

Assessment of the differentiated aspiration process of palivizumab

Análise do processo diferenciado de aspiração do palivizumabe

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Descritores

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Abstract

Objective: Assess the differentiated aspiration process of palivizumab, from planning to administration, and from the patient's profile to obtained savings as a result of the optimization of doses.

Methods: Cross-sectional study carried out by means of secondary data obtained from the medical records of 858 children. Variables of the study were as follows: information on the profile of cared children, amount of acquired and administered doses, vaccination procedure, and optimized doses. Data were extracted from care management reports.

Results: The innovative technique and the vaccination planning allowed for 98 children to be favored by leftovers of the medication, implying savings of R\$ 1.144.347,52 in 2012 and 2013.

Conclusion: The employment of the differentiated aspiration process favored the availability of the medication to 54 children other than those previously programmed, and the application of 78 leftovers. The establishment of a previous management planning process of programmed contents to be administered to children, in compliance with their profile, especially their body weight, favored the inclusion of other admitted newborns. The systematization process of the team work toward the administration of palivizumab implied the reduction of public expenditures.

Resumo

Objetivo: Analisar o processo diferenciado de aspiração do palivizumabe, do planejamento para a administração, do perfil da clientela e da economia obtida pela otimização das doses.

Métodos: Estudo transversal realizado com dados secundários obtidos nos prontuários de 858 crianças. As variáveis de estudo foram: informações sobre o perfil das crianças assistidas, quantidade de doses adquiridas e administradas, procedimento de aplicação diferenciado e doses otimizadas. Os dados foram extraídos dos relatórios de gestão da assistência.

Resultados: A técnica inovadora e o planejamento da administração assegurou a 98 crianças serem beneficiadas com 166 sobras da medicação e implicou em economia de gastos na ordem de R\$ 1.144.347,52 em 2012 e 2013.

Conclusão: A aplicação do processo diferenciado de aspiração favoreceu a viabilização do medicamento para 54 crianças além das programadas, com utilização de 78 sobras. A gestão do agendamento das crianças com planejamento prévio do volume preparado, de acordo com o perfil das mesmas, em especial o peso corporal atualizado, favoreceu a inclusão de novos neonatos internados. A sistematização do processo de trabalho da equipe para a administração de palivizumabe implicou em redução de gastos públicos.

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Introduction

Acute respiratory infections show expressive indicators of morbidity-mortality in children. The infections are characterized by acute inflammatory infectious or non-infectious processes that affect alveoli, bronchioles, bronchi, and interstitial spaces. The respiratory syncytial virus is one of the major etiologic agents involved in the acute respiratory infection.⁽¹⁾

Worldwide, it is estimated that this virus leads to 2.3% of deaths among newborns from 0 through 27 days of age, as well as 6.7% among children between 28 and 364 days of age. Additionally, respiratory infection episodes affect nearly 34 million children below five years of age and cause 10% of these cases to be admitted in hospitals. In the United States, from 1997 to 2006, between 132,000 and 172,000 children with less than five years of age were estimated to be admitted in hospitals as a consequence of infections produced by the respiratory syncytial virus.⁽²⁾

In Brazil, the virus has been accountable for 75% of bronchiolitis and 40% of pneumonia in children below one year of age. Usually, the evolution of the infection results in a common cold; however, 25% of children present complications and are ultimately admitted in hospitals.⁽¹⁾ In Sao Paulo, Southeastern Brazil, 147,532 children were admitted in hospitals under the diagnosis of bronchiolitis/acute bronchitis and pneumonia between 2008 and 2012. In the first six months of 2013, 10,745 admittance processes were reported.⁽³⁾

The risk factors associated with the infection of the lower respiratory tract, and therefore susceptible to infections by the virus, are: children with less than six months of age, particularly those who are born during the first half of the birth seasonality; children that go to day care centers; babies and children with subjacent pulmonary disease, such as chronic pulmonary disease; babies born prior to 35 weeks of pregnancy; babies and children with congenital cardiac disease; children who are exposed to passive smoking; and immunocompromised patients (for instance, serious immunodeficiency, com-

bined leukemia or bone marrow disease, or lung transplant recipients). Genetic predisposition has also been pointed out as a potential factor.⁽²⁾

