ORIGINAL ARTICLE

Selective Vaccination Strategy with BCG: Are We Identifying All Eligible Newborns?

Zulmira K. Abdula[1], Susana Alexandre[1], Ana Rita Constante[1], Raquel Carreira[1], Alcina Sousa[2], Luísa Preto[1], Catarina Gomes[1]

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Abstract

Introduction: In Portugal, a selective vaccination strategy with bacillus Calmette-Guérin was adopted in January 2017. The efficacy of this strategy relies on the precise identification of high-risk groups. We designed a study to evaluate the implementation of the Portuguese guideline on bacillus Calmette-Guérin vaccination in the surrounding area of our hospital.

Methods: Retrospective study of a cohort of children born in our hospital from January 2017 to June 2018. The data was collected through a telephone questionnaire.

Results: We included 233 children in the study (95% confidence level, 6% margin of error). Of them, 46 (19.7%) were eligible for bacillus Calmette-Guérin immunization, mostly (82.6%) because they had a parent, cohabitant, or frequent contact in a high-risk country. Of these eligible children, 21 (45.7%) had not been identified and were unvaccinated. From the total sample, there were 38 vaccinated children, of which 47.4% were referred during the first month of age (age range of 0-20 months).

Discussion: We identified 45.7% of unreferred high-risk children, a quarter of which with risk factors not often inquired about: close contacts with substance abuse or human immunodeficiency virus infection. About half of the parents denied or did not recall being asked about the criteria in our maternity or in further routine health consultations. Larger studies would be important to ascertain the regional and national performance rates. A significant number of unreferred children was found, revealing that our risk identification must be improved. There is still a failure to reassess the risk in all routine visits and probably not all the risk criteria are excluded.

Keywords: BCG Vaccine/standards; Child; Portugal; Tuberculosis/epidemiology; Tuberculosis/prevention & control; Surveys and Questionnaires

Introduction

The bacillus Calmette-Guérin (BCG) vaccine is a public health preventive strategy to decrease tuberculosis incidence. It is most effective for the severe forms of disease – meningitis or disseminated tuberculosis – and the younger the child is, the higher the protection, with the maximum amount being in the neonatal period.[1] Recent studies demonstrated that it also has a modest protective effect in the reduction of the pulmonary primary infection.[2]

Vaccine strategies can be universal (all healthy neonates) or selective (high-risk children). Studies in low incidence countries have shown that the additional protection conferred by universal strategies is small and less cost-effective when compared to the targeted vaccination strategy.[3-5] The World Health Organization (WHO) recommends that countries with a high incidence of tuberculosis (defined as a notification rate of more than 40 cases per 100,000 population) to vaccinate universally. In countries with low incidence (notification rate of fewer than 10 cases per 100,000 population), a selective strategy is of higher cost-effectiveness.[4] However, the efficacy of this strategy depends on the existence of a reliable surveillance system, capable of providing notification rates of bacteriologically positive cases and the average annual rate of tuberculosis meningitis in children younger than 5 years old.[3,4]

In Western Europe, currently all countries have selective strategies, with some differences in the risk criteria and age-groups of the target population. The timing of the discontinuation of the universal strategy varied greatly, and there are some cases where it was made at incidence rates between 10 and 20 cases per 100,000 population, e.g. Sweden, Spain, and United Kingdom.[3,6-8] Theoretical model tests predict an elevation in incidence rates, particularly in childhood cases and in severe forms of the disease.[9] Reports from Sweden and United

1. Department of Pediatrics, Centro Hospitalar do Oeste, Unidade das Caldas da Rainha, Caldas da Rainha, Portugal
2. Department of Obstetrics, Centro Hospitalar do Oeste, Unidade das Caldas da Rainha, Caldas da Rainha, Portugal
Corresponding Author
Zulmira K. Abdula
https://orcid.org/0000-0002-2755-2425
Zk.abdula@gmail.com
Rua Diário de Notícias, 2500-176 Caldas da Rainha, Portugal
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Kingdom after their change reflected this initial increase in the incidence rates, mostly in the migrant population (or their descendants).[10-12] This data reinforces the importance of a well-defined and reliable identification process for eligible children.

