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FACTORS RELATED TO COMPLIANCE WITH PALIVIZUMAB PROPHYLAXIS FOR RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION – DATA FROM POLAND

CZYNNIKI ZWIĄZANE Z PRZESTRZEGANIEM ZALECEŃ (COMPLIANCE) PROFILAKTYKI ZAKAŻEŃ WIRUSEM RS (RSV) PRZY UŻYCIU PALIWIZUMABU – DANE Z POLSKI

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Abstract

Aim: *To evaluate compliance and health outcomes in children receiving palivizumab prophylaxis and to identify factors that could impact parental compliance with the recommended regimen of palivizumab immunoprophylaxis.*

Material and methods: *A retrospective, multicentre, non-interventional study of children enrolled in the Polish National Programme for Respiratory Syncytial Virus (RSV) Immunoprophylaxis who received ≥1 dose of palivizumab during two consecutive RSV seasons (I: 2008-2009, II: 2009-2010). For each child qualified to receive palivizumab, the following data were collected: sociodemographic factors, clinical characteristics at enrolment, and in the course of palivizumab prophylaxis.*

Results: *One thousand twenty-one infants were enrolled into the Registry at 29 sites across Poland and received a total of 3,241 palivizumab injections (average: 3.2 doses per child). The incidence of adverse reactions was 3.33%; nervousness was the most frequently reported event (1.23%). Overall, 771 (75.5%) children received all of their expected injections, whereas 635 (62.2%) children received their injections within the appropriate interdose interval. Compliance was lower in male infants. None of the other demographic, social, or clinical factors seemed to impact compliance. Non-compliant children had a higher rate of hospitalisation due to respiratory illness (22% vs 9.9%, p<0.0001, and 18.4% vs 9.5%, p<0.0001, for compliance defined by the number of expected injections received and by the interdose interval, respectively).*

Conclusions: *Palivizumab prophylaxis was conducted in accordance with recommendations and was well tolerated in at-risk infants. Non-compliance was higher among male infants and was related with a higher rate of hospitalisation due to respiratory illness.*

Key words*: respiratory syncytial virus infections, palivizumab, prematurity*

Streszczenie

Cel: *Ocena przestrzegania zaleceń i stanu zdrowia dzieci otrzymujących profilaktykę paliwizumabem oraz identyfikacja czynników mogących mieć wpływ na przestrzeganie zasad immunoprofilaktyki przez rodziców.*

Materiał i metody: *Retrospektywne, wieloośrodkowe, nieinterwencyjne badanie przeprowadzone w grupie dzieci objętych Ogólnopolskim Programem Zapobiegania RSV (OPZRSV), które otrzymały przynajmniej jedną dawkę paliwizumabu podczas dwóch kolejnych sezonów RSV (I: 2008-2009, II: 2009-*

-2010). U wszystkich dzieci zakwalifikowanych do programu profilaktyki paliwizumabem rejestrowano następujące dane: demograficzne, socjalne i kliniczne oraz przebieg profilaktyki paliwizumabem.
Wyniki: *Rejestr obejmował 1021 dzieci z 29 ośrodków z całej Polski, którym podano łącznie 3241 dawek paliwizumabu (średnio 3,2 dawki w przeliczeniu na dziecko). Częstość występowania działań niepożądanych wynosiła 3,33%, przy czym najczęściej obserwowano niepokój (1,23%). Ogółem, 771 (75,5%) dzieci otrzymało wszystkie należne dawki, podczas gdy 635 (62.2%) dzieci otrzymało należne dawki paliwizumabu z zachowaniem właściwego odstępu między kolejnymi dawkami. Stosowanie się do profilaktyki było gorsze u niemowląt płci męskiej. Żaden z innych czynników demograficznych, socjalnych i klinicznych nie wpływał na przestrzeganie zaleceń. Zaobserwowano wyższy odsetek hospitalizacji z przyczyn oddechowych w grupie niemowląt, u których nie przestrzegano dawkowania (22% vs 9,9%, p<0.0001 oraz 18,4% vs 9,5%, p <0.0001 – odpowiednio dla zgodności określonej liczbą dawek należnych oraz jako podanie należnych dawek we właściwym czasie).*
Wnioski: *Profilaktykę paliwizumabem przeprowadzono zgodnie z rekomendacjami i była ona dobrze tolerowana w grupie niemowląt wysokiego ryzyka. Odstępstwa od zalecanego schematu podawania były większe wśród niemowląt płci męskiej i wiązały się z częstszą hospitalizacją z powodu chorób układu oddechowego.*