Currently, the prophylactic treatment given to this viral infection is performed by the application of an IgG-class humanized monoclonal antibody, which neutralizes the F protein of the virus and hinders its access to the inside of the host cell, hence preventing the formation of syncytia.⁽⁴⁾

Such immunoprophylaxis has been approved by the Food and Drug Administration (FDA) toward preventing serious lower respiratory tract diseases provoked by respiratory syncytial virus in children of up to two years old who comply with one or more of the following high risk criteria: gestational age lower than 35 weeks; chronic pulmonary disease; cyanotic congenital cardiopathy; or other complexities.⁽⁴⁾

In Brazil, palivizumab is commercialized under the Synagis® trademark and has been recommended by the National Commission of Technology Incorporation to the Unified Health System in July 2012 toward preventing serious infections associated with the respiratory syncytial virus in children belonging to the highest risk subgroup to hospitalization or complication processes, that is, premature babies with gestational age lower than 28 weeks and children of up to two years old who have chronic pulmonary disease and congenital cardiac disease.⁽¹⁾

Packaged in a vial, the lyophilized whitish powder-based drug becomes clear and lightly opalescent following its reconstitution, and must be used in a maximum period of 6 hours. The recommended posology is 15 mg/kg, administered via intramuscular shot once a month within the seasonality period of the respiratory syncytial virus, five months a year. Stronger doses of 1 ml must be subdivided.⁽⁵⁾

The Sao Paulo State Secretariat of Health has been making the drug available to patients on a legal basis since 2006.⁽⁶⁾ The technical board of the Hospital Maternidade Leonor Mendes de Barros, one of the hospitals located in the southeastern area of the city of Sao Paulo, has been carrying out a program based on a local legislation established in

2008. Some children who were appointed to take the drug started receiving it during their hospitalization process, as the institution seeks to comply with the recommendation of the Unified Health System and also with the mother-child binomial. As of 2010, specific cases started being effectively reported and therefore, up to 2013, the unit immunized a total of 1,141 children between 1 day and 2 years of age.

After the incorporation of the technology in the state of Sao Paulo, and more recently nationwide,⁽⁷⁾ a systematized process has been created in order to manage the administration of this medication, aiming at reducing costs as a result of the optimization of doses.

Aiming to collaborate with the construction of knowledge concerning new techniques that favor the optimization of resources and the reduction of child mortality, the objective of this present study was to assess the differentiated aspiration process of palivizumab, from planning to administration, from the patient's profile to the savings obtained by the optimization of doses in the systematized management process created to the administration of such drug in the referred hospital.

Methods

Cross-sectional study on the differentiated aspiration process of palivizumab carried out in the medication administration center of the Hospital Maternidade Leonor Mendes de Barros.

The variables of the study were as follows: information on the profile of cared children; amount of doses acquired and administered; differentiated application procedure; and optimized doses. Data were collected from care management reports in 2012 and 2013 and organized in Excel® spreadsheets by the unit's team, who later submitted them to the researchers, following the agreement of the institution's technical director.

The study complied with national and international ethical guidelines for studies involving human beings.

Results

Since the onset of the implementation of the immunobiological medication administration center of the Hospital Maternidade Leonor Mendes de Barros, the technical team was focused on optimizing the resources as a way of broadening the access of children indicated to take palivizumab. Among the developed strategies, a more accurate aspiration of the drug has been assessed and improved, especially motivated by the perception of leftovers in the vials after the dilution process (diluent and solute), in compliance with the recommendations of the manufacturer.

Figure 1 depicts the palivizumab vial and the usually employed aspiration needle (on the left), and the Quincke spinal needle (on the right), showing the reach of the needles to the solution and the flexibility that can provide the technician with the



Figure 1. Vial with the palivizumab solution with common needle and spinal needle

possibility of aspirating the whole wall of the vial, a process named here as “off-label use”.

The second strategy created by the immunization team was to develop a care management process that could allow for the full use of the prepared medication by the group of children scheduled and confirmed to receive the drug.