In Portugal, the incidence of the disease has shown a progressive decline in recent years, reaching and maintaining rates lower than 20 cases per 100,000 population since 2015.[13] Due to this tendency, in 2017, the vaccination strategy was changed to a selective BCG immunization approach.[14,15] Children are identified according to the criteria defined by the Direção Geral da Saúde. The first guideline was published in February 2016[14] and an update of the criteria was issued in a second guideline in June 2016[15] (Table 1). Initially having a parent, cohabitant, or frequent contact who in the last 10 years had lived in a high-risk country was considered as a risk factor. In June, it was changed to a parent, cohabitant or frequent contact born in one of those countries. Although the total incidence has been decreasing, the number of cases in younger children has increased (Table 2). National reports revealed that, in 2017 and 2018, there were 66 cases in children under the age of 6 years, with eight cases of severe disease (Table 2).[13,16,17] All of these severe cases were in unvaccinated children and three of them were in a high-risk group.[13] Data from the tuberculosis surveillance and monitoring in Europe[18] show 40 cases in children 0-4 years old notified in 2019.

Our study aims to evaluate the implementation of the national guideline for BCG vaccination in our maternity through the assessment of the number of eligible children identified/not identified and the most common risk factors correctly identified/not identified.

Methods

A retrospective observational study of a cohort of children born in our hospital between January 2017 and June 2018. The study sample was obtained by systematic sampling and selecting the first newborn of the day in the timeframe of the study.

The Portuguese BCG vaccination guideline establishes the eligibility criteria (Table 1).[15] We designed a standardized form based on this document that included the demographic data, risk factors as defined by the guideline, vaccination status, timing of referral and previous similar inquiries during maternity stay, or in routine medical visits. Data were collected by telephone interview with one of the parents, after obtaining verbal consent.

Of a population of 1,692 newborns, we defined a target study sample of 314 children, for a 95% confidence level (5% margin of error). The inclusion criteria were being born in our maternity between January 2017 and June 2018 and being a resident in the surrounding area of our hospital. We excluded children with unsuccessful contact attempts, deceased newborns, and absence of verbal consent to participate in the study.

We obtained an initial sample of 521. We excluded 288 and gathered a final sample of 233 children (95% confidence level, 6% margin of error), corresponding to 13.8% of the newborns in the timeframe of the study (Fig. 1).

Descriptive analysis of the data was performed with Excel, Microsoft Office Professional Plus 2016®, by the calculation of the frequencies (absolute and relative) and ranges.

Table 1. Definition criteria for BCG vaccination (high-risk group for tuberculosis)[15]

Children < 6 years, unvaccinated/without BCG scar and…	Notes
High incidence country provenance	Duration of stay of at least three months
Submitted and at the end of contact screening and/or prophylactic therapy	Evaluated by the local public health unit
Parents, cohabitant, or frequent contact with high-risk conditions	HIV infection
	Drug or alcohol abuse
	Born in a high incidence country
	History of tuberculosis
Belonging to a high-risk community	Defined by the local public health unit
Traveling to a high incidence country	Duration of stay of at least three months or if a high risk of infection

BCG - bacillus Calmette-Guérin; HIV - human immunodeficiency virus.

Table 2. Tuberculosis incidence in Portugal 2016-2018[13,16,17]

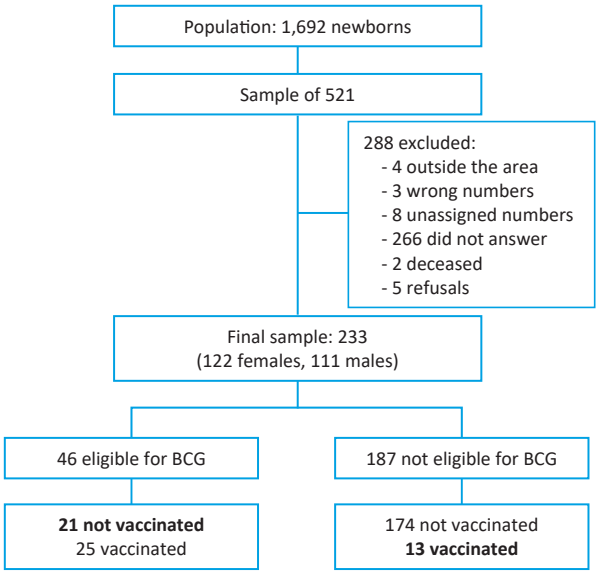
Year	Incidence rate	Number of cases < 6 years	Pediatric severe disease
2016	16.5/100,000	19	2
2017	15.6/100,000	32	4
2018	15.4/100,000	34	4