Słowa kluczowe*:* zakażenia syncytialnym wirusem oddechowym, paliwizumab, wcześniactwo

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INTRODUCTION

Respiratory syncytial virus (RSV) is a significant cause of lower respiratory tract infection (LRTI) in young children, infecting almost all children by two years of age [1]. RSV infection is associated with substantial morbidity and is a common worldwide cause of hospitalisation in the first year of life. It has been estimated that worldwide RSV infection accounts for about 33.8 million episodes of acute LRTI in children under the age of five, 3.4 million hospitalisations, and is the cause of 66,000-199,000 deaths per year [2].

RSV-related morbidity and mortality are higher in infants with certain co-existing medical conditions such as prematurity, chronic bronchopulmonary disease (BPD), hemodynamically significant congenital heart disease, neuromuscular diseases, and immune deficiency syndromes. Non-medical factors that are associated with an increased risk of severe RSV infection are: date of birth during the start of the RSV season, male gender, lower socio-economic status, crowding or siblings, smoking exposure, and day-care attendance [3-5]. Serious RSV disease requiring hospitalisation places a burden both on families and on the health care system, thus it is an important issue to prevent and modify the severity of RSV infection in high-risk children.

Palivizumab is a humanised monoclonal immunoglobulin G, directed against an epitope in the A antigenic site of the fusion protein of RSV. It is the only immunoprophylaxis therapy approved for prevention of serious LRTI caused by RSV in high-risk patients. Palivizumab is administered once a month at a dose of 15 mg/kg of body weight by intramuscular injection. It is recommended that patients receive up to five doses of the drug at one month intervals. In premature infants and infants with BPD, this dose maintains a mean trough serum concentration above 40 μg/mL (a level that resulted in a 99% reduction of pulmonary RSV in the cotton rat model) [6, 7].

There is evidence that palivizumab is effective in reducing the incidence of serious, RSV-induced LRTI in preterm children, children with chronic lung disease, or children with congenital heart disease [8, 9]. A recent meta-analysis of three randomised controlled trials comparing palivizumab with a placebo in 2,831 patients indicated that palivizumab prophylaxis was associated with a significant reduction in RSV hospitalisations (risk ratio 0.49, 95%, confidence interval: 0.37 to 0.64) when compared to placebo [10].

The Polish National Programme for RSV Immunoprophylaxis (OPZRSV) was initiated in 2008. Within the programme, patients who had received RSV prophylaxis were closely monitored. Furthermore, data on demographics, living conditions, clinical characteristics and palivizumab prophylaxis outcomes in infants were registered. Results of the OPZRSV support the effectiveness of palivizumab prophylaxis in preventing severe LRTI [11], however, the most effective palivizumab prophylaxis is observed when administration of immunoglobulin is regular and completed in the RSV season.

Detailed knowledge of factors related to palivizumab prophylaxis compliance may have implications in clinical practice, supporting appropriate neonatal counselling and the implementation of a more effective health programme. So far, no data has been published on compliance among children from the OPZRSV registry.

OBJECTIVES

The objectives of this study were to evaluate compliance and health outcomes in children receiving palivizumab prophylaxis during two consecutive RSV seasons (2008-2009 and 2009-2010) and to identify demographic factors, living conditions, and neonatal course-related factors which

could impact parental compliance with the recommended regimen of palivizumab immunoprophylaxis.

MATERIAL AND METHODS

The study includes children enrolled into the OPZRSV who received at least one dose of palivizumab funded by the National Health Fund (NFZ) during two consecutive RSV seasons (season I: 2008-2009 and season II: 2009-2010). The inclusion criteria evolved as the NFZ guidelines were updated. First (season I), prophylaxis was given to infants with BPD who met one of the following criteria:

- preterm birth in 2008 and at 30 weeks gestation or less,
- preterm birth in 2007 and at 26 weeks gestation or less,
- severe BPD requiring ongoing medical treatment.

