A study of the incidence of BCG vaccine complications in infants of Babol, Mazandaran (2011-2013)

Abstract

Background: BCG vaccination which is administered to prevent tuberculosis is sometimes associated with serious complications. This study aimed to determine the incidence of complications of BCG vaccination in Babol.

Methods: All infants who received BCG vaccination between 2011-2013 in health centers of Babol entered the study. Data regarding complications of vaccine were extracted according to the National Inventory of babies. All complicated cases were confirmed by the Academic Committee to review the adverse consequences of the vaccine.

Results: Among the 15984 vaccinated neonates, 150 (0.93%) cases presented lymphadenitis. 46.5% were females and 53.5% were males; 43% were rural residents and 57% were urban residents. No cases of lymphadenitis including 1% of lymphadenitis with abscess formation were recovered without treatment. Disseminated infection occurred in 3 cases of immune deficient patients who responded to the treatment. Most complications occurred during 4 months after vaccination.

Conclusion: According to the results of this study, the prevalence of lymphadenitis in Babol was higher than the standard of WHO. This may be attributed to type and vaccine storage and injection technique. These findings justify further training of health-center workers.

Keywords: BCG vaccination, Complications, Lymphadenitis, Disseminated TB, Urine discoloration.

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Complications of BCG vaccine

Severe complications include suppurative lymphadenitis, osteomyelitis, osteitis and disseminated infection caused by the vaccine and the global incidence has been 100-1000 and 1-700, and 2 in a million, respectively (5). Most complications from vaccine occur when there are changes in the species of bacteria used in the vaccine or by its low percentage as a result of laboratory errors or vaccine storage and injection technique, the lack of vaccine’s cold chain and inappropriate vaccine doses (6). The complications are more common in people who have a history of previous exposure to tuberculosis cases (7), and in particular, the incidence of complications.

Recent observations have indicated higher than expected number of patients who present to health center clinics because of complications of BCG vaccination. For these reasons, the present study was conducted to investigate the frequency of major complications caused by BCG vaccine in children under the full coverage of health centers of Babol, Mazandaran.

Methods

The population of this study included all children born in 2012-2013 who have received BCG vaccination in Babol. After vaccine-injection, the parents of the vaccinated children were asked to inform regarding the development of any local or systemic manifestations such as swelling, nausea, vomiting, any change in the color of urine, restlessness and frequent urination immediately to health centers. All vaccinated children were followed-up after vaccination and examined by a physician or experts in health centers two weeks after vaccination, then monthly for 3 months until recovery of side effects. Data were obtained from the checklist extracted from the National Inventory in Form 2 and were sent to Communicable DisEASE Prevention and Control Unit. The sent items were discussed in vaccine committee of its adverse effects in the presence of experts among the faculty members; after the confirmation of the effects of the BCG vaccine, questionnaires were approved in the study plan.

Results

In this study, 150 out of 15,984 vaccinated neonates (0.93%) presented with Lymphadenitis among which 70 (46.7 %) cases were females and 80 (35.3%) males; 65 cases (43%) were rural residents and 85 (57%) were urban residents. 99% with lymphadenopathy, lymphadenitis, 1% abscess, in which 99.8 cases recovered without intervention (drug, drainage or surgery) and 3 (0.02 %) cases, including two girls and one boy received diet therapy for 12 months because they had disseminated infection due to a severe immune deficiency; diet therapy included: two months with isoniazid, rifampin, ethambutol, clarithromycin and ten months with isoniazid and rifampin.

In 159 (0.1 %) cases the appearance of urine changed to orange color on the second day after vaccination and recovered after a week. 31 (0.2%) cases had severe restlessness 48 hours to 10 days after injection. 48 (0.3%) cases had nausea and vomiting from the second day of birth to 2 weeks and in the followed examinations, some had cases of GERD who were referred for treatment while the others recovered.

In terms of interval between onsets of symptoms, most complications developed 2-4 after vaccination. The onset of complications at different ages are shown in table 1.

Table 1. Prevalence of complications of BCG vaccine at different ages

| Age (Months) | ≤2 | 2-4 | 4-6 | 6-8 | ≥8 |
|--------------|----|-----|-----|-----|----|
| Complication level (%) | 24 | 35 | 26 | 9 | 6 |

Prevalence of complications varied from 0.6 % to 1.7% across different health cares

Discussion

The results of this study indicate a low prevalence of complications after BCG vaccination with rare severe adverse reactions (8). In this study, disseminated TB infection occurred in children with history of immune deficiency (9 and 10) although there are also reports of disseminated infection in healthy individuals (11). Others reported adverse reactions that included lymphadenitis, erythema, stiffness and abscess at the injection site and lymphadenopathy (12 and 13). In this study, the most common complication was lymphadenitis which was observed similar to other studies, but greater than the standard of WHO (2, 3, 5, 14, 15). Lymphadenitis in the under an area which does not need treatment and can recover by itself. Our cases with immune deficiency were similar to
other studies treated and recovered by drugs like other studies (1, 16).

