase in the number of visits to emergency units does not necessarily correspond to a growth in true medical-psychiatric emergencies, such as suicidal and self-injurious behavior.[3] Although there is no data about this situation in Portugal, it is reasonable to assume that a similar pattern of what is seen in other countries also occurs here, with behavior changes without a specific diagnosis, suicidal behavior, depression, aggression, substance abuse, and situations of violence topping the list reasons why patients arrive at emergency units for psychiatric causes.[4-5] This recent trend indicates the need to adjust the space and environment of emergency units by increasing mental health resources for subjects in this age group and training emergency healthcare workers on how to better cater to the needs of this patient group, particularly in services where emergency pediatric psychiatric care is not offered yet.[5-6]

Episodes of psychomotor agitation in children and adolescents are relatively frequent events in emergency units. Psychomotor agitation is a highly nonspecific sign,[6-8] which manifests in a wide variety of non-psychiatric and psychiatric conditions.[3-6] It is often underappreciated and quickly labeled as a symptom of psychiatric origin without much consideration of other causes, including a few potentially severe ones.[8]

Self- and hetero-aggressive behaviors, as well as agitation, represent a challenge for pediatric emergency unit teams. Several authors have noted that more than half of emergency unit workers feel inadequately prepared to manage patients with these symptoms.[9]

This article brings together evidence and consensus statements published in the literature. Its purpose is to provide practical support to teams dealing with agitated patients in pediatric emergency care. A non-systematic review was performed on medical databases PubMed, ScieELO, and Google Scholar based on search terms "Psychomotor agitation," "Child," "Adolescent," and "Emergency medical services" in English, Portuguese, and Spanish. The guidelines from the National Institute for Health and Care Excellence (UK) (NICE)[10] were also reviewed, although they apply to aggressive and violent behavior, not psychomotor agitation. Although the two situations are different, we looked for overlapping applicable elements.

There is no official guideline and a notable lack of literature on the subject. This article focuses on reaching a consensus on the non-pharmacological and pharmacological approaches applicable to pediatric patients suffering from psychomotor agitation.

DIAGNOSTIC INVESTIGATION

Many are the potential etiologies of psychomotor agitation in children and adolescents.[3-8] Patient evaluation starts from the first moments of observation and moves into assessing the level of development, language, and general physical appearance.[11] Caregivers must be interviewed for information about environmental factors and events that might trigger psychomotor agitation episodes, factors that sustain a state of agitation,[11,12] relevant elements in the patient's medical-psychiatric history, previous episodes of agitation, and response to medication.[8]

Non-psychiatric causes of psychomotor agitation in pediatric patients may include infection, metabolic and endocrine disorders, tumors, vitamin deficiencies, traumatic brain injury, accidental or intentional medicine overdose, paradoxical reaction to medication – a widespread event in this population, drug abuse to abstinence from substances, and expression of pain in children or adolescents with severe limitations in language and communication.[8,11-13] Although rare, Munchausen syndrome by proxy must be considered.

Delirium, also called acute confusional state, is an important non-psychiatric cause of refractory agitation in children, mistakenly labeled as psychiatric for frequently presenting with auditory and visual hallucinations. It is mainly distinguished by changes in the state of consciousness combined with fluctuation of symptoms. It is potentially fatal if the underlying cause is left untreated.[6,8,12]

It is difficult to estimate the relative frequency of different non-psychiatric causes of pediatric agitation in emergency care, given the highly non-specific nature of this symptom, which might be present in all medical causes of agitation.