In the 2009-2010 season (season II), prophylaxis was also funded by NFZ, but more restricted inclusion criteria were applied. Children with BPD and complying with one of the following criteria were enrolled into the programme:

- gestational age of <30 weeks and younger than 3 months of age at the beginning of the RSV infection season (born after 1.08.2009);
- gestational age of <28 weeks and younger than 6 months of age at the beginning of the RSV infection season (born after 1.05.2009).

The exclusion criteria were: hypersensitivity to palivizumab, contraindications for passive immunisation, and lack of parental or legal guardian consent for participation.

The study was retrospective, observational, multicentre, and non-interventional. A total of 29 pediatric centres throughout the country actively participated in the study. For each child qualified for receiving palivizumab prophylaxis, the local physician investigator reviewed medical records and retrospectively entered patient sociodemographic data, without identifiers, into a standardised form. Collected data included: baseline data on patient demographics, living conditions, prior medical history, neonatal course, and details of palivizumab administration. Data on any episodes of respiratory illness or respiratory illness-related hospitalisations with admission whose onset was no later than 35 days after the last palivizumab administration were also gathered.

Statistical analysis

Data analysis included examination of the following factors: demographic, social status and clinical characteristics at enrolment, the course of palivizumab prophylaxis, and compliance.

Compliance was evaluated by two methods:

- comparing the actual number of doses received with the expected number of doses,
- interdose interval.

According to the palivizumab Summary of Product Characteristics, the expected number of palivizumab doses was calculated assuming monthly injections from the first dose to the end of the RSV season. The start and the end of the RSV season was defined based on available epidemiological data for Poland [12]. For example, children who received their first dose in November or December were expected to receive a total of five doses, and those who received their first dose in March would be expected to receive two doses. Any child who received all the expected doses was considered compliant. For the interdose interval, intervals of 30 ± 5 days were considered to be compliant. However, an interval of 20 ± 5 days between the first and second dose was likely to result in higher trough levels after the first dose, potentially offering better RSV protection. Thus, an interval of 16-35 days between the first and the second injection was considered to be compliant.

Qualitative variables were expressed as numbers and percentages. Quantitative data were expressed as means ± standard deviations (SD). Data were summarised for the entire study population by the RSV season and by compliance. Chi-square and Kruskal-Wallis tests were conducted for categorical and continuous variables, respectively. A logistic regression analysis was used to assess the relationship between demographics, clinical and living condition-related factors, and adherence to palivizumab prophylaxis. Data analyses were performed using Statistica for Windows 10.0 (Statsoft) software and p-values of <0.05 were considered significant.

RESULTS

Characteristics of study population

In the consecutive RSV seasons analysed, a total of 1,021 infants were enrolled into the registry (557 and 464 in RSV seasons 2008-2009 and 2009-2010, respectively) by 29 sites in Poland (fig. 1). The mean number of children per participating site was 35.2 ± 27.9 (range 2-68). Detailed characteristics of children enrolled with regard to RSV season are shown in table I. There were 505 (49.5%) males and 516 (50.5%) females enrolled. The average completed gestational age was 26.6 ± 1.8 weeks and the average birth weight was 937 ± 262 grams. Parental education and place of residence were evenly distributed across the groups. Fifty-five percent of the children enrolled had at least one sibling and more than 25% shared a bedroom with a sibling. It should be emphasised that although the parents were aware of the dangers of tobacco smoke, nearly 30% of the children were exposed to tobacco smoke. Only four children attended day-care.

Palivizumab utilisation

A total of 3,241 palivizumab injections were administered, with each child receiving an average of 3.2±1.04 injections (range of 1 to 5 doses). The mean number of injections was higher in the RSV season 2008-2009 compared to the RSV season 2009-2010 (3.6±1 and 2.7±0.8).

Adverse events and safety

In total, the percentage of adverse reactions was 3.33% (108/3,241). Nervousness was the most frequently reported event (1.23%; 40/3,241). The remaining adverse reactions were less common and similar in terms of incidence (fig. 2).

