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IMMUNODEFICIENT STATES IN PRETERM AND TERM INFANTS WITH RECURRENT RESPIRATORY DISEASES

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იმუნოდეფიციტური მდგომარეობები მორეციდივე რესპირატორული დაავადებების დროს დღენაკლ და დროულ ახალშობილებში.

[1] თსსუ პედიატრიის კათედრა, ინგოროყვას მაღალი სამედიცინო ტექნოლოგიების საუნივერსიტეტო კლინიკა, [2] თსსუ პედიატრიის დეპარტამენტი, [3] თსსუ იმუნოლოგიის დეპარტამენტი, ვლ.ბახუტაშვილის სახელობის სამედიცინო ბიოტექნოლოგიის ინსტიტუტი

რეზიუმე

მძიმე რესპირატორული დაავადებები იმუნოდეფიციტის ხშირი გამოვლინებაა. ჩვენი კვლევის მიზანია იმუნოდეფიციტური მდგომარეობების გამოვლენა დღენაკლულ ჩვილებში, ხშირი მძიმე რესპირატორული დაავადებებით, მართვის ტაქტიკის, რეციდივების პროფილაქტიკის და ფილტვების შემდგომი დაზიანების მინიმიზაციის მიზნით. კვლევა შემთხვევა-კონტროლი ტარდებოდა 8 თვის განმავლობაში.

53 დღენაკლული ბავშვი, რომლებმაც გადაიტანეს მწვავე რესპირატორული დისტრესი და ფილტვების ხელოვნური ვენტილაცია ნეონატალურ პერიოდში, რომელთაგან ექვსს, კომპიუტერული ტომოგრაფიით გამოუვლინდათ პათოლოგიური ცვლილებები (ფიბროზული ინფილტრატები, მოზაიკური მილევა, გაუმჭვირვალე მინის ტიპის დაჩრდილვა), შევადარეთ 32 დროულ ახალშობილს, საკონტროლო ჯგუფიდან.

ორივე ჯგუფი ხასიათდებოდა ხშირი რესპირატორული ავადობით. IgG და IgA დეფიციტი გამოუვლინდა ძირითადი ჯგუფის 18 (33,96%) პაციენტს და საკონტროლო ჯგუფის 1 (3,125%) პაციენტს. ფიშერის ტესტის ზუსტი სტატისტიკური მნიშვნელობა P-მნიშვნელობა შეადგენს 0,0009. იმუნოგლობულინის ინტრავენური გადასხმა ჩაუტარდა 18 დღენაკლი ახალშობილიდან 8-ს. მომდევნო 3-7 თვის განმავლობაში რესპირატორული დაავადებების რეციდივი არ დაურეგისტრირდა 6 (75%) პაციენტს. 1 (12,5%) პაციენტს ერთჯერადად აღენიშნა მსუბუქი სიმპტომები, ზედა სასუნთქი გზების მხრივ, 1 (12,5%) პაციენტი განმეორებით იქნა ჰოსპიტალიზებული სუნთქვის უკმარისობით. 3–7 თვის განმავლობაში, სულ მცირე ერთი განმეორებითი ჰოსპიტალიზაცია დაურეგისტრირდა 10-ს, 18 დღენაკლი პაციენტიდან, რომლებსაც არ ჩაუტარდა იმუნოგლობულინის ინტრავენური გადასხმა.

ჩვენი კვლევის მიზანი გულისხმობს შესაძლო მიზეზ-შედეგობრივი კორელაციის გამოავლენას მორეციდივე რესპირაციულ დაავადებებსა და იმუნოდეფიციტურ მდგომარეობებს შორის ნაადრევად დაბადებულ ახალშობილებში. აღნიშნული მოგვცემს საშუალებას გავაუმჯობესოთ პაციენტების მართვა, შევამციროთ ავადობის რეციდივი, ფილტვის შემდგომი დაზიანება და ჰოსპიტალიზაციის სიხშირე.

Pediatric respiratory tract infections are a universal clinical problem across the whole childhood that is associated with significant morbidity and mortality [4,6]. The role of pediatricians is to discriminate among the child with transient increased morbidity and child with increased, complicated respiratory morbidity, which evokes the possible immune defect.

