

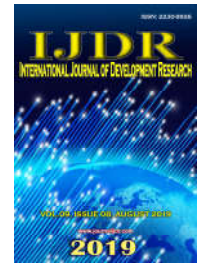


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REVIEW ARTICLE

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EVALUATION OF DELIRIUM IN INTENSIVE PEDIATRIC THERAPY UNITS: AN INTEGRATIVE REVIEW

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ABSTRACT

Delirium is a change in attention or awareness associated with changes in cognition, which occurs over a short period of time, may originate from cortical and subcortical dysfunctions, due to problems in the concentrations of neurotransmitters, responsible for cognitive function, behavior and mood. This study aimed to analyze the specialized literature regarding the incidence, evaluation and treatment of delirium in pediatric critical care. It is a study of bibliographical review of the integrative type, based on the analysis of scientific articles, with a quantitative focus on incidence, risk factors and evaluation of Delirium in the Pediatric Intensive Care Unit. Cohort studies, case studies and online surveys were considered, resulting in a final sample of 17 articles. There was a predominance of recent publications, between 70 and 70% of the cohort, prospective, 58.8%, use of pCAM-ICU, 35.7% of the evaluated articles, and 45.4% indicating more than 30% of occurrence of delirium in their samples, occurring more frequently in patients submitted to mechanical ventilation, 46.2%. Through the research, it was verified that few tools are applied in the diagnosis of delirium, which should be encouraged in health institutions.

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INTRODUCTION

The critical pediatric patients present fast deterioration which skin lesions, infections and respiratory diseases (asthma and bronchiolitis) the most common causes of hospital admission and they might need intensive care assistance (BENNEYWORTH *et al.*, 2015). The intensive care exposes the patients to pain and stressful events, thus analgesia and sedation are essential to these patients care, especially the ones in mechanical ventilation. The main indication to use analgesia and sedation are: pain management, anxiety and physical agitation; improve the synchronization with the mechanical ventilation; avoid the loss of catheters and endotracheal tubes and reduce the cellular metabolism (VET *et al.*, 2013; HARRIS *et al.*, 2016). However, the excessive sedation due to the concern of lost devices and accidental extubation result in increasing time of mechanical ventilation and more time of hospitalization in the Intensive Care Unit (ICU), brain

dysfunction, medicine toleration, abstinence syndrome and delirium. To improve the sedated patient care, the scales and protocols of analgesia and sedation integrated to a brief daily interruption of sedation result in lower using of it, mechanical ventilation and hospitalization in ICU. (HUGHES; GIRARD; PANDHARIPANDE, 2013; KEOGH; LONG; HORN, 2015; MOTTA *et al.*, 2016). The complications of pediatric sedation are: respiratory problems, medication error, difficulty with intravenous puncture and pulmonary aspiration and might cause nausea, vomiting, pain and delirium (BECKE *et al.*, 2014). *Delirium*, from Latin *de-lira* (be out of the place) is a neurocognitive disorder resulting of somatic disease or its treatment. It is a behavior manifestation of brain dysfunction associated to underlying medical illness. It presents as a floating changing in the mental state. It is a known and prevalent problem in adults and children intensive care and may lead to an increase of mortality and in the medical assistance costs. This imbalance happens because of the illness itself or administration of psychoactive medications (SCHIEVELD *et al.*, 2015; SILVA, 2015; SILVER *et al.*, 2015; PISANI *et al.*, 2009; KUDCHADKAR; YASTER;

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PUNJABI, 2014). Delirium presents repercussions in short and long term: catheters removal, accidental extubations, increasing in mechanical ventilation use, more time of hospitalization, bigger rate of mortality, cognitive damage in long term and post traumatic disorder (SALLUH *et al.*, 2010). In view of the above, the question is: What is the current panel of incidence, risk factors and assessment of *Delirium* in Pediatrics Intensive Care Unit? Therefore, the main goal of this study is analyze the produced knowledge in relation to the incidence, assessment and treatment of delirium in the care of critical pediatric patients.

METHODOLOGY

This study is an integrative review, which constitutes a broader methodological approach regarding other revisions, where there is the possibility of insertion of experimental or non-experimental studies, in order to have a subsidy for a complete understanding of the phenomenon. The steps to the elaboration of this study were: theme identification, delimitation of the guiding question, definition of inclusion and exclusion criteria, establishment of the most relevant information to be selected in the researches, minacious analyses of the included studies in review, interpretation and presentation of results. To the sample selection were used scientific articles in Portuguese and English language published in the last 10 years in reference timing from 2006 to 2017, which were related to the topic *Delirium in pediatric patients in Intensive Care Unit*.