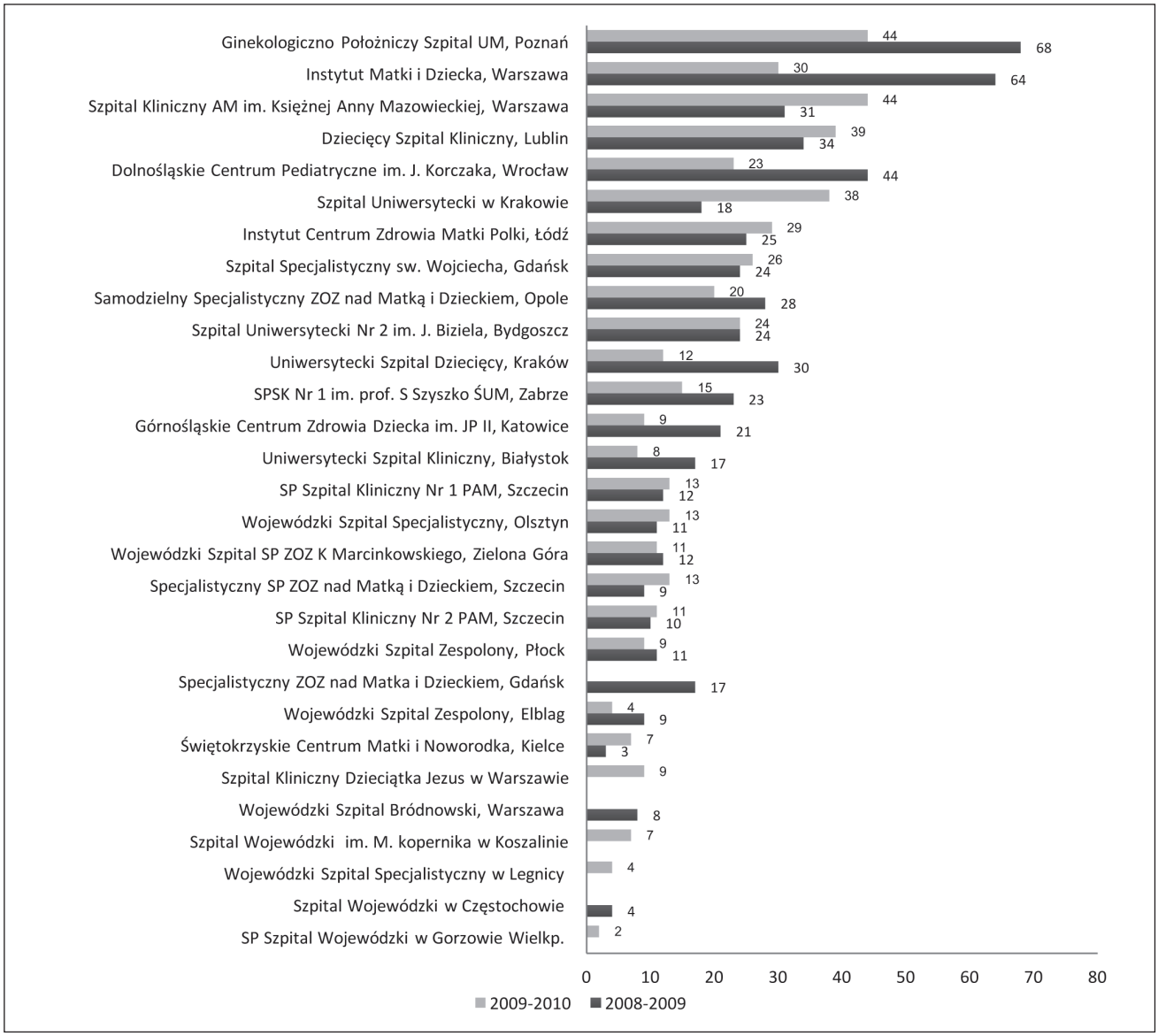

Fig. 1. Number of children receiving palivizumab prophylaxis at different participating centres by the RSV season.

Ryc. 1. Liczba dzieci otrzymujących profilaktykę paliwizumabem w poszczególnych ośrodkach w zależności od sezonu RSV.

