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Original Research Article

BCG-SSI® vaccine-associated lymphadenitis: Incidence and management

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ABSTRACT

Background and objective: There is a high incidence of childhood tuberculosis in Latvia, including children aged less than 1 year, while BCG-associated lymphadenitis is one of the most frequent adverse events requiring surgical treatment. The aim of this study was to analyze the incidence of purulent BCG adenitis through-out the population of Latvia after the introduction of BCG-SSI® vaccine and to evaluate the treatment results.

Material and methods: The study included 194 patients. All patients had received the BCG-SSI® vaccine during the first week of life routinely or at a later time according to the indications. The indications for surgical treatment were lymph node destruction also affecting the skin. All patients in this study received surgical treatment – the affected lymph node extirpation.

Results: The mean age of the patients was 5.12 ± 0.96 months. A total of 172 patients had purulent axillar lymphadenitis, 14 had purulent supraclavicular lymphadenitis, 8 patients had lymphadenitis at both localizations. During the whole study period the incidence of BCG adenitis varied from 0.02% to 0.36%, while the mean rate was 0.11% ± 0.08% from 184,068 vaccinated children during the study period. We observed an increasing trend in the incidence of BCG lymphadenitis during the study period. The primary and complete healing rate at the end of period was 99.5% ($n = 193$) following an affected lymph node extirpation. The mean hospitalization time after the operation was 3.71 ± 0.18 days.

Conclusions: The incidence of BCG-SSI® vaccine associated purulent lymphadenitis varied widely with an increasing trend, followed by the return to the product characteristic limits. Indications for the surgical treatment should not be changed. Extirpation of the purulent BCG adenitis is a safe treatment method and leads to the primary wound healing in the majority of cases.

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1. Introduction

Bacillus Calmette–Guerin (BCG) vaccination is a part of the immunization programs in the countries with a risk of childhood tuberculosis [1–4]. In different countries there are different schedules for BCG vaccination, starting from the maternity home [5] to the 6th year of life [6]. The vaccine was recommended in Europe in 2005 for children under one year of age in 12 different countries, for older children in 5 countries, only at risk groups in 10 countries, and no routine vaccination in 7 countries [6]. The early BCG vaccination between 2 and 5 days after the birth is a part of the compulsory childhood immunization program in Latvia, due to the high incidence of childhood tuberculosis, including the children under one year of age [7,8].

BCG lymphadenitis is one of the BCG vaccination's adverse events, related to the Category NR1 – Abnormal BCG primary complex [9,10]. Its incidence differs depending on the particular vaccine, the age of the child at the time of vaccination and probably some other factors [6,9].

The treatment of BCG lymphadenitis is still controversial [5,11–14]. While indications for the surgical treatment are rather clear, particular treatment methods are still discussed and opinions differ among different countries, centers and authors [5,15–18].

Today there is only one BCG vaccine available in the European Union – BCG-SSI® vaccine from Staten's Serum Institute (M Bovis, Danish Strain 1331), which is distributed in vials, containing 10 doses of 0.1 mL of vaccine for children over 12 months of age and adults, or 20 doses of 0.05 mL for infants under 12 months. The BCG-SSI® vaccine has been the only one used in the Republic of Latvia since the year 2005.

The clinical effects and the elevated number of the adverse reactions of the BCG-SSI® vaccine have been described in a number of publications. Those about the adverse reactions give different results, and try to concentrate mostly on the vaccine-related reasons [5,6,10,19–21]. A sudden increase in incidence of the purulent BCG adenitis was recognized also in Latvia in 2010 and 2011. It lead to a tri-lateral discussion among the State Drug Agency (the Government's Pharmacovigilance Office), the Statens Serum Institute and the Latvian Association of Paediatric Surgeons, followed by the implementation of the BCG-SSI® vaccine manufacturing changes and an instruction campaign about the vaccination procedure, performed by The State Drug Agency in the first part of 2012 [22]. After this successful campaign we observed a decline in the incidence of BCG adenitis in the subsequent years.

The aim of this study was to analyze the incidence dynamics of purulent BCG adenitis through-out the population of Latvia after the introduction of BCG-SSI® vaccine and to evaluate the treatment results.

2. Material and methods

A retrospective study was undertaken and medical records of 194 children, admitted to the only reference center in Latvia for major BCG vaccination associated adverse events, from the year 2005 to 2013, were reviewed. The study included patients from 1 to 17 months of age with the diagnosis of histologically proven purulent BCG lymphadenitis. All patients received the BCG-SSI® vaccine (M Bovis, Danish strain 1331) on the ipsilateral arm via an intradermal injection. 163 patients (84.02%) received the BCG-SSI® vaccine during the first week of life, while 31 patients (15.98%) received it later due to different medical or social reasons. Observing the signs and symptoms of BCG adenitis all patients were consulted by a pediatrician specializing in child tuberculosis and an immunologist. Indications for surgical treatment were assessed by a pediatric surgeon. The indications for surgical treatment were lymph node destruction with the overlying skin involvement. All patients in this study received surgical treatment – purulent lymph node extirpation. All patients were consulted and operated in one reference center by one pediatrician specializing in child tuberculosis, one immunologist and operated by two pediatric surgeons. All patients had postoperative outpatient follow-up controls up to 18 months. The incidence of purulent BCG lymphadenitis of less than 0.1% reported by the producer in the ''Description of BCG vaccine SSI'' was considered as a comparator [23]. The study was approved by the Institutional Ethics Review Board.

Data were analyzed using descriptive and analytical statistical methods. Mean values and 95% CI of the age of the hospitalized patients, time after vaccination, incidence of purulent BCG adenitis and postoperative time were calculated. The Mann–Kendall trend test was used to determine possible trends in the occurrence of purulent BCG lymphadenitis over the particular time. A P value of less than 0.05 was chosen as the level of significance.

3. Results

A total of 184,068 children had received the BCG-SSI® vaccine countrywide during the whole study period, from 17,633 to 23,123 children each year [24]. Of these 615 patients developed BCG lymphadenitis, while 194 patients aged from 1 to 17 months (the mean age was 5.12 ± 0.96 months) were admitted for surgical treatment of purulent BCG lymphadenitis. The main characteristics of the study population and study findings are presented in Table. All children were healthy and none had reported close contact with any tuberculosis patient prior to hospitalization. The number of patients in each year of the study varied, and the maximum incidence was observed in the period between 2010 and 2012 with the peak in 2011 (Table). During the whole study period the incidence of BCG adenitis varied, while the mean incidence was $0.11\% \pm 0.08\%$ (Figure). A total of 180 patients had purulent axillar lymphadenitis, from 4 to 59 each study year, 14 patients had purulent supraclavicular lymphadenitis, from 0 to 6 each study year. Of the 194 patients, 8 had lymphadenitis at both localizations.

There was a statistically significantly increasing trend in the incidence of BCG vaccine associated purulent lymphadenitis during the period 2005–2013 (Kendall's tau = 0.667; $P = 0.013$), especially in the 3-year span between 2010 and 2012 with the peak incidence in 2011 (0.36%, 95% CI 0.28–0.45, $P = 0.05$) that significantly differed from the mean incidence of the whole 9-year period.