The data were collected in BVS (Biblioteca Virtual de Saude/Health Virtual Library), MedLine, PubMed, LILACS (Literatura Latino – Americana e do Caribe em Ciências da Saude) e SCIELO (Scientific Electronic Library online - Brazil). It was inserted the keywords: “*delirium*”, “*pediatria / pediatric*” and “*unidade de terapia intensiva / intensive care unit*”, The data collection was performed from July to August 2017. The inclusion criteria were: Available texts, completed or summarized, in Portuguese or English, published from 2007 to 2017 which were categorized as cohort, case control, observational, prospective or longitudinal studies. It were not included literature review studies. The exclusion criteria were studies published before 2007, repeated and the ones which do not have the theme or content related to this study. Initially, it was performed the reading of the article’s titles, then the abstract focusing in the inclusion and exclusion criteria. In cases which the title and the abstract do not match with the searched topic, the complete publication was searched in order to be able to prove whether or not it answered the guiding question. Regarding *Delirium*, the analysis was done in quantitative terms, presenting the data to be constructed in tables that included incidence, risk factors, prevention with sedatives and assessment tools of delirium in pediatric ICUs.

RESULTS AND DISCUSSION

From the literature review, it was found 6232 articles related to the keyword *Delirium*; after inclusion of the ICU keyword, the sample decreased to 669; Pediatric descriptor was then included and the sample changed to 23 articles. Of these, it was considered cohort studies, case studies and online surveys, resulting in a final sample of 17 articles (TABLE 1). The selected articles were organized and analyzed systematically from the elaboration of an Excel sheet (Table 1) containing the descriptors: title, authors, published year, study type,

sample size, study place and goals of the analyzed studies and categorizations according to the aims of the research. According to table 2, there is a predominance of recent publications, from 2015 to 2017, 70.6% of the articles selected.

Table 1. Description of the selected sample. São Luís, Maranhão, 2019

Articles	Total	Selected
Keyword		
<i>Delirium</i>	6232	
<i>Delirium</i> ; UTI	669	5563
<i>Delirium</i> ; UTI; Pediatric	23	
Studies types		
Literature review		6
Coorte studies	12	
Case studies	2	
Online Survey	3	
TOTAL	17	

Table 2. Selected studies by publication year. São Luís, Maranhão, 2019

Ano	n	%
2007	1	5,9
2010	1	5,9
2011	2	11,8
2014	1	5,9
2015	5	29,4
2016	3	17,6
2017	4	23,5
TOTAL	17	100

The study type more prevalent among the selected ones was cohort, prospective was 58.8% of the sample, online survey was 17.6%. These were performed by physicians in different countries.

Table 3. Selected publications by study type. São Luís, Maranhão, 2019.

Study type	n	%
Cohort, prospective	10	58,8
Online Survey	3	17,6
Case study	2	11,8
Multicentric research	1	5,9
Cohort, prospective, of validation	1	5,9
TOTAL	17	100,0

The assessment tool more used to evaluate *delirium* in ICU was the pCAM-ICU scale according to 35.7% of the evaluated articles, following of DSM-IV with 21.4%, CAP, Clinical suspicious e PAED had 14.3% of use and SBS with 7.1%.

Table 4. Assessment tools of *Delirium* used at pediatric ICU according to the selected studies. São Luís, Maranhão, 2019

Authors (APENDICE A)	%	Assessment tools
4, 7, 10, 15, 17	35,7	pCAM-ICU
1, 6, 9	21,4	DSM-IV
2, 12	14,3	CAPD
8, 13	14,3	Clinical suspicious ¹
3, 14	14,3	PAED
1	7,1	SBS

¹The clinical suspicious is determined as “confusion, agitation, moans, behavior disorder without acceptable medical explanation”

The pCAM-ICU scale was one of the most reported in the study of Gusmao-Flores (2015) which made a multinational inquiry with pediatric ICU professionals to determine the

practices related to the assessment and management of delirium, verifying superior frequency among the Brazilian interviewed when compared to international professionals interviewed (83.0% versus 43.5% respectively; $p < 0,001$). In Brazil, the use of the validated method was higher (85,0% versus 55,1%; $p < 0,001$). This tool was used in the research by Rosen, Mervitz, Cravero (2016), described by most of the professionals investigated in their study on the experience and opinions of Canadian pediatric anesthesiologists on the incidence of *Delirium*. Smith *et al.*, (2011) shows that Pediatric Confusion Assessment Method for Intensive Care Unit (pCAM-ICU) has validity and reliability to delirium assessment when compared to DSM-IV criteria (sensitivity of 83% and specificity of 99%). This questionnaire also was used on his research in 2017 (SMITH *et al.*, 2017).