Psychiatric causes include a wide variety of conditions. In emergency care, once organic causes have been ruled out, patients must be probed for psychiatric and medication history, family, social, and support status, particularly in emergency departments without pediatric psychiatry service, so that a referral decision can be made when needed.[4,6,11] Psychiatric agitation in children and adolescents is more often reactive to experiential and situational events. In rare cases, it can be purposeful and voluntary or stem from various environmental, physical, and individual factors.[11]

The most frequent psychiatric causes of pediatric agitation are anxiety, intellectual development disorder, autism spectrum disorder, various neurodevelopmental conditions, conduct and behavior disorders, adjustment disorder, post-traumatic stress disorder, and depression.[8,12] However, a definitive diagnosis based on symptoms and clinical history must be attained once behavioral changes have been controlled.[4]

Children with depression often present with irritability and agitation. Non-organic hallucinations and psychotic

disorders and manic or mixed states in bipolar disorder are infrequent causes of agitation in this population.[12]

No data is available on the relative frequency of different causes of pediatric agitation in emergency care since this symptom may result from multiple non-psychiatric causes. Regarding agitation for psychiatric causes, longitudinal assessment of the patient is often needed before a diagnosis is established, in an effort that involves many more than just the staff working in the emergency department, which goes beyond the scope of this work. Finally, socio-cultural factors and family dynamics may also precipitate sometimes severe episodes of agitation without an apparent underlying condition.

In the rapid assessment of agitated children or adolescents, the mnemonic "AEIOU TIPS" – widely used by medical students – can be used to remind the staff of the leading causes of changes in a patient's mental status: Alcohol, Electrolyte, Insulin (hypoglycemia), Opiates and Other Drugs (drugs, anticholinergic and sympathomimetic medications, serotonin syndrome), Uremia, Trauma, Infection (meningitis/encephalitis), Psychiatric disorder, Space-occupying lesion. Table 1 summarizes pediatric agitation's leading non-psychiatric and psychiatric causes in emergency departments.[14]

In an emergency care context, evaluating non-psychiatric causes of agitation takes precedence over psychiatric ones. Promptly assuming that agitation is due to psychiatric reasons and consequently prescribing psychotropic drugs may decrease the patient's level of activity and agitation and alleviate symptoms. Still, without addressing the cause, the ensuing false sense of resolution might delay diagnosis and deteriorate the patient's condition.

Finally, in the presence of both non-psychiatric and psychiatric etiologies, it may be necessary to intervene in acute agitation in cases where observation, evaluation, and administration of complementary diagnostic methods are challenging. In other words, intervention to contain agitation is possible as the causes of the symptom are investigated, and decisions must be based on the risks and benefits at play in each specific case.

ENVIRONMENTAL MEASURES AND NON--PHARMACOLOGICAL MANAGEMENT

There is consensus among authors that diagnosis should inform the choice of therapy and that care delivery should be individualized, multidisciplinary, and collaborative. Drugs and physical restraint should be seen as a last resort, an element of a broader short-to-medium-term therapeutic plan that goes beyond pharmacological therapy.[6,3-8] Non-pharmacological measures to reduce the escalation of agitation should be implemented early to allow patient collaboration whenever possible.[6,11-12]

The noises, the smells, the numerous patients and staff moving about, and the invasive procedures patients often undergo explain why the emergency department is a stressful environment for patients. Children and adolescents with intellectual disability, autism spectrum disorder, attention deficit disorder, or low frustration tolerance are particularly susceptible to environmental stimuli.[11] The environment patients are in, and the structural organization of that place must be considered.

Table 1. Leading psychiatric and non-psychiatric causes of pediatric agitation in emergency departments[14].

Psychiatric	Non-Psychiatric
Anxiety and acute reaction to adverse life events	*Delirium*
Adjustment disorder	Traumatic brain injury
Conduct and behavior disorders (e.g., oppositional defiant disorder)	Infectious and autoimmune diseases (e.g., meningitis, encephalitis)
Attention deficit and hyperactivity disorder	Metabolic disorders (e.g., hypoglycemia, uremia, fluid and electrolyte imbalance, vitamin deficiencies)
Disruptive mood dysregulation disorder	Poisoning/withdrawal from substance abuse or toxic substances (e.g., toxicants, drugs, alcohol)
Intellectual development disorder	Intentional and accidental medicine overdose (e.g., insulin, anticholinergic and/or sympathomimetic drugs, serotonin syndrome) or paradoxical reaction to medication (e.g., benzodiazepines)
Autism spectrum disorder	Space-occupying lesions of the central nervous system
Post-traumatic stress disorder	
Depressive disorder	
Munchausen and Munchausen by proxy syndrome (both rare)	
Psychotic disorder (with delusions and hallucinations – rare)	
Bipolar disorder (manic and mixed episodes – rare)	

*Adapted from *Bhatia R*[14].

