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Original research

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Events following BCG vaccination during neonatal period and factors that might affect potency and side effects

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Abstract

Introduction: In Sri Lanka, BCG vaccine is given during neonatal period. There are many myths regarding BCG vaccine and sequelae of vaccination are not clearly documented in medical literature. *Objectives:* Objectives of this study were to describe the sequelae of BCG vaccination and to find out the scientific basis of beliefs related to it. *Methods:* A prospective observational study was carried out at Ragama teaching hospital and two private hospitals in Gampaha district. 125 babies each from government and private sector were recruited, with consent from parents. Vaccine was administered by a consultant Paediatrician. Vaccine site was cleaned with 70 % alcohol and allowed to dry before vaccination. All babies were bathed on same day. Babies were followed up until a scar was detected. *Results:* Only 182 babies completed the follow up and all babies developed a scar. Time taken for a reaction varied, but all babies had a reaction by 8 weeks and a scar by 14 weeks. None had fever or other adverse reactions attributable to the vaccine. *Conclusions:* Cleaning the vaccination site with alcohol, bathing and time of vaccination has no influence on side effects or efficacy of the vaccine. BCG is a safe vaccine provided correct technique of administration is employed.

Keywords: BCG vaccine; BCG scar; neonate

Introduction

Developed by Albert Calmette & Camille Guérin, BCG vaccine was first used on humans in 1921. Countries with high Tuberculosis prevalence like Sri Lanka, give the BCG vaccine during neonatal period [1]. Intradermal administration of BCG in a small, wriggly baby is difficult for an inexperienced administrator. To avoid inadvertent subcutaneous injection, needle should be withdrawn and re-injected if no resistance is felt during vaccination. Subcutaneous injection of BCG vaccine results in abscess formation and suppurative lymphadenitis [2]. Due to thin dermis intradermal injection can result in double puncturing of skin, if neonate moves during vaccination. An experienced vaccinator with good assistance is important for successful BCG vaccination.

Scar formation is generally taken as evidence of successful vaccination. Current recommendation in Sri Lanka is to revaccinate if no reaction observed within six months of vaccination [3]. According to a Sri Lankan study, 97% of children had a scar following BCG vaccination during neonatal period [4]. Different Studies have given variable rates. A study from United Arab of Emirates found a rate of 92% [5], while in Peru it was 99% [6]. In another Sri Lankan study out of 923 children who had BCG vaccine, only 89% had a Scar [7]. According to available information in literature, first a papule appears at the BCG vaccination site, followed by a pustule, ulcer, scab and finally a scar in 8 -14 weeks [8]. Previous studies give timing of some of these reactions, but a detail description is not available [9-10]. Parents become concern when no reaction takes

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place after BCG vaccination and seek medical advice. Knowing timing of different reactions will help to identify non-reactors early and give precise advice to parents.

There are many beliefs about BCG vaccination which are not scientifically tested. BCG vaccine cause fever, vaccinations should be only in the morning and bathing is contraindicated after vaccinations are among them. In addition skin is not cleaned prior to vaccination with antiseptics or 70% alcohol, fearing inactivation of the vaccine [3]. This has no scientific basis, as alcohol has no residual antiseptic action once it evaporates. Primary outcome of this study was to describe the timing of different reactions taking place after BCG vaccination during neonatal period. Secondary outcome was to test varies believes associated with BCG vaccination.

Methods

A prospective observational study was conducted between July 2011 and December 2011, at Teaching hospital Ragama and two main private hospitals in Gampaha district, Sri Lanka.

Subject selection

According to results from previous studies on BCG vaccination, it was assumed about 8% of vaccine recipients will not develop a scar. A sample size of 221 is required to estimate this within 4% (prevalence of 8% and 95 confidant interval 4 -12%) with an estimated dropout rate of 25%. To ensure inclusion of a socio-economically mixed sample, 125 babies born at Teaching Hospital Ragama (government sector hospital) and 125 babies born at two main private hospitals in Gampaha district were selected for the study. Babies were included on all inclusive consecutive basis until the required number was recruited. Only babies in the postnatal wards were included in the study, so that babies born before 35 weeks of gestation were not included. A family history of immune deficiency was obtained prior to vaccination and none had. An information sheet was provided to parents with details of the study. Informed written consent was obtained from mothers and all consented. In accordance to the immunization schedule no other vaccine was received by babies until two months of age.