The flow of such care conventionally begins at the Sao Paulo State Secretariat of Health, which receives the requirements and medical prescriptions to the children applying for the treatment and who meet the pre-established criteria toward accessing the intervention. These patients are distributed among the several immunobiological medication administration centers, such as the Hospital Maternidade Leonor Mendes de Barros, or specialized drugstores that receive the vials

(on legal basis), and the medication is administered at the site chosen by the person responsible for the child.

The Health Secretariat issues an electronic list of authorized children, counting on the following information: name of the person responsible for the child; identification of the child; telephone number; and town of residence. With such information in hand, the hospital's team contacts the person responsible for the child by telephone, complementing and updating data; the most relevant piece of information is the estimated and updated weight of the child, which is the basis for the calculation of the total preparation of doses. Such information allows for the planning of the necessary volume for a one-day work. In this process, it is also necessary to acknowledge the basic clinical conditions of the child, such as eventual occurrences of fever, infection signals, among others, which contraindicate the administration of the medication in the scheduled date. The process is then rescheduled for a time when the child is fully ready to receive the drug.

In 2012, 409 children were scheduled to receive palivizumab at the Hospital Maternidade Leonor Mendes de Barros. Nevertheless, only 393 effectively showed up, configuring an absenteeism index of 3.9%. The major cause of absence (56.2%) was the impossibility of locating the child due to incorrect or insufficient records. From the assisted children, the majority (34.0%) presented a prematurity diagnosis, followed by cardiopathy, 12.0%. The largest amount of children (34.0%) lived in Sao Paulo, Southeastern Brazil; 33.7% were less than one year of age. In 2013, the absenteeism index reached 2.7%; however, in 84.6% of cases, the major reason was the hospital admittance process within the period of administration of some doses. A total amount of 478 children received referrals and the medication was administered in 465 of them, with a predominance of 34.6% of premature children (similar to the records in 2012), 18.1% came from Sao Paulo and 13.5% were less than one year of age.

As for the savings obtained by the health team as a result of employing the new aspiration technique, chart 1 shows the dose, vial and expenditure figures related to the administration of palivizumab.

The cost of the aspiration process of palivizumab that employed spinal needles in 2012 reached R\$373.70 (101 used needles) and R\$436.60 (118 used

needles) in 2013. Subtracting the value applied to purchase the needles, the total amount saved with the process reached R\$1,143,537.22, that is, over a million, one hundred thousand reais (Chart 1).

Chart 1. Comparison between doses and consumed vials, and expenditures with palivizumab

Doses/consumed vials/expenditures	2012	2013
Correlation between administered dose and consumed vial	1,367/1,360	1,704/1,605
Total expenditure of consumed vials	R\$ 5,717,576.00	R\$ 6,748,399.05
Doses to be made available at specialized drugstores*	1,455	1,782
Total expenditure of vials made available at specialized drugstores	R\$ 6,117,707.55	R\$ 7,492,615.02
Expenditure difference between the medication administration in the centers and the medication made available at specialized drugstores	R\$ 400,131.55	R\$ 744,215.97
Total savings with palivizumab	R\$1,144,347.52	

* For this calculation, the study did not take into account those children who would need two vials as a result of a medical prescription that exceeded 1 ml of the drug

Discussion

One of the limitations to a more detailed analysis of the results of this research is the fact that 54 patients who received the leftovers of palivizumab were not followed up. Studies have shown that the application of the medication in children significantly reduces the number of hospitalization processes caused by the respiratory syncytial virus.

The objective of the present study was to show the differentiated aspiration process and management of palivizumab, aiming to optimize the dosing and expand the coverage of patients in need of the administration process that is carried out by the health team of the Hospital Maternidade Leonor Mendes de Barros.

In view of the daily observation of palivizumab, a few strategies started being tested by the hospital's team so that a full aspiration of the medication could be carried out, as the leftovers were quite significant.

Among the hospital's byproducts identified in the institution's daily practices, a certain type of needle allowed for the full removal of the solution from the vial, the spinal needle. The primary characteristic of such needle is its Quinke tip, described by the manufacturers as a bevel-tip needle that enables a more effective aspiration of palivizumab, thus facilitating the collection of the whole remaining drug solution. The second

characteristic is the flexibility of the needle, allowing for its contact with all the internal walls of the vial and allowing for the maximized aspiration of the solution. A third feature is the length of the needle, which reaches the total height of the vial.