To minimize risks for patients and healthcare workers, the environment must be safe, without elements or sharp objects that can be thrown, with furniture fixed to the walls.[6-8,11-12] Healthcare workers must position themselves between the patient and the exit door to leave the room quickly if needed. The evaluation of an agitated patient must never be conducted by a healthcare worker alone.[8]

When possible, aid from a patient family member should be sought. If the case requires it, the security team should be advised in advance of patients at risk of becoming agitated.[6-8,11-12] Caregivers may provide valuable advice on how to contain the patient and discuss strategies that have been useful in similar circumstances.

An agitated child or adolescent must be provided with a comfortable space away from other people, where they can move more freely, away from noise and bright lights, with sensory toys and other distractions of their liking, food, and beverages. Reuniting the child with their parents or removing them from the scene, depending on the situation, can be simple and effective measures to calm the child down.[11]

Unnecessary interventions should be avoided. Explaining the procedures, particularly the invasive ones, using clear and empathetic communication and a calm tone of voice, clarifying the processes and rules of interaction, asking for authorization before anything is done to the patient, mimicking the procedures on the parents before they are performed on the patient, avoiding confrontations with the patient while maintaining a neutral attitude, and avoiding negative comments or criticism is helpful.[6-8]

Training emergency teams in communication skills and dialectical behavior therapy may be helpful, as well as simulating interactions to recognize risk factors for agitation and disruptive behavior to improve performance and avoid escalation and the use of physical or pharmacological restraints.[9]

Adopting a neutral stance does not mean accepting or consenting to whatever the patient does. The aim is to contain and resolve the situation with the least possible risk.

PHYSICAL RESTRAINT

The literature describes physical restraint as a last resort, reserved for cases where all other measures (implemented in the following order: environmental, communication, and pharmacological) have not been effective. Since they have been associated with injury and death in children/adolescents, the use of restraints may prevent the formation of a therapeutic alliance with the patient, cause trauma, and hinder subsequent etiological investigation.[12] Although indicated to contain aggressive and violent behavior and not psychomotor agitation, the NICE Guidelines do not recommend the use of physical restraints in children.[10]

Once the symptoms subside, the behaviors and situations experienced during agitation must be discussed to analyze what worked and what might be done in future episodes.

PHARMACOLOGICAL MANAGEMENT

The pharmacological management of agitation in children and adolescents must consider the specificities of this age group. Medication absorption is generally similar to that of adults. However, liver metabolism, glomerular excretion, and drug distribution are more pronounced in younger people. Doses may be higher than the ones used in adults and proportional to body weight.[4]

When established, diagnosis generally directs drug prescription.[6] There are no drugs approved specifically for the control of agitation. Prescriptions are made on an off-label basis.[12]

Collecting information about current prescriptions, previous drug reactions, and medications used in earlier episodes may guide the choice of therapy, prevent side effects and drug interactions, and decrease risk.[6] Differences in the susceptibility of pediatric patients to adverse effects of psychiatric medication call for caution in prescription.[12] In an emergency, many healthcare workers prescribe the drugs they are more comfortable with. However, there may be more suitable options, hence the need to reflect and analyze pharmacological interventions.

Generally, patients should be offered oral medication before injectable drugs are considered. If possible, intravenous administration should be preferred over intramuscular.[6,8] Ideally, the choice to proceed with pharmacological treatment for agitation should be considered with the involvement and consent of caregivers.[15] If the patient is medicated, it is reasonable to use half the salvage dose, which may be sufficient to manage agitation.[6,8,11]

Several authors prefer monotherapy to the combination of several medications due to the risk of drug interactions in children and adolescents. Close monitoring of patient response (level of consciousness, vital signs, adverse effects, electrocardiogram, among others) is strictly recommended.