The most commonly reported other adverse reactions were diarrhoea (4 cases) and vomiting (4 cases).

Compliance with dosing

Throughout two RSV seasons, 771 children (75.5%) received all of their expected injections, whereas 635 (62.2%) children received their injections within the appropriate interdose interval.

Compliance was higher in the RSV season 2009-2010 vs 2008-2009, as defined by the number of expected injections (80.4% vs 71.5%, respectively; p=0.0009). No difference was observed in the percentage of children who were compliant, as defined by the interdose intervals (63.4% and 60.8% in RSV seasons 2008-2009 and 2009-2010, respectively; p=0.391).

A significant association between compliance (regardless of evaluation method) and infant gender was observed, with a greater proportion of male children among non-compliant subjects (tab. II). There were no significant differences between the compliant and non-compliant groups by either evaluation in terms of the following variables: birth weight, gestational age, age of parents, education of parents, siblings, smoke exposure, living conditions, or place of residence (tab. II). Furthermore, the incidence of adverse events from palivizumab was comparable among compliant and non-compliant children.

Over the two RSV seasons, an episode of respiratory illness during palivizumab prophylaxis was reported in 444 (43.5%) children. The incidence was higher in non-compliant children, as defined by the interdose interval (48.2% vs 40.6%; p=0.018). However, no difference was observed in terms of compliance, as defined by the number of expected doses (p=0.173; tab. II).

One hundred and thirty-one (12.8%) children required hospitalisation for respiratory illness. Notably, a

Table I. Characteristics of study population by RSV season.

Tabela I. Charakterystyka populacji badanej z podziałem na sezon RSV.

Characteristics ***Charakterystyka***	**Total** ***Ogółem***	**RSV season** ***Sezon RSV***	
		2008 to 2009 2008 do 2009	2009 to 2010 2009 do 2010
Number of infants enrolled *Liczba niemowląt włączonych do badania*	1021	557	464
Male infants, n (%) *Płeć męska, n (%)*	505 (49.4)	255 (45.8)	250 (53.9)
Gestational age, mean ± SD, wk Wiek ciążowy, średnia ± SD, tyg.	26.6 ± 1.8	27.0 ± 2.0	26.6 ± 1.4
Birth weight, mean ± SD, g *Urodzeniowa masa ciała, średnia ± SD, g*	936 ± 262	941 ± 281	931 ± 238
Maternal age, mean ± SD, y *Wiek matki, średnia ± SD, l.*	29.5 ± 5.6	29.7 ± 5.7	29.36 ± 5.5
Paternal age, mean ± SD, y *Wiek ojca, średnia ± SD, l.*	32.0 ± 6.7	32.0 ± 7.0	31.9 ± 6.3
Mother's education:* *Wykształcenie matki:**			
primary *podstawowe*	236 (23.3)	133 (23.9)	103 (22.5)
secondary *średnie*	408 (40.2)	230 (41.3)	178 (39.0)
higher *wyższe*	370 (36.5)	194 (34.8)	176 (38.5)
Father's education:* *Wykształcenie ojca:**			
primary *podstawowe*	313 (31.3)	180 (32.6)	133 (29.8)
secondary *średnie*	420 (42.0)	234 (42.3)	186 (41.6)
higher wyższe	267 (26.7)	139 (25.1)	128 (28.6)
Residence:* *Miejsce zamieszkania:**			
rural area *wieś*	311 (30.5)	178 (32.0)	133 (28.7)
urban area with ≤100,000 inhabitants *miasto ≤100 000 mieszkańców*	356 (34.9)	194 (34.8)	162 (35.0)
urban area with >100,000 inhabitants *miasto >100 000 mieszkańców*	353 (34.6)	185 (33.2)	168 (36.3)
Living area, mean ± SD, square m* *Powierzchnia mieszkalna, średnia ± SD, m²**	80.4 ± 55.6	79.8 ± 53.3	81.8 ± 58
Smoke exposure, n (%)* *Narażenie na dym tytoniowy, n (%)**	292 (28.8)	161 (28.9)	131 (28.2)
One or more siblings, n (%)* *Posiadanie rodzeństwa, n (%)**	556 (54.7)	313 (56.2)	243 (52.8)
Siblings sharing the child's room, n (%)* *Dzielenie pokoju z rodzeństwem, n (%)**	276 (27.2)	161 (28.9)	115 (25.0)
Day-care attendance, (%) *Uczęszczanie do żłobka, (%)*	4 (0.4)	2 (0.4)	2 (0.4)

*Data missing for an individual item ranged from 0.1% to 2.1%.