Severe respiratory diseases are common manifestations of immunodeficiencies [4,6]. Prognosis is greatly dependent on infectious and non-infectious respiratory complications. Thus it is extremely important to diagnose PIDs instantly to prevent significant morbidity and mortality [2,8]. Regular examinations by the appropriate tests should reveal the respiratory and immunologic pathologies in the

early stages. Raising awareness of PIDs improves the prognosis of these patients. However, deciding which children to investigate and when is quite challenging for physicians.

The most common clinical manifestation of predominant humoral and/or combined immunodeficiencies are prolonged and recurrent infections involving the respiratory tract, e.g., rhinosinusitis, otitis media, bronchitis, bronchiectasis, and pneumonias [1,4,6]. Respiratory infections in PIDs patients are usually severe, persistent, and recurrent in comparison with infections in non-PID patients. The clinical symptoms in humoral deficiencies, typically tend to occur after the first 6 months of life (after the disappearance of maternal IgG), however, sino-pulmonary infections may occur earlier [3,5]. Clinical history is the most important aspect of suspecting a diagnosis of primary humoral immunodeficiency. Therefore, patients at any age with recurrent upper or lower respiratory infections, where the frequency, severity, course of an isolated pathogen is unusual should be investigated for possible humoral or other type immunodeficiencies [2,8].

Patients with frequent respiratory conditions who are suspected of having immunodeficient states may be evaluated for having:

1. predominantly humoral (antibody) deficiencies,
2. combined T-cell and B-cell immunodeficiencies,
3. other well-defined immunodeficiency syndromes,
4. congenital defects of number and/or function of phagocytes,
5. complement deficiencies,
6. defects of immune dysregulation,
7. autoinflammatory disorders
8. defects in innate immunity.

Among all the immunodeficiencies, antibody deficiencies are the most frequent and comprise approximately 70–75% of all PIDs [1,2,7]. These patients are typically characterized by different respiratory symptoms and complications due to the inherited immune defect. In children, respiratory symptoms are a typical initial presentation of various PIDs. However, also the other groups and classes of PIDs can be associated with significant respiratory morbidity and manifestations Through two simple widely available tests – serum immunoglobulin concentration (IgG, IgA, IgM, and ±IgE) and differential leukocyte cell count – the majority of the PID can be detected and revealed. Therefore, these two simplex tests can be in general recommended as screening tools for PIDs in primary care [8].

Material and methods. The goal of our study is to reveal immunodeficient states in preterm infants with frequent severe respiratory diseases to improve management plans, prevent recurrences and minimize further lung damage.

A case-control study was performed for 8 months.

85 patients who had multiple severe respiratory conditions (bronchiolitis and/or pneumonia) in anamnesis and were hospitalized for respiratory distress syndrome in our clinic were further investigated.

Upon admission to our hospital, all 85 patients expressed increased breathing rate (RR 60-80) (100%), grunting (89%), nasal flaring (72%), retractions (100%), wheezing (100%).

The experimental group contained 53 infants who were born preterm, had ARDS after birth (42%), were exposed to mechanical ventilation in the neonatal period, had multiple (at least twice a month) severe respiratory conditions (bronchiolitis and/or pneumonia) in anamnesis (100%) and were hospitalized for respiratory distress syndrome in our clinic (100%).

6 of the 53 preterm patients showed CT scan abnormalities (fibrotic infiltrates, mosaic attenuation, ground-glass opacity). 32 patients were born term, had frequent severe respiratory conditions in anamnesis (100%), and were hospitalized for respiratory distress syndrome in our clinic (100%).

Blood immunoglobulin tests were performed in all these patients. Both IgG and IgA were deficient in 18 (33.96%) patients of the study group and 1 (3.125%) patient from the control group. IgG and IgM were deficient in 6 (11.3%) preterm infants, IgA was deficient in 4 preterm infants (7.55%). 2 of the patients are diagnosed as having Bruton agammaglobulinemia. Genetic tests were not performed on other patients. The Fisher exact test statistic P-value is 0.0009.

IVIG was transfused in 8 of the 18 preterm infants. During the next 3 to 7 months recurrence of the respiratory conditions was not reported in 6 (75%) patients; 1 (12.5%) patient experienced mild upper respiratory symptoms once, 1 (12.5%) patient was readmitted with respiratory failure.

During 3 to 7 months at least one readmission was reported in 10 of 18 preterm patients who were not transfused IVIG.

None of the term patients were transfused IVIG and 6 of them experienced mild upper respiratory disease once during the next 3 to 7 months.