The adverse effects as a result of the BCG vaccine were also dependent on the type of vaccine. In our study, vaccine type was 0, which like other studies, it was observed that lymphadenitis occurs in the SSI BCG vaccine more than the other types (17, 12). Previous studies, showed the occurrence of some complications. Within 2 years after vaccination. Nonetheless, most of these complications occurred in the first 20 weeks after vaccine-injection (12); these results were similar to the results of a recent study in which the most effects have been seen within 2-4 months which can be attributed to the lack of T helper 1 in the early neonatal period.

Other complications reported in the current study was the development of orange color urine which was not reported in other studies. The cause of urine discoloration in the present study was detected and remained to clear. However, it was not a serious complication and was self-limiting. In this study, the incidence of complications varied across different health centers, which can be attributed to inappropriate dosages, storage and types of vaccine and variations in vaccination injection techniques (2).

In conclusion, the results of this study indicate that the development of complications particularly lymphadenitis in health care centers of Babol is higher than expected and suggests further training of health center staff regarding injection techniques, storage type of vaccine and replacing it with a vaccine with fewer side effects.

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References
1. Afshar Paiman S, Siadati A, Mamishi S, Tabatabaie P, Khotaeeg D. Disseminated mycobacterium bovis Infection after BCG Vaccination. Iran J Allergy Asthma Immunol 2006; 5:133-7.
2. Venkataraman A, Yusuff M, Liebeschuetz S, Riddell A, Prendergast AJ. Management and outcome of Bacille Calmette-Guérin vaccine adverse reactions. Vaccine 2015; 33: 5470-4.
3. Mahmoudi Sh, Khaheshi S, Pourakbari B, et al. Adverse reactions to mycobacterium bovis bacille Calmette-Guérin vaccination against tuberculosis in Iranian children. Clin Exp Vaccine Res 2015; 4:195-9.
4. Kumar Govindarajan K, Yih Chai F. BCG adenitis-need for increased awareness. Malaysian J Med Sci 2011; 18: 66-9.
5. World Health Organization. Department of vaccines and biologicals. Supplementary information on vaccine safety. Part 2: Background rates of adverse events following immunization. 2000. Available at: http://apps.who.int/iris/bitstream/10665/66675/1/WHO_V-B_00.36_eng.pdf. Accessed July 2015.
6. Hassana RH, Abel-Elah Alyb K, Kandila SM, El Sayed Zakie M. Post-Bacillus Calmette-Gue’r’in lymphadenitis in Egyptian children: an outbreak. Ann Pediatr Surg 2012, 8: 69–73.
7. Tobiume M, Shinohara T, Kuno T, et al. BCG-induced pneumonitis with lymphocytic pleurisy in the absence of elevated KL-6. BMC Pulm Med 2014; 14; 35.
8. Murphy D, Corner AL, Gormley E. Adverse reactions to Mycobacterium bovis bacille Calmette–Guérin (BCG) vaccination against tuberculosis in humans, veterinary animals and wildlife species. Tuberculosis 2008; 88: 344-57.
9. von Reyn CF, Kimambo S, Meit L, et al. Disseminated tuberculosis in human immunodeficiency virus infection: ineffective immunity, polyclonal disease and high mortality. Int J Tuberc Lung Dis 2011; 15: 1087-92.
10. Atikan BY, Cavusoglu C, Dortkardesler M, Sozeri B. Assessment of tuberculosis infection during treatment with biologic agents in a BCG-vaccinated pediatric population. Clin Rheumatol 2014 Dec 18. [Epub ahead of print]
11. Delibalta G, Seringeç M, Öncül O. A case diagnosed with chronic granulomatous disease after disseminated infection following BCG vaccination. Mikrobiyol Bul 2015; 49: 461-6.
12. Turnbull FM, McIntyre PB, Achat HM, et al. National study of adverse reactions after vaccination with Bacille Calmette-Gue´rin. Clin Infect Dis 2002; 34: 447-53.
13. Dommergues MA, de La Rocque F, Guy C, et al. Local and regional adverse reactions to BCG-SSI vaccination: a
12-month cohort follow-up study. Vaccine 2009; 27: 6967-73.

14. Daei Parizi M, Kardoust Parizi A, Izadipour S. Evaluating clinical course of BCG lymphadenitis and factors affect on it during a 5-year period in Kerman, Iran. J Trop Pediatr 2014; 60: 148-53.

15. Gołebiowska M, Andrzejewska E, Stryjewska I, Baranowska H, Drazkiewicz A. Adverse events following BCG vaccination in infants and children up to 36 months of age. Przegl Epidemiol 2008; 62: 71-5.

16. Rezai MS, Khotaei G, Mamishi S, Kheirkhah M, Parvaneh N. Disseminated Bacillus Calmette-Guerin infection after BCG vaccination. J Trop Pediatr 2008; 54: 413-6.

17. Alrabiaah AA, Alsubaie SS, Bukhari EI, Gad A, Alzamel FA. Outbreak of Bacille Calmette-Guérin-related lymphadenitis in Saudi children at a university hospital after a change in the strain of vaccine. Ann Saudi Med 2012; 32: 4-8.