**Odsetek brakujących danych dla poszczególnych parametrów wynosił od 0,1% do 2,1%.*

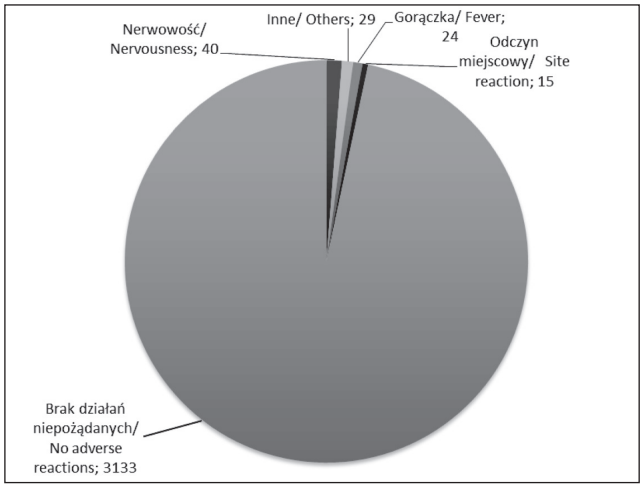

Fig. 2. Incidence of adverse reactions.

Ryc. 2. Częstość występowania działań niepożądanych.

significant association was observed between compliance and respiratory illness-related hospitalisations, with the greater proportion of hospitalisations among non-compliant children (22% vs 9.9%, p<0.0001 and 18.4% vs 9.5%, p<0.0001, for compliance defined by the number of expected injections received and by the interdose interval, respectively; table II).

Furthermore, children who were non-compliant by the number of expected doses required significantly longer hospitalisation (15.8±14.0 days vs 11.4±7.9 days, respectively; p=0.021), compared to those who were compliant, whereas a trend towards longer hospital stays was observed for non-compliant children, as defined by the interdose interval (14.8±12.76 days vs 11.4±8.3 days, respectively; p=0.061). No association between compliance (whether measured by the number of doses received or by the interdose interval) was observed in terms of re-hospitalisations or total length of hospital stay (tab. II).

DISCUSSION

As effectiveness of palivizumab in preventing severe LRTI highly depends on compliance with the monthly dosing regimen during the RSV season, recognising potential barriers to adherence is a priority. This observational study provides data on palivizumab utilisation and compliance throughout the two RSV seasons (from 2008 to 2010) in high-risk children registered in the OPZRSV who were given at least one dose of palivizumab.

In our study, compliance rates over the two RSV seasons were 75.5% and 62.2%, by the expected number of doses and the interdose interval, respectively, and were within the ranges of the previously published data from Canada and the USA (72%–82.7% and 60.9%–69.5%, by the expected number of doses and the interdose interval, respectively) [13-15].

We observed a higher compliance rate in the second RSV season. This increase may reflect the improved knowledge and experience of health care providers as well as greater awareness of the risk of severe RSV disease and benefits of prophylaxis among parents. In addition, these results may be attributed to a lower mean number of injections or lower gestational age of the children who were eligible to receive prophylaxis in the 2009 to 2010 season, compared to those enrolled during the RSV season 2008 to 2009. With regard to a younger age at the beginning of the prophylaxis, this is in line with the findings from the Italian study by Pignotti et al. [16]. Families with younger children were more compliant than those with older children [16]. It seems that the family's perception of their child's health gradually changes with their growth and the older children were perceived as being healthier and therefore not requiring prophylaxis [16].

Previous studies recognised various demographic and environmental factors as potential barriers to achieving full compliance, including: lower parental expectations for the benefits of RSV prophylaxis, minority race, exposure to smoking, socioeconomic level, born of multiple birth, siblings, maternal education level, language difficulties, distance to clinic, and cost of palivizumab prophylaxis [13, 17, 18].

