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REVIEW ARTICLE

- ² Viral bronchiolitis in young infants:
- $_{\scriptscriptstyle 3}$ new perspectives for management and treatment $^{
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Iornal de

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KEYWORDS Abstract Objective: The aim of this review was to address advances in management and treatment of Viral bronchiolitis; acute viral bronchiolitis in infants. 10 Infants: Sources: A systematic review search was made including all articles published in English 11 Respiratory syncytial between 2010 and 2017, and available in the electronic databases PubMed and Cochrane Cen-12 virus tral Register of Controlled Trials (CENTRAL) and specialized register of the Acute Respiratory Q3 13 Infections Group (Cochrane review group). The following MESH terms in English were included, 14 using different Boolean operators for the search strategy: "bronchiolitis, viral," "diagnosis," 15 "epidemiology," "etiology," "therapy," "virology," "prevention and control," "respiratory 16 syncytial virus, human," Additional filters were used. 17 Summary of findings: Few effective interventions are recommended for the management of 18 RSV bronchiolitis in young infants. The main goal is to ensure an adequate oxygen supplemen-19 tation and fluid balance whenever deemed necessary. Hypertonic saline nebulization is helpful 20 only for hospitalized infants. Numerous antiviral drugs and specific vaccines for RSV are under 21 evaluation and foretell advances in disease management in the near future. 22 Conclusion: A number of promising new technologies are advancing in the field. Until new 23 interventions became feasible, early detection and modification of preventable risk factors is 24 essential to improve outcomes. 25 © 2017 Sociedade Brasileira de Pediatria. Published by Elsevier Editora Ltda. This is an open 26 access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/ 27 4.0/).

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PALAVRAS-CHAVE Bronquiolite viral; Neonatos; Vírus sincicial respiratório

Bronquiolite viral em neonatos jovens: novas perspectivas para manejo e tratamento

Resumo

Objetivo: O objetivo desta análise é abordar avanços no manejo e no tratamento de bronquiolite viral aguda em neonatos.

Fontes: Uma pesquisa de análise sistemática foi realizada e incluiu todos os artigos publicados em inglês entre 2010 e 2017 e disponíveis nas bases de dados eletrônicas PubMed, no Registro Central de Ensaios Controlados (CENTRAL) da Cochrane e no registro especializado do Grupo de Infecções Respiratórias Agudas (grupo de revisão Cochrane). Os seguintes termos MESH em inglês foram incluídos na abordagem utilizando diferentes operadores booleanos para a estratégia de pesquisa: "bronquiolite, viral", "diagnóstico", "epidemiologia", "etiologia", "terapia", "virologia", "prevenção e controle", "vírus sincicial respiratório, humano". Foram utilizados filtros adicionais.

Resumo dos achados: Poucas intervenções efetivas são recomendadas para o manejo da bronquiolite por VSR em neonatos jovens. O principal objetivo é garantir uma suplementação de oxigênio adequada e equilíbrio de fluidos sempre que considerado necessário. A nebulização de solução salina hipertônica ajuda apenas em casos de neonatos hospitalizados. Vários medicamentos antivirais e vacinas específicas contra VSR estão em fase de avaliação e predizem avanços no manejo da doença no futuro próximo.

Conclusão: Várias novas tecnologias promissoras estão avançando no campo. Até que as novas intervenções se tornem viáveis, a detecção precoce e a modificação de fatores de risco de prevenção são fundamentais para melhorar os resultados.

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53 Introduction

Respiratory syncytial virus (RSV) bronchiolitis is the most 54 frequent cause of lower respiratory tract illness (LRTI) and 55 hospitalization in young infants worldwide.^{1,2} This disease 56 is associated with up to 199,000 deaths every year in chil-57 dren under the age of 5 years, and approximately million 58 hospitalizations annually.¹⁻⁴ Of these deaths, 99% occur in 59 developing countries.¹ In developed countries, RSV deaths 60 are infrequent and associated with chronic lung disease, 61 neuromuscular disorders, heart disease, Down's syndrome, 62 and preterm birth.⁵ By the age of 2 years, over 95% of the 63 children have been infected by the virus. 64

Acute RSV bronchiolitis is a seasonal disease, which often 65 starts every year between fall and spring, and peaks in win-66 67 ter. The tropics are the exception, and there is no specific seasonality in these regions, although some epidemics are 68 hypothesized to be associated with the rainy season.² RSV 69 infection is typically mild and begins with upper respira-70 tory tract signs, mimicking a common cold.^{7,8} After a few 71 days, some patients will progress to experience disease 72 affecting the distal bronchioles, with clinical signs of tachyp-73 nea, wheezing, crackles, rhonchus, and chest retractions.^{7,9} 74 Approximately 1-3% of infected children develop feeding 75 difficulties, apnea, or are unable to maintain adequate 76 oxygen saturation (SpO₂), requiring hospital admission for supportive therapy.^{2,4,10} A small number of infants, espe-78 cially those with co-morbidities, will progress to respiratory 79 failure or death.^{1,2,5} There are several studies suggesting an 80 81 association between severe bronchiolitis by RSV and recurrent wheezing, an association that disappears by the end of 82 the first decade of life.¹¹⁻¹³ With greater frequency than RSV, 83

rhinoviruses, when combined with early life atopic sensitization, are associated with asthma.¹⁴ In 2009, the total cost for hospitalizations due to bronchiolitis in the United States was close to two billion dollars. Although trends in hospitalizations rates in the US have declined between 2000 and 2009, costs have raised at the expense of increased use of intensive care for high-risk patients.¹⁵ Despite its high morbidity, the economic expenses, concerning mortality rates in developing countries, and the association of RSV with transient lung sequelae (e.g., recurrent wheezing), treatment of RSV LRTI is still symptomatic and has significant gaps. Moreover, over fifty years after its discovery, no licensed vaccine against RSV is available. Palivizumab, an effective humanized monoclonal antibody (mAb) against the RSV fusion (F) protein, is available for preterm infants, infants with BPD, and infants with cyanotic congenital heart disease.¹⁶ Even though palivizumab significantly reduces severe RSV LRTI, the drug is expensive and requires several doses, limiting its use in industrialized and developing countries. Therefore, safe and inexpensive vaccines and treatments are urgently needed to decrease the impact of RSV in children.

Sources

A systematic review search was conducted, and it 106 included articles published in English between 2010 107 and 2017, available in electronic databases PubMed, 108 Cochrane Central Register of Controlled Trials (CENTRAL), 109 and specialized register of the Acute Respiratory Infec-110 tions Group (Cochrane review group). Recent guidelines 111 reports were also searched. The following MESH terms 112 in English were included in the approach using different 113

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