The classes of drugs more commonly used in clinical practice to treat pediatric agitation, in order of frequency, are benzodiazepines (lorazepam), antipsychotics (chlorpromazine and haloperidol), and antihistamines (diphenhydramine and hydroxyzine).[15,16] These drugs are generally well tolerated. However, no specific guidelines or comparative trials exist for the different medications (with sizable populations or comparative analysis of effects and impact).[15,16]

The use of antipsychotics in children and adolescents, particularly second-generation ones, has increased in recent years.[12] The list of first-generation antipsychotics used to treat children includes chlorpromazine, levomepromazine, haloperidol, and droperidol (the latter withdrawn from clinical use in Europe). The literature indicates efficacy is similar to that of second-generation antipsychotics. However, first-generation

antipsychotics are not recommended as the drugs of first choice[17] since side effects, namely extrapyramidal symptoms and cardiotoxicity, [11,17] are more frequent.

Haloperidol is effective in managing agitation and delirium.[12] However, its heightened potency increases the risk of acute dystonia, akathisia, and neuroleptic malignant syndrome. Yet, the drug lowers the seizure threshold to a lesser extent than other drugs in the same class.[17] It is an exception to the rule that monotherapy is preferable whenever possible over drug combinations. Some authors prefer the association with lorazepam instead of an additional dose of haloperidol in the absence of a complete response in the first administration.[6]

Second-generation antipsychotics used in the treatment of agitation include risperidone, olanzapine, ziprasidone, and aripiprazole. This drug class provides a better risk profile, although they may more rarely cause the same adverse events as those present in first-generation antipsychotics.[17] In this group of medications, olanzapine may have the most potent sedative effect with a lower incidence of extrapyramidal and cardiac adverse effects.[6] However, due to the risk of severe respiratory depression and death, the association with benzodiazepines or other central nervous system depressants is not recommended.[6,12,17] Aripiprazole appears to be less effective than the other drugs and may help prevent excessive sedation.[17] It is also less used in patients with autism spectrum disorders or other neurodevelopmental disorders due to the potential for activation and akathisia in the context of emergency care.[11]

Most authors advise against the intravenous administration of antipsychotics because of an association with increased incidence of torsade de pointes and sudden death, in addition to the risk of drug interactions and the lack of studies on drug safety.[12]

Benzodiazepines are the most frequently prescribed medications in the treatment of agitation in emergency settings.[16] Lorazepam appears preferable to diazepam due to complete and rapid absorption, rapid onset, short half-life, and active metabolite-free elimination.

Midazolam, although useful as a sedative, should be avoided in the treatment of agitation.[17] Intranasal midazolam has been studied in preoperative sedation to reduce the impact of anxiety or help manage uncooperative patients. Still, no studies have examined its efficacy and safety in acute agitation.

Benzodiazepines should be avoided in patients with a history of paradoxical reactions or in the treatment of delirium.[6]

Paradoxical reactions occur more frequently in patients with intellectual disability, neurodevelopmental disorders, neurological conditions, and organic brain disease. The exact frequency of occurrence is unknown.[17]

Diphenhydramine and hydroxyzine are also frequently prescribed in the management of agitation. However, they may worsen symptoms of delirium due to an anticholinergic effect. These drugs have also been associated with paradoxical agitation in children.[12,17] They constitute reasonable options in the treatment of agitation secondary to anxiety or exacerbation of an underlying anxiety disorder.[17]

Antiepileptics are ineffective and poorly tolerated.[12] Barbiturates and opioid analgesics should not be prescribed to manage agitation alone.[6] Some authors have suggested the use of clonidine, although the drug requires constant monitoring due to the associated cardiocirculatory risks.[15] Other authors are investigating a possible role for intranasal ketamine in agitation,[18] although more research is still needed.

Whenever possible, treatment should be directed at the cause of agitation. Delirium is a clear example of where it is essential to treat the organic cause underlying the symptom. The pharmacological management of delirium must include the discontinuation of drugs that may worsen the patient's condition. As mentioned, benzodiazepines, anticholinergics, and opioids should be avoided.[6,11] Second-generation antipsychotics are recommended as a complementary therapy for delirium. Risperidone, olanzapine, and quetiapine are the most prescribed.[6]

In agitation secondary to drug poisoning and withdrawal, treatment is directed and based on the suspected substance of abuse. Haloperidol and lorazepam may be considered in cases of severe agitation.[11]

Children with neurodevelopmental disorders are more vulnerable to paradoxical reactions to medication, which is why benzodiazepines should be avoided.[6] In the event of communication difficulties, the cause of agitation can be ascertained through careful observation and investigation of the patient's history.