In contrast, in our study, we found that no demographic or neonatal characteristics seemed to impact compliance except for gender. In univariate analysis, male children were more likely to be non-compliant. To the best of our knowledge, no previous study has reported the direct association between child gender and compliance to palivizumab prophylaxis.Nevertheless, male gender has been recognised as a risk factor for RSV-related hospitalisations in young children, including those who had undergone palivizumab prophylaxis [15, 19]. The reason seems to be that males have shorter and narrower airways and are more likely to develop bronchial obstruction in cases of RSV infection [3, 20]. In fact, after correction for respiratory illness-related hospitalisation, the effect of gender on compliance failed to be significant (data not shown). Different patient populations (including variability in terms of ethnicity and cultural norms), country-specific epidemiological data, difference in health care programmes, health insurance coverage, and/or funding availability may account for the differences observed in factors affecting palivizumab compliance. Nevertheless, the factors associated with compliance in our study remained unclear or not defined and studies designed to capture other potential factors are warranted.

With regard to respiratory-related outcomes, we observed that episodes of respiratory illness during palivizumab prophylaxis were associated with decreased compliance, defined by the interdose interval, but not by the expected number of doses. This may suggest that in our study population, children who experienced respiratory infection did not miss their palivizumab dose, but had it administered at a longer interval. Further evaluation addressing this issue is needed.

In line with previous studies, our data also indicates that complete dosing as well as timing compliance to the monthly dosage may decrease hospital admission rates attributable to respiratory disease [8, 15, 19, 21,

Table II. Characteristics of study population stratified by the compliance.

Tabela II. Charakterystyka populacji badanej w zależności od compliance.

Characteristics *Charakterystyka*	**Compliance based on the expected number of injections: Compliance określane liczbą dawek należnych**		**P-value Wartość p**	**Compliance based on the interdose interval: Compliance określane jako należne dawki we właściwym czasie**		**P-value** ***Wartość*** **p**
	compliant *compliant* n=771	non-compliant *non-compliant* n=250		compliant *compliant* n=635	non-compliant *non-compliant* n=386	
Male infants, n (%) *Płeć męska, n (%)*	403 (52.3)	149 (59.6)	**0.043**	323 (50.9)	229 (59.3)	**0.009**
Gestational age, mean ± SD, wk *Wiek ciążowy, średnia ± SD, tyg.*	26.69 ± 1.82	26.5 ±1.63	0.230	26.66 ±1.82	26.61 ± 1.69	0.230
Birth weight, mean ± SD, g *Urodzeniowa masa ciała, średnia ± SD, g*	937.15 ± 264.25	936.35 ± 255.09	0.962	934.8 ±. 261.04	940.5 ± 263.64	0.728
Adverse event, n (%) *Działania niepożądane, n (%)*	64 (8.3)	20 (8.0)	0.279	45 (7.1)	39 (10.1)	0.147
Respiratory illness at RSV prophylaxis, n (%) *Choroba dróg oddechowych w trakcie profilaktyki RSV, n (%)*	326 (42.3)	118 (47.2)	0.173	258 (40.6)	186 (48.2)	**0.018**
Respiratory illness-related hospitalisations: *Hospitalizacje z powodów oddechowych:*						
Hospitalisation at RSV prophylaxis, n (%) *Hospitalizacja w trakcie profilaktyki RSV, n (%)*	76 (9.9)	55 (22.0)	**< 0.0001**	60 (9.5)	71 (18.4)	**< 0.0001**
Length of the first hospitalisation, mean ± SD, days *Długość pierwszej hospitalizacji, średnia ± SD, dni*	11.4 ± 7.9	15.8 ± 14.0	**0.021**	11.4 ± 8.3	14.8 ± 12.76	0.061
Re-hospitalisations, n (%) *Wielokrotne hospitalizacje, n (%)*	7 (0.9)	3 (1.2)	0.684	5 (0.8)	5 (1.3)	0.424
Total length of hospital stay, mean ± SD, days *Łączny czas hospitalizacji, średnia ± SD, dni*	14.3 ± 12.5	17.4 ± 14.9	0.185	14.7 ± 13.7	16.3 ± 13.6	0.499
Maternal age, mean ± SD, y *Wiek matki, średnia ± SD, l.*	29.4 ± 5.5	29.7 ± 6.1	0.268	29.4 ± 5.6	29.6 ±5.9	0.783
Paternal age, mean ± SD, y *Wiek ojca, średnia ± SD, l.*	31.9 ± 6.6	32.1 ± 6.7	0.496	31.9 ± 6.4	31.9 ± 6.7	0.994

Table II. Cont.