The psCAM-ICU is an assessment tool of delirium highly valid and reliable for children critically sick and school age children. The availability of monitoring tool of delirium as psCAM-ICU and PCAM-ICU, offers an opportunity to detect delirium in pediatric cohorts in different ages (SMITH *et al.*, 2016). The Kudchadkar, Yaster e Punjabi (2014) study, with the goal of examine the treatment of pediatric sedation in intensive care, the sleep promotion and the screening practice of delirium for intubated and mechanical ventilated children, discovered that most of the intensive care professional do not use the validate methods of assessment of sedation to guide their choices, even there are many different validated methods. The COMFORT index still being the punctuation system more used, even though the American professionals report the increased in the use of the Sedation and Agitation Scale of SBS. This one was projected and validated in 2006 to identify the *continuum* of sedation- agitation in children. The Silva's (2015) study, using the CAPD tool had as result the fake positive, once the CAPD presents lower specificity in patients with development delay, thus the use of an efficient observational tool to detect *Delirium* in children favors the screening of hospitalized patients in intensive care units.

According Somaini *et al.*, (2015), in his results had some difficulty to differentiate delirium and pain using the PAED score. "No eye contact", "No intentional action" and "No place consciousness" were significantly related to *delirium*. 'Inconsolability' and 'Restlessness' are not reliable enough to identify pain or delirium in the fifteen first minutes after awake. This score also was used by Shin, Lee e Kim (2016), in their study case this score was very efficient on the patient's diagnosis. In relation to the DSM-IV, the author Schievelde *et al.*, (2007) considers that DSM-IV's criteria are not useful in pediatric *delirium* cases, especially in the ICU.

This is a topic of concerning and indicates that delirium is not mentioned on the DSM-IV section about pediatric psychiatric. DSM-IV describes as an essential feature of delirium the "consciousness disorder" leading to "harm the concentration, changing and keep focus skills", which the authors consider with little relevance in critical patient's case. The DSM-IV also was used by Malarbi *et al.*, (2011) and Silver *et al.*, (2015). Among the evaluated articles, 11 show in their results the incidence of Delirium in pediatric ICUs, however the studies also show heterogeneous results. It was possible notice that 45.4% of the study indicates more than 30% of delirium and the others (54, 5%) indicates until 30% of occurrence.

Table 5. Incidence of Delirium in Pediatric ICUs according to the selected literature. São Luís, Maranhão, 2019

Incidence of <i>Delirium</i>	n	%
Until 20%	3	27,3
20 to 30%	3	27,3
More than 30%	5	45,4
TOTAL	11	100,0

In accordance with the Smith *et al.*, (2011) results, the DSM-IV assessments diagnosed *delirium* in 13, 2% of the evaluated patients, while pCAM-ICU diagnosed only 11% of *delirium* in these patients. Smith *et al.* (2016) study reveals that the general prevalence of *delirium* of this cohort using the psCAM-ICU was 44% of the evaluated patients. The *delirium* rate was 53% in patients younger than 2 years old against 33% in 2 to 5 years old patients. Additionally, using the psCAM-ICU, the hypoactive delirium (81%) was extremely predominant when compared to the hyperactive subtype (19%). On Silva's (2015) study, 32% of the patients present at least one positive evaluation to *delirium*. Few studies performed with children show a variable incidence: 5% (SCHIEVELD *et al.*, 2007), 4 to 16% (VAN DIJK *et al.*, 2012), 30% (SMITH *et al.*, 2013). Differently from these articles, Smith *et al.*, (2017) found high frequency of 44% of delirium during at least once per day as on the Schievelde *et al.*'s (2007) study where 61% of their evaluated patients were diagnosed with *delirium*. On the study made by Traube *et al.*, (2017) among 835 evaluated patients, 25% was diagnosed positively to delirium, superior result to the Somaini *et al.*'s study (2015) which 21% of the results were positive. Fewer studies reported about the risk factor related to Delirium on the selected literature, being the mechanical ventilation the factor that were more mentioned (46.2% of the articles). The using of Benzodiazepine as anesthetic (15.2%) and children younger than 2 years old (15.4%), was verified factor, as the time of hospitalization at ICU (7.7%).