Vaccination process

All babies were vaccinated within 24 hours of birth. As hospital authorities instructed not to interfere with ward routines, babies in government sector had the vaccine only in the morning, while babies from private sector at different times of the day, to facilitate early discharge. BCG vaccine produced at serum institute of India was used. A special auto disabling BCG syringe was used in the government sector, while single use insulin syringe was used in private sector. After explaining the vaccination process to parents, left upper deltoid area was cleaned with 70% alcohol. After alcohol was evaporated completely, BCG vaccine (0.5 ml) was injected intradermally to the upper outer deltoid region. The vaccinator was a consultant Paediatrician, with over 10 years' experience in neonatal BCG vaccination. All aseptic precautions were taken during vaccination. Resistant was not felt during injection in one baby, so reinjection was done after withdrawing the needle. Double puncturing of skin occurred in another. These two babies were excluded from the study because accuracy of vaccination could not be ensured, but were followed up separately. Two other babies were recruited in place of them. All babies were bathed within 24 hours of vaccination.

Follow up

Babies were observed while in the hospital for fever or local reactions. On discharge parents were advised to report back immediately if baby developed fever or any other complication. If the baby was not in the hospital a telephone call was given on 3rd day after vaccination to inquire the condition of the baby. A special clinic was conducted to follow up these babies. Follow ups were done weekly up to four weeks and fortnightly thereafter, until a scar was present. At each follow up reaction at the vaccination site was recorded. The reaction was recorded as no reaction, induration without visible papule, visible papule, pustule, ulcer or scar. The reaction was recorded by a pre-intern doctor, who was trained by a consultant Paediatrician. Observations of parents regarding the reaction at vaccination site, in between follow ups were also recorded.

Data analysis

Statistical package for social sciences, version 16 was used to analyse the data.

Ethical issues

Ethical approval to conduct the study was obtained from research and ethics committee of faculty of Medicine, University of Kelaniya, Sri Lanka. Permission was obtained from relevant hospital authorities. Parents of babies recruited had no additional expenses other than for travelling. Children who had fever or any other medical problem was seen by a consultant Paediatrician and appropriate actions were taken.

Results

Out of 250 babies recruited for the study, 86 from government sector and 96 from private sector were followed up until a scar was detected. Rest defaulted follow up at different stages. Out of babies completed the study, 10.9% were small for gestational age and 51% were females. Babies with different gestational ages were included in the sample. Table 1 gives the breakdown of the sample according to period of gestation.

Table 1 Breakdown of study population according to period of gestation

POA	*Frequency*
35	02(01.1%)
36	04(02.2%)
37	19(10.4%)
38	47(25.8%)
39	43(23.6%)
40	63(34.6%)
41	04(02.2%)
Total	182(100%)

Reaction at the site

All babies developed a visible scar at the site of vaccination, but the duration taken varied. Minimum duration to produce a scar was 6 weeks and maximum was 14 weeks, with a median of 8 weeks. Breakdown of duration taken to produce a scar is depicted in Table 2.

Table 2 Duration taken to develop a scar

No. of weeks	*Number of babies*
06	28 (15.4%)
08	91 (50.0%)
10	49 (26.9%)
12	11 (06.0%)
14	03 (01.6%)
Total	182 (100%)

Earliest reaction noted at the vaccine site was an induration and mild colour change, without a visible papule. This was noted as early as one week in 66 (36%) babies. Minimum duration taken to produce a visible papule was two weeks. All babies had a visible papule by eight weeks. In 38 (21%) babies, pustular or ulcer stages were not detected or reported by parents. A visible papule directly gave way to a scar in these babies. Breakdown of durations taken to produce different types of reactions is depicted in Table 3.

Table 3 Duration taken to produce different types of reactions

Duration (weeks)	*Visible papule*	*Papule*	*Pustule*	*Ulcer*	*Scar*
Minimum