Tabela II. Cd.

Mother's education:* *Wykształcenie matki:**			0.284			0.192
primary *podstawowe*	171 (22.3)	65 (26.3)		137 (21.7)	99 (25.9)	
secondary *średnie*	318 (41.5)	90 (36.5)		266 (42.1)	142 (37.2)	
higher *wyższe*	278 (36.2)	92 (37.2)		229 (36.2)	141 (36.9)	
Father's education:* *Wykształcenie ojca:**			0.448			0.861
primary *podstawowe*	238 (31.4)	75 (31.0)		197 (31.6)	116 (30.8)	
secondary *średnie*	311 (41.0)	109 (50.0)		258 (41.4)	162 (43.1)	
higher *wyższe*	209 (27.6)	58 (24.0)		169 (27.0)	98 (26.1)	
Residence:* *Miejsce zamieszkania:**			0.250			0.124
rural area *wieś*	241 (31.3)	70 (28.1)		203 (32.0)	108 (28.0)	
urban area with ≤100,000 inhabitants *miasto ≤100 000 mieszkańców*	274 (35.5)	82 (32.9)		227 (35.8)	129 (33.5)	
urban area with >100,000 inhabitants *miasto >100 000 mieszkańców*	256 (33.2)	97 (39.0)		205 (61.2)	148 (38.5)	
Living area, mean ± SD, square m* *Powierzchnia mieszkalna, średnia ± SD, m^2**	80.36 ± 53.96	80.37 ± 60.38	0.997	80.04 ± 53.39	80.9 ± 59.03	0.509
Smoke exposure, n (%)* *Narażenie na dym tytoniowy, n (%)**	213 (27.7)	79 (32.1)	0.183	179 (28.3)	113(29.7)	0.649
One or more siblings, n (%)* *Posiadanie rodzeństwa, n (%)**	418 (54.4)	138 (55.6)	0.723	348 (54.8)	208 (54.6)	0.948
Siblings sharing the child's room, n (%)* *Dzielenie pokoju z rodzeństwem, n (%)**	205 (26.7)	71 (28.7)	0.528	169 (26.8)	107 (28.4)	0.671

*Data missing for an individual item ranged from 0.1% to 2.1%.

**Odsetek brakujących danych dla poszczególnych parametrów wynosił od 0,1% do 2,1%.*

22]. In addition, children who received all the expected palivizumab doses may experience less severe illness, requiring shorter hospital stays compared with non-compliant children. Taken together, these findings imply that higher compliance is necessary to avoid respiratory illness-related outcomes, including hospitalisations. It is also important in terms of the cost of palivizumab prophylaxis and health care resources. Therefore, further optimisation of the prophylaxis programme is warranted. Recently, home-based programmes for the administration of palivizumab have been associated with improved compliance compared to office- or clinic-based administration [14, 15, 23]. This, together with other activities such as extensive counselling of parents or reminder telephone calls, may be used to enhance compliance [18].

The limitation of the study, which needs to be mentioned, is that all respiratory illness-related data were captured with no distinction for RSV (RSV testing was not routinely performed). Therefore, the true relationship between the palivizumab compliance and respiratory illness-related outcomes may have been missed and findings must be interpreted with caution.

CONCLUSIONS

Palivizumab prophylaxis was conducted in accordance with recommendations and was well tolerated in at-risk infants. The compliance rates observed in our study align closely with the previously published data from non-European countries, but factors affecting compliance may vary, be country-specific, or have not yet been defined. Our study reinforces the findings of other studies by showing the potential association between compliance with palivizumab and a lower rate of respiratory illness-related hospitalisations. Further studies are needed to define new factors which may shape palivizumab utilisation patterns in the Polish population.

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