Table 6. Risk factors to Delirium in Pediatric ICUs according the selected literature. São Luís, Maranhão, 2019

Risk factors	n	%
Mechanical ventilation	6	46,2
Benzodiazepine	2	15,4
Younger than 2 years old	2	15,4
Time of hospitalization at ICU	1	7,7

In their study Smith *et al.* (2017) searched to determine associations between pediatric delirium and modifiable risk factors, the exposition to benzodiazepines is associated to the development, more duration of delirium and less probability of discharge at ICUs. The author also present in their study that there is a significantly relation between long staying at ICUs and the usage of this medication. Traube *et al.* (2017) identified the prevalence of delirium in children critically sick and the risk factors associated to. Those one who stayed for 6 or more days in the pediatric ICUs had a higher prevalence of delirium (about 38%). The Silver *et al.*'s study (2015) reports that the mechanical ventilation was statistically consider more significant in the prediction of pediatric delirium (OR = 3, 86 (1,81, 8,24), $p = 0,0005$). In relation to the medical inquiry made using the online survey. In this study were evaluated 990 physicians who work in pediatric ICUs in different countries. When they were questioned about the use of medication to avoid Delirium, their answers pointed among 17 and 82% of them chose Midazolam.

Table 7. Sedative used to treat Delirium according to the Online Surveys

Articles	Propofol	Midazolam	Fentanyl	Haloperidol	Dexmedetomidine
15	42	31	10		5
16		82	76		
17		17	3	66	30

Among 3 to 76% of them prescribe Fentanyl. Only one of the articles identified that 66% of the physicians chose Haloperidol as a treatment medication to Delirium. And 42% of them prescribe Propofol as a treatment medication (ROSEN; MERVITZ; CRAVERO, 2016; KUDCHADKAR; YASTER; PUNJABI, 2014; GUSMAO-FLORES, 2015). In accordance with Traube *et al.* study (2017), the time of hospitalization in the pediatric ICU was increasing in children who developed delirium (Odds ratio: 2,3; CI = 2,1-2,5; p <0,001), the duration of mechanical ventilation use (4 vs 1 d; p <0,001). Delirium also was a strong predict factor of mortality (odds ratio: 4,39; IC = 1,96-9,99; p <0,001). According to Silva's study (2015) presents that at the moment that the delirium were detected, 57% of the patients were using mechanical ventilation. Also on SchievelD *et al.* study (2007) the mechanical ventilation was the support used by 85% of the patients with delirium. The patients that need invasive ventilation used to be considered more critical and possibly more susceptible to develop delirium. However, in 37% of the positive evaluation to delirium, the patients were using only oxygen therapy. It was analyzed 3 articles based on online surveys, where the interviewed professionals who work in pediatric UCIs pointed that the most common medication used to treat Delirium was Midazolam and Fentanyl, followed by Dexmedetomidine, Propofol and Haloperidol. Currently, the systematic review shows that the use of some medication categories is related to the increase of the risk to develop delirium. Opioids (RR=2,5; IC 95%: 1,2-5,2), benzodiazepines (RR=3,0; IC 95%: 1,3-6,8), dihidropiridines (RR=2,4; IC 95%: 1,3-6,8); and antihistamine (RR=1,8; IC 95%: 0,7-4,5). The authors recommend the reduction or suspension of benzodiazepines, while the opioids should be administrated with precaution to control the pain. (CLEGG; YOUNG, 2011). The using of venous anesthesia in the pediatric population shows advantage related to the faster recover, the reduction of vomiting and nausea, the decreasing of delirium in post-operative (BORGES *et al.*, 2016).

Conclusion

Through this research, it was possible identify some tools used to diagnose Delirium. This practice should be encouraged in the health institutions, since delirium is a relevant complication of critical illness on children, with identifiable risk factors. It is essential to analyze these risk factors to be possible the efficient prevention and treatment that could be medication or the patient environment. Multicenter researches, control study case and longitudinal studies would be useful to determine the precision of the screening tools in the pediatric ICU and the related risk factors. It is also crucial to encourage the implantation of protocols of systematic evaluation of delirium, leading to define efficient interventions. The incidence decreasing of delirium in the pediatric ICUs should be considered as a quality indicator which represents the improvement of the patient care assistance.