In patients previously diagnosed with attention deficit disorder and other common psychiatric causes of agitation, it is often practical to prescribe an extra dose of the patient's usual medication or have the patient take it if the cause of agitation is the fact that the patient has forgotten to take the medication.[6]

Considering the rare nature of acute cases of psychosis or manic states in preadolescence, after organic causes have been ruled out, it is recommended that individuals showing signs of agitation are referred to a pediatric emergency service for observation.

Table 2 shows the medications more commonly prescribed for agitation with doses for pediatric patients.[19] The list was adapted from the consensus statement of the American Association for Emergency Psychiatry.[6] Some drugs and formulations mentioned in the table are unavailable in emergency units in Portugal or Brazil. However, they might be included in local formularies once adequate studies have been performed.

Table 2. Medications and doses prescribed in pediatric agitation.[19]

Medication	Dose	Peak Effect	Max daily dose	Notes/monitoring
Diphenhydramine (antihistaminic)	PO/IM: 12.5–50mg 1 mg/kg/dose	PO: 2 hours	Child: 50–100 mg Adolescent: 100–200 mg	Avoid in delirium. Can be combined with haloperidol or chlorpromazine if concerns with EPS are present. Can cause disinhibition or delirium in younger or DD youth.
Promethazine IM (antihistaminic)	<12 years: 25–50mg (max 100mg/day) >12 years: 50-100mg	> 60 minutes	Child: 50mg Adolescent: 100mg	An effective sedative, although it has a slow onset of action. Helpful if the cause of behavioral disturbance is unknown and there is a concern about the use of antipsychotic medication in a child or young person
Lorazepam (benzodiazepine)	PO/IM/IV/NGT: 0.5 mg-2 mg 0.05 mg-0.1 mg/kg/dose	IV: 10 minutes PO/IM: 1–2 hours	Child: 4 mg Adolescent: 6–8 mg Depending on weight/prior medication exposure	Can cause disinhibition or delirium in younger or DD youth. Can be given with haloperidol, chlorpromazine or risperidone. Do not give with olanzapine (especially IM due to risk of respiratory depression.
Midazolam (benzodiazepine)	IM: 0.1–0.15mg/kg PO: 300–500µg/kg or 6–10 years = 7.5mg >10 years = 10mg	PO: 15-30 minutes IM: 10-20 minutes IV: 1-3 minutes		Quicker onset and shorter duration of action than lorazepam or diazepam. IV administration should only be used (usually as a last resort) with extreme caution and where resuscitation facilities are available. Shorter onset and duration of action than haloperidol.
Diazepam IV (benzodiazepine) (Not for IM administration)	IV: 0.1mg/kg/dose by slow IV injection.	1-3 minutes	Child: 40mg Adolescent: 60mg	Long half-life that does not correlate with length of sedation. Possibility of accumulation. Never give as IM injection
Clonidine (alpha2 agonist)	PO: 0.05 mg-0.1 mg	PO: 30–60 minutes	27–40.5 kg: 0.2 mg/day 40.5–45 kg: 0.3 mg/day >45 kg: 0.4mg/day	Monitor for hypotension and bradycardia. Avoid giving with BZD or atypicals due to hypotension risk.
Chlorpromazine (antipsychotic)	PO/IM: 12.5–60 mg (IM should be half PO dose) 0.55 mg/kg/dose	PO: 30–60 minutes IM: 15 minutes	Child <5 years: 40mg/day Child >5 years: 75mg/day	Monitor hypotension. Monitor for QT prolongation
Haloperidol (antipsychotic)	PO/IM: 0.5 mg-5 mg (IM should be half a dose of PO) 0.55 mg/kg/dose	PO: 2 hours IM: 20 minutes	15–40 kg: 6mg >40 kg: 15 mg Depending on prior antipsychotic exposure	Monitor hypotension. Consider EKG or cardiac monitoring for QT prolongation, especially for IV administration. Note EPS risk with MDD > 3mg/day, with IV dosing having very high EPS risk. Consider AIMS testing.
Olanzapine (antipsychotic)	PO/ODT or IM: 2.5–10 mg (IM should be half or 1/4 dose of PO)	PO: 5 hours (range 1–8 hours) IM: 15–45 minutes	10–20 mg Depending on antipsychotic exposure	Do not give with or within 1 hour of any BZD given risk for respiratory suppression
Risperidone (antipsychotic)	PO/ODT: 0.25–1mg 0.005–0.01mg/kg/dose	PO: 1 hour	Child: 1–2 mg Adolescent: 2–3 mg Depending on antipsychotic exposure	Can cause akathisia (restlessness/agitation) in higher doses.
Quetiapine (antipsychotic)	PO: 25–50 mg 1–1.5 mg/kg/dose (or divided)	PO: 30 minutes-2 hours	>10 years: 600 mg Depending on prior antipsychotic exposure	More sedating at lower doses Monitor hypotension.