Results

Our final sample of 233 children consisted of 52.4% females and 47.6% males. They were born in 2017 (65.2%) and 2018 (34.8%). At the moment of data collection, the age range of the included children was between 3-21 months. According to our questionnaire, 46 children (19.7%) were eligible for BCG vaccination (Fig. 1). The most common risk factor was having a parent, cohabitant, or frequent contact with a person born in a high incidence country - accounting for 82.7% - and 17 (36.9%) had more than one risk factor. Among the eligible children, 21 did not have the vaccine. Of these, seven were not eligible according to the first guideline criteria[14] and nine had parents or frequent contacts that were born in Brazil, a country with a risk status that has varied over time.

Of the 233 enquired children, only 38 had been vaccinated (Table 3) and almost all of them have been identified in our maternity or primary care unit. In two cases, there was a prenatal indication from their mother obstetrician. The age of referral varied between the neonatal period and 20 months of age, with most referred within four weeks (Table 3). Of the vaccinated children, 13 were not eligible according to our questionnaire, although nine had criteria for the first guideline.[14]

When asked if the eligibility questionnaire was previously conducted, only 51.1% of the parents confirmed it was, 41.2% denied having been asked, and 7.7% did not remember or did not know.



BCG - bacillus Calmette-Guérin.

Figure 1. Study sample.

Discussion

The present study revealed that, in our sample, 45.7% of the eligible children were not vaccinated (21/46). This was an alarming finding. In Portugal, an increase in severe childhood disease has been observed in recent years (Table 2).[13,16,17] It is possible that a failure in the identification of eligible children could be one of the factors for these results, similar to what has been reported in other European countries.[9-12] Studies with more representative samples would be important to ascertain the regional and national performance rates and a possible relation to the incidence rates.

Our results demonstrate how the identification of high-risk children must be improved. Even though about 40% of the parents denied ever being asked about the risk factors, it is possible that a considerable number of them simply do not remember. Another possible explanation is that, until 2017, the vaccine was administered in the maternity. Therefore, most professionals possibly do not remember revisiting it throughout the next visits. As highlighted in Direção Geral da Saúde guidelines, the presence or absence of risk is dynamic.[19]

During data collection, parents often mentioned that questions about high-risk countries and the history of tuberculosis were asked, but they had never been asked if there was a history of human immunodeficiency virus (HIV) infection or substance abuse, which are still taboo subjects, especially in wards where privacy is limited. This must not be an excuse to not address it, however. In our sample, all of the children whose criteria for vaccination was having contact with a human immunodeficiency virus positive person (4) had not been referred (Table 4).

Several organizational aspects may have played a role in our results, especially changes in the list of high-risk countries and the existence of two distinct guidelines.[14,15] Almost half of the unreferred children (9/21) had as a risk factor having a cohabitant and/or frequent contact with someone who was born in Brazil and this country was removed from the high incidence list for a few months. Moreover, many health professionals did not realize the changes made in the eligibility criteria, which could explain seven of the unreferred cases (Table 4).

In November 2018, Direção Geral da Saúde sent an updated list of risk criteria to hospitals and primary care units, adding contact with someone who was imprisoned in the last five years as a risk factor. Despite this, the information on the Direção Geral da Saúde website has not yet been changed. As nowadays many health professionals look for information online, many of them may be misguided by the outdated list and guideline[14] currently available on the website (at the time of submission of the article).

Table 3. Vaccinated children's results

Referral	n	%	Time to vaccination	n	%	Age at referral	n	%
Obstetrician	2	5.3%	< 1 week	4	10.5%	Neonatal	18	47.5%
Maternity	15	39.5%	1-2 weeks	9	23.7%	1 month	8	21.1%
Primary care unit	15	39.5%	2-4 weeks	10	26.3%	2 months	3	7.9%
Pediatrician	2	5.3%	1-3 months	6	15.8%	3 months	1	2.6%
Unknown	4	10.5%	Unknown	9	23.7%	4 months	1	2.6%
						6 months	1	2.6%
						12 months	1	2.6%
						20 months	1	2.6%
						Unknown	4	10.5%

Table 4. Frequency of risk factors in the vaccinated versus unvaccinated eligible children

Risk factors identified	Vaccinated	Unvaccinated
Parents/cohabitant born/frequent contact from high incidence country	15	10
- Born in Brazil	4	9
- Born in other countries but living in Portugal for more than 10 years	5	7
Parents/cohabitant/frequent contact with a personal history of tuberculosis	6	1
Parents/cohabitant/frequent contact with an HIV infection	0	4
Parents/cohabitant/frequent contact with drug or alcohol dependence	2	3
Long duration (> 3 months) travel to a high incidence country	4	0

HIV - human immunodeficiency virus.