The “off-label use” of the needle enables a full aspiration of the drug solution, thus contributing to its complete reutilization.

The commercialized cost of the Quincke bevel-tip spinal needle is nearly R\$3.70 (cost paid by the Sao Paulo State Health Secretariat in 2013), whereas the common needle for medication administration costs less than three cents of a real.⁽⁶⁾ At a first glance, it seems strange and unnecessary the use of a more expensive technology for such an accurate aspiration process. Nevertheless, when it is taken into account that the palivizumab vial, after being diluted, reaches a volume of approximately 1 ml and costs R\$4,204.61⁽²⁾ to the Secretariat of Health, to leave 0.1 ml in the vial corresponds to a relative cost of R\$420.00 therefore implying the possibility for a child weighing 700 grams to be covered by the medication and thus contributing to the child's insertion into the health care system.

As for the planning process to the application of the medication, the dose administered at the hospital is prepared the day prior to the child's appointment at the institution, taking into account the weight the person responsible for the child reported on the previous telephone contact.

The careful work process carried out by the health team enabled them to realize that despite their commitment toward not wasting the drug, there were daily leftovers of the medication. The reutilization process resulted from the accurate aspiration process of the drug, as well as the use of vials that were not used due to the absence of children in the scheduled day, or the prescribed amount of the drug that did not match the child's weight. These doses were reutilized and administered in children admitted in the institution who complied with the pre-requisites to receive the medication.

Whenever the administered dose respects its correct ratio, complies with the posology of paliv-

izumab recommended by the Ministry of Health, added to the aseptic dilution technique and the proper post-dilution storage norms, it contributes to the rational use of the medication.⁽⁸⁾

The administration of drugs collaborates toward significant savings when compared to the disposal of the vial. Certain children only use a fraction of a vial and the leftovers could be reutilized to be administered to one or more patients, depending on the prescribed dosage and according to previously described criteria.

In 2012, the immunobiological medication administration center of the referred hospital received 1,360 vials from the State Secretariat of Health. This amount of vials was administered to 44 hospitalized children; 88 dose leftovers were reutilized. In 2013, from the 1,605 received doses, 78 leftovers were reutilized in 54 children.

Among the fractioned doses, the most frequently used volumes in 2012 reached 0.90-0.99 ml (20.8%) and 0.60-0.69 ml (19.1%) in 2013. The preparation of the medication was performed right in the beginning of the work shift, taking into account the respective weight indicated by the person responsible for the child on the telephone call. The exact calculation of the dosage to be applied was carried out moments prior to the administration of the medication, following the verification of the child's weight and eventual correction of the prescription.

Regarding the savings achieved by the employment of the new aspiration technique, when compared with individual doses received by patients that acquired the drug at specialized drugstores in the state of Sao Paulo, nearly 272 vials would be saved, reaching a financial amount of R\$ 1,144,347.52, based on the cost of R\$ 4,204.61 per vial paid by the Secretariat of Health in 2013. If the calculation considered the commercial cost of the medication (R\$ 6,748.54), the savings would reach R\$ 1,835,592.00.

The evidences of the efficacy of the use of palivizumab against the respiratory syncytial virus have already been extensively indicated in systematic reviews; however, a concern is left regarding the high cost of the drug and the access of the complying population. Economic studies have been carried out in order to check and determine which popula-

tions could be favored in a more cost-benefit manner, as many studies point to a lack of cost-effective processes for all children.⁽⁹⁾

In Brazil, back in 2012, the National Commission of Technology Incorporation to the Unified Health System recommended the incorporation of palivizumab in prevention processes against serious infections associated with the virus in children from the highest risk subgroup to hospitalization and complication processes, that is, premature babies of less than 28 weeks and children of up to 2 years of age with chronic pulmonary disease or congenital cardiac disease under the following conditions: elaboration of application guidelines by the Ministry of Health; and significant reduction of the medication's cost.⁽¹⁾

In 2012, from a total amount of 393 instruments, 252 were assessed. As for admittance processes, 91 did not carry out the diagnostic exam for respiratory syncytial virus. In 2013, 258 out of 463 cases responded positively, being 42 hospitalization processes and 39 that did not perform the diagnostic exam.