PO, by mouth; *IM*, intramuscular; *IV*, intravenous; *NGT*, nasogastric tube; *mg*, milligram; *EPS*, extrapyramidal symptoms; *DD*, developmental disability; mg/kg, milligrams per kilogram; *BZD*, benzodiazepines; *EKG*, electrocardiogram; *AIMS*, Abnormal Involuntary Movement Scale; *MDD*, major depressive disorder; *ODT*, orally dissolving tablet. *Adapted from Gerson R, Malas N, Mroczkowski MM[19]

FINAL CONSIDERATIONS

Agitation may be challenging to manage in an emergency care setting. There is a lack of guidelines stipulating the emergency measures required for pediatric patients.

Diagnostic evaluation is an essential element in the definition of therapy, as is the analysis of the risks and benefits of the medication prescribed to manage agitation.

Case series should be developed and analyzed so that preventive and management measures for pediatric agitation

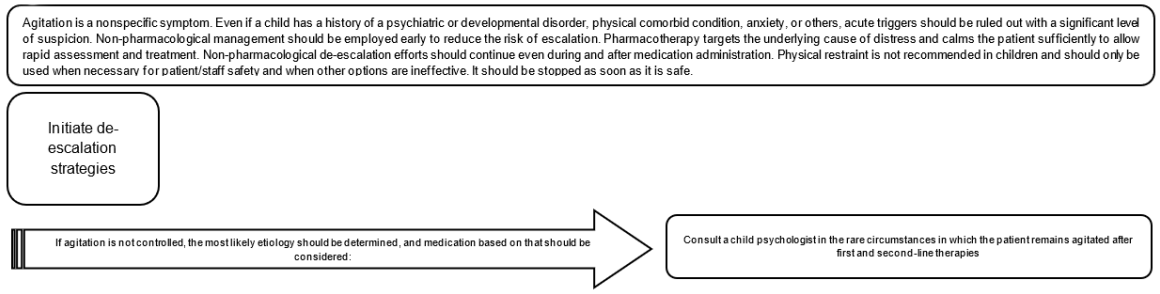
are defined. Emergency care teams should also be adequately trained to deal with agitation, mainly when pediatric psychiatry services are unavailable in the emergency unit.

Chemical restraint should only be considered once environmental and communication strategies have been implemented. This may require reorganizing the spaces in the emergency department and providing, for example, rooms away from the overly stimulating emergency department area and specific training for healthcare workers on agitation management. The primary objective is to calm the patient without sedating them to reduce suffering and anxiety, the risk of injury to themselves, healthcare workers, and others, and allow the correct assessment of the patient, ideally with their collaboration and involvement, and avoid traumatic events.

The use of medical resources must be based on evidence, not on the list of the "most prescribed" drugs. If implemented by trained professionals, behavioral and environmental measures may diminish the need for other measures.