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Quadro 1. Planilha descritiva de artigos utilizados na revisão de literatura

Artigos	Autores	Ano	Tipo de estudo	Local do estudo	Amostra	OBJETIVO	Incidência de Delirium	Sexo	Fatores associados a delirium	Escala de avaliação de delirium
1	SCHIEVELD et al.	2007	Coorte, observacional, prospectivo	UK	61	Estudar a fenomenologia, correlatos clínicos e resposta ao tratamento do delirium em crianças gravemente doentes em unidade de terapia intensiva pediátrica (UTIP)	65	62% M	VM 85%	DSM-IV
2	RASS	2015	Coorte, observacional, prospectivo	BR	47	Conhecer a incidência de delirium na Unidade de Terapia Intensiva pediátrica do Hospital Materno Infantil de Brasília.	32	60% F	VM 57%	CAPD
3	SOMAINI, et al.	2015	Coorte, observacional, prospectivo	EUA	150	Avaliar a possibilidade de distinguir entre Delirium e dor.	21			PAED
4	SMITH, et al.	2017	Coorte, observacional, prospectivo	EUA	300	Determinar associações entre delirium pediátrico e fatores de risco modificáveis.	44		Benzodiazepine 75%	CAM-ICU
5	TRAUBE, et al.	2017	Coorte, observacional, longitudinal	EUA	1547	Descrever a frequência de delirium em crianças gravemente doentes, sua duração, fatores de risco associados e efeitos nos desfechos intra-hospitalares, incluindo mortalidade.	17		Tempo de UTI / VM	
6	SILVER, et al.	2015	Coorte, observacional, prospectivo	EUA	99	Descrever um estudo piloto de instituição única sobre prevalência e fatores de risco para o delirium em crianças criticamente doentes	21	57% M	Idade, VM 54	DSM-IV
7	SMITH, et al.	2011	Coorte, observacional, prospectivo	EUA	68	Validar um instrumento diagnóstico para o delirium pediátrico em crianças gravemente doentes	13,2	77% M		CAM-ICU
8	SMEETS, et al.	2010	Coorte, observacional, prospectivo	NL	147	Investigar, sob circunstâncias de cuidados de rotina, o impacto do delirium pediátrico (PD) no tempo de permanência na unidade de terapia intensiva pediátrica.	33			Clínica

9	MALARBI, et al.	2011	Coorte, observacional, prospectivo	AUS	198	Determinar os comportamentos centrais do Delirium que discriminam a condição de dor e birra em crianças pequenas e agrupar esses comportamentos de acordo com os critérios principais de diagnóstico do DSM-IV / V e os comportamentos associados ao delirium	-					DSM-IV
10	SMITH, et al.	2016	Coorte, observacional, prospectivo, de validação	EUA	300	Determinar a validade e a confiabilidade de uma ferramenta de avaliação de delirium fundamentalmente objetiva e adequada ao desenvolvimento para crianças gravemente enfermas e crianças em idade pré-escolar e para determinar a prevalência de delirium.	44	63% M	VM 43			CAM-ICU
11	TRAUBE, et al.	2017	Pesquisa multicêntrica	EUA	994	Determinar a prevalência de delirium em crianças criticamente doentes e explorar fatores de risco associados	25			idade inferior a 2 anos, ventilação mecânica, benzodiazepínicos		
12	SIMONE, et al.	2017	Coorte, observacional, prospectivo	EUA	1875	Examinar o impacto de um pacote de UTI natriagem e prevalência de delirium e descrever características de casos de delirium	17					CAPD
13	MESQUITA	2016	Estudo de caso	BR	1	Apresentar estudo de caso de um paciente pediátrico em delirium na UTI	-	55% M				Clínica
14	SHIN; LEE; KIM.	2016	Estudo de caso	IND	1	Apresentar o resultado do tratamento com ríspidona em um paciente pediátrico em delirium na UTI	-					PAED

Quadro 1. Planilha descritiva de artigos utilizados na revisão de literatura. (continuação)

Artigos	Autores	Ano	Tipo de estudo	Local do estudo	Amostra	OBJETIVO	Propofol	Midazolam	Fentanyl	Haloperidol	Dexmedetomidina	Escala de avaliação de delirium
15	ROSEN; MERVITZ; CRAVERO	2015	Pesquisa online		209	Extraíra experiência e opiniões de anestesiolistas pediátricos canadenses sobre a incidência de delirium.	42%	31%	10%		5%	CAM-ICU
16	KUDCHADKAR; YASTER; PUNJABI	2014	Pesquisa online		345	Examinar práticas de controle de sedação pediátrica intensiva, promoção do sono e delirium para crianças intubadas e mecanicamente ventiladas.		82%	76%			SBS
17	GUSMAO-FLORES	2015	Pesquisa online		436	Conduzir um inquérito multinacional com profissionais de unidades de terapia intensiva para determinar as práticas relacionadas à avaliação e ao manejo do delirium		17%	3%	66%	30%	CAM-ICU