The study showed a 47.2% reduction in hospitalization processes between 2012 and 2013, which allows to infer a clear reduction trend; however, the accuracy of the data would depend on confirmatory diagnostic exams, which have not been performed in the majority of the hospital admittance processes.

Conclusion

The results of the study allowed to conclude that the application of the aspiration technique of the drug by employing the “off-label use” of the spinal needle favored the reutilization of the medication by 54 non-scheduled children, by means of the administration of 78 leftovers. The scheduling management of children, added to the previous planning of prepared volumes, in compliance with the children's profiles, especially the updated weight, favored the coverage of new hospitalized babies. The systematization of the health team's work process toward the ad-

ministration of palivizumab implied a monetary reduction of public expenditures.

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Collaborations

Albuquerque RS and Mariani Neto C have collaborated with the critical review of the relevant content and final approval of the version to be published. Arone GAC; Bersusa AAS and Leandro VP have contributed with the conception of the project, implementation of the research and drafting of the article.

References

1. Brasil. Ministério da Saúde. Secretária de Ciência Tecnologia e Insumos Estratégicos. Relatório de recomendação da Comissão Nacional de Incorporação de Tecnologia no SUS- CONITEC. Tecnologia Palivizumabe para prevenção da infecção pelo vírus sincicial respiratório. Brasília (DF); 2012. [citado 2013 Out 29] Disponível em: <http://portalsaude.saude.gov.br/images/pdf/2014/janeiro/28/Palivizumabe-VirusSincicial-final.pdf>.
2. Barr FE, Graham BS, Edwards MS, Redding G, Torchia MM. Respiratory syncytial virus infection: Clinical features and diagnosis. Up to date: Philadelphia; 2013 [cited 2013 Oct 29]. Available from: <http://www.uptodate.com/contents/respiratory-syncytial-virus-infection-clinical-features-and-diagnosis>.
3. Brasil. Ministério da Saúde. Departamento de Informática do SUS. Informações de Saúde. Assistência à Saúde [internet]. DATASUS: Brasília (DF); [citado 2013 Nov 1]. Disponível em: <http://www2.datasus.gov.br/DATASUS/index.php?area=0202>.
4. Frogel MP, Stewart DL, Hoopes M, Fernandes AW, Mahadevia PJ. A systematic review of compliance with palivizumab administration for RSV immunoprophylaxis. *J Manag Care Pharm*. 2010;16(1):46-58. Review.
5. Abbott Laboratórios do Brasil. Modelo de bula para o paciente. SYNAGIS [internet]. ABOIT: São Paulo; 2013 [citado 2013 Nov 1]. Disponível em: https://www.abbottbrasil.com.br/abbott/upload/bulario/1369342010bu_05_synagis_mai.13_

vp.pdf?PHPSESSID=u3dbmfe2b95vq4c3fvv5n0l1b5.

6. Chieffi AL, Barata RB. ["Judicialization" of public health policy for distribution of medicines]. *Cad Saúde Pública*. 2009;25(8):1839-49. Portuguese.
7. Brasil. Ministério da Saúde. Secretaria de Ciência, Tecnologia e Insumos Estratégicos. Portaria Nº 53, de 30 de novembro de 2012 que dispõe sobre a incorporação do palivizumabe no SUS. Diário Oficial da União seção 1 de 3 de dez de 2012. [citado 2013 Nov 13]. Disponível em: <http://www.in.gov.br/imprensa/visualiza/index.jsp?jornal=1&pagina=78&data=03/12/2012>.
8. Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Portaria Nº 522, de 13 de maio de 2013. Aprova o protocolo de uso do Palivizumabe. [citado 2013 Nov 13]. Disponível em: http://bvsms.saude.gov.br/bvs/saudelegis/sas/2013/prt0522_13_05_2013.html.
9. Wang D, Cummins C, Bayliss S, Sandercock J, Burls A. Immunoprophylaxis against respiratory syncytial virus (RSV) with palivizumab in children: a systematic review and economic evaluation. *Health Technol Assess*. 2008;12(36):iii, ix-x,1-86. Review.