Results and discussion. In general, a thriving child with recurrent respiratory infections does not suffer from a serious underlying disease. Most of the children do not have an immunodeficiency, but if they do, this often concerns an antibody deficiency [1,7]. The most common clinical manifestation of predominant humoral (and combined immunodeficiencies with associated antibody defects) are recurrent and prolonged infections involving the respiratory tract, either upper airways (e.g., sinusitis and otitis media) or lower respiratory tract [e.g., pneumonia, bronchiectasis, and interstitial lung diseases (ILDs)] [4,5]. The complications from the lower respiratory tract are usually considered to be more important and also more specific for PIDs and they determinate patients' prognosis [4,6]. Predominantly humoral immunodeficiencies represent clinically the most important group of inherited immune defects. The most frequent defects are selective deficiency of IgA, deficiencies of IgG subclasses [2,3,8].

In our study, all the patients had symptoms of respiratory distress upon admission to our hospital, but the course of the disease was far more severe in preterm patients with humoral immunodeficiencies. According to the obtained data, the IgG and IgA deficiency was the most common (33.96%) humoral immunodeficiency in tested patients. IgG and IgM were deficient in 11.3% of preterm infants, IgA was deficient in 7.55%. 2 of the patients were diagnosed as having Bruton agammaglobulinemia. The cause of the immunodeficiency in other patients is still in the research process, it is not determined whether the immunoglobulin deficiency is because of the primary immunodeficiencies or it is transient immunodeficient states in preterm infants whose immune system is not still mature. Repetitive evaluation of blood immunoglobulin levels was done in those patients who were transfused IVIG. 4 of the 8 patients had normal Ig levels on repetitive tests, 4 patients were still IgG deficient, and considering the deficient level of IgG, 3 of them were transfused IVIG again. Frequency and/or severity were decreased in all of those patients. 6 patients were satisfactory on regular follow-ups, 1 patient had a mild respiratory disease and 1 patient had severe respiratory failure once during 3 to 7 months.

The appropriate therapy using the immunoglobulin substitution and antibiotics usually leads to the significant decline of the frequency and severity of infections with a significant impact on the life quality and prognosis of these patients [6,7]. All our patients were treated for their specific infectious diseases, 8 of them were transfused IVIG.

Conclusion. The newborn infant is especially vulnerable to a range of respiratory diseases, that are presenting with signs of respiratory distress. Thorough clinical assessment and appropriate investigation are required for all infants presenting with signs of respiratory distress to ensure accurate diagnosis and correct treatment.

The research may reveal a correlation between frequent respiratory diseases and immunodeficiencies as either the cause or the result of the conditions in preterm babies, thus allowing us to improve management techniques to decrease recurrences and reduce further lung damage and readmission rates in the patients.

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IMMUNODEFICIENT STATES IN PRETERM AND TERM INFANTS WITH RECURRENT RESPIRATORY DISEASES

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SUMMARY

Severe respiratory diseases are common manifestations of immunodeficiencies.

The goal of our study is to reveal immunodeficient states in preterm infants with frequent severe respiratory diseases to improve management plans, prevent recurrences and minimize further lung damage.

A case-control study was performed for 8 months. 53 preterm infants who had ARDS and were exposed to mechanical ventilation in the neonatal period, 6 of which showed CT scan abnormalities (fibrotic infiltrates, mosaic attenuation, ground-glass opacity), were compared to 32 term infants from the control group. Both groups presented with frequent severe respiratory diseases. IgG and IgA were deficient in 18 (33.96%) patients of the study group and 1 (3.125%) patient from the control group. The Fisher exact test statistic P-value is 0.0009.

IVIG was transfused in 8 of the 18 preterm infants. During the next 3 to 7 months recurrence of the respiratory conditions was not reported in 6 (75%) patients; 1 (12.5%) patient experienced mild upper respiratory symptoms once, 1 (12.5%) patient was readmitted with respiratory failure. During 3 to 7 months at least one readmission was reported in 10 of 18 preterm patients who were not transfused IVIG.

The research may reveal a correlation between frequent respiratory diseases and immunodeficiencies as either the cause or the result of the conditions in preterm babies, thus allowing us to improve management techniques to decrease recurrences and reduce further lung damage and readmission rates in the patients.

Keywords: respiratory distress. Immunodeficiency, diagnostics, infant, preterm infant