With this study, we conclude that there is a significant number of eligible children born in the first 18 months after the implementation of the selective vaccination strategy that were not identified or referred. This is probably due to:

- Changes in the list of the high-risk countries;
- Lack of knowledge of the current guideline;
- Previous inexistence of a standardized questionnaire;
- Lack of a routine habit to repeat the questionnaire until the child is 5 years old;
- Incomplete questionnaires.

After the conclusion of the study, in our hospital a checkbox was added to the newborn clinical diary on the eligibility for BCG vaccination.

It is likely that Direção Geral da Saúde surveillance noted similar findings nationwide, as in November 2018, a new standard questionnaire was issued that was included in the vaccine online registry. These actions will probably result in an improvement in the identification of these children. It would be interesting if a new assessment is carried out in our hospital and that more healthcare units conduct similar audits.

The study results and analysis are limited due to its retrospective design and memory bias. The relatively small sample size may overestimate the proportion of unidentified children. Studies with a larger sample would be useful to confirm these numbers with higher confidence.

WHAT THIS STUDY ADDS

- According to our research, this is the first national study after the change in our vaccination strategy that evaluates the implementation of the norm.
- In our area, the identification of eligible children was still suboptimal, as 45.7% were missed.
- A standard questionnaire and scheduled key moments for its application was missing in order to increase adherence to the repeated re-evaluation of all the risk factors.
- For the success of the current strategy, it is important that all healthcare professionals are kept informed and updated on the risk evaluation and current performance.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

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Protection of human and animal subjects

The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Provenance and peer review

Not commissioned; externally peer reviewed

Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

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Estratégia de Vacinação Seletiva com BCG: Estamos a Identificar Todos os Recém-Nascidos Elegíveis?

Resumo:

Introdução: Em Portugal, foi adotada em janeiro de 2017 uma estratégia de vacinação seletiva com o bacilo Calmette-Guérin. A eficácia desta estratégia baseia-se na identificação precisa de grupos de alto risco. Delineamos um estudo para avaliar a implementação da norma portuguesa de vacinação contra a tuberculose na área do nosso hospital.

Métodos: Estudo retrospetivo de uma coorte de crianças nascidas no nosso hospital no período entre janeiro de 2017 e junho de 2018. Os dados foram obtidos através de um questionário telefónico.

Resultados: Foram incluídas no estudo 233 crianças (nível de confiança 95%, margem de erro de 6%). Destas, 46 (19,7%) eram elegíveis para a imunização com o bacilo Calmette-Guérin, a maioria (82,6%) por terem um dos pais, coabitantes ou contato frequente de um país de alto risco. Destas crianças elegíveis, 21 (45,7%) não foram identificadas e não foram vacinadas. Do total da amostra, 38 crianças foram vacinadas, das quais 47,4% foram encaminhadas durante o primeiro mês de idade (faixa etária de 0-20 meses).

Discussão: Identificamos 45,7% de crianças de alto risco não referenciadas, um quarto das quais com fatores de risco raramente questionados: contatos próximos com abuso de substâncias ou infeção pelo vírus da imunodeficiência humana. Cerca de metade dos pais negou ou não se lembra de ter sido questionado sobre os critérios, nem na nossa maternidade nem noutras consultas de saúde de rotina. Estudos de maior dimensão são importantes para determinar as taxas de desempenho regionais e nacionais. Foi encontrado um número significativo de crianças não referenciadas, o que revela que a nossa identificação de risco deve ser melhorada. Ainda há uma falha na reavaliação do risco em todas as visitas de rotina e provavelmente nem todos os critérios de risco são excluídos.

Palavras-Chave: Criança; Inquéritos e Questionários; Portugal; Tuberculose/epidemiologia; Tuberculose/prevenção e controlo; Vacina BCG/normas