More studies are needed about the drugs used in an emergency setting, including evaluations of short- and long-term drug safety and comparative studies between the available options and the optimal ones that should be integrated into emergency department practice. Discussing this subject and planning interventions may be the first step to improving the knowledge and quality of management practices. Figure 1 shows a proposal for a clinical decision flowchart[20] to assist emergency care teams in managing pediatric agitation. The flowchart presented below was adapted from the consensus statement of the American Association for Emergency Psychiatry.[6]

Figure 1. Medical decision flowchart.[20]



Environmental	Behavioral	Psychological	Personal Space	Body Language	Ask about what might be helpful	Other
Decrease stimulation (dim lights, play music, or favorite TV program).	Provide age-appropriate distraction, set reasonable limits, and explain consequences.	Provide one-on-one verbal support, use open questions, listen without rushing, stay calm, and manage pain/hunger.	Keep a distance of at least two times your arm's length.	Maintain calm posture, expression, and behavior.	Ask about techniques and tools that have helped in the past.	Reward cooperation and active listening, and develop empathy with the patient.

It is Delirium (Acute onset/fluctuating symptoms, inattention, disorganized thinking, or altered level of consciousness)	→ History, DAU, physical examination	- Manage the underlying medical conditions - Manage pain - Avoid benzodiazepines and anticholinergics since they may worsen delirium	→ Patient still agitated, needs medication	PO: quetiapine, olanzapine, risperidone or clonidine IM: olanzapine, chlorpromazine, haloperidol IV: haloperidol +/or Lorazepam or Diazepam if there is risl of seizures or catatonia
	→	Unknown substance: BZD, + haloperidol in case of severe agitation or hallucination	Withdrawal from alcohol/BZD or stimulant drug poisoning: BZD, +	Withdrawal from opioids: Clonidine and/or replacement with Methadone/Buprenorphine/Tramadol +

Is it substance poisoning or withdrawal syndrome?			haloperidol in case of severe agitation or hallucination	drugs to manage symptoms (ibuprofen, loperamide, ondansetron…)
		PCP: BZD	Poisoning by alcohol/BZD: Haloperidol or Chlorpromazine	Negative DAU? Consider synthetic cannabinoid or cathinone: BZD +/- Haloperidol or Chlorpromazine (PO/IM)
Patient with developmental delay or autism? (Greater risk of delirium and adverse or paradoxical reactions to medication)	Yes →	- Try behavioral interventions - Assess pain, hunger, and other physical needs - Consider visual communication and sensory tools - Ask caregivers about what usually calms the child - Ask about previous responses to medication (positive and negative), mainly BZDs e diphenhydramine.	Ainda agitado Precisa de medicação →	- Consider an extra dose of MH. - Avoid BZDs due to risk of disinhibition. - Avoid IM medication Clonidine or diphenhydramine or antipsychotics (risperidone, chlorpromazine, or olanzapine)
Is there a clear psychiatric diagnosis?	Yes →	Agitated catatonia: BZD	ADHD: clonidine or diphenhydramine or risperidone (in case of risk of hypotension)	Mania or psychosis (rare!): - If the patient is on antipsychotics, consider an extra dose of MH. - Risperidone or Chlorpromazine or olanzapine or haloperidol +/-BZDs
		Anxiety/trauma/PTSD: BZD or clonidine (if there is risk of disinhibition)	Conduct disorder: chlorpromazine or BZD or olanzapine or risperidone	
Unknown cause	Yes →	Mild agitation/verbal aggression: - Environmental and behavioral measures	Moderate agitation, aggression directed to objects: - Diphenhydramine or BZDs or olanzapine	Severe agitation, self-aggression, and aggression toward persons: - Chlorpromazine or haloperidol + BZD or Olanzapine

PO, by mouth; IM, intramuscular; IV, intravenous; BZS: benzodiazepines (lorazepam, diazepam, midazolam…); PCP: phencyclidine and/or ketamine; PTSD: post-traumatic stress disorder; ADHD: attention deficit and hyperactivity disorder.

→ Olanzapine and BZD must not be prescribed together due to the risk of respiratory depression (see Table 2).

→ Diazepam, avoid intramuscular route of administration (see Table 2).

*Adapted from Gerson R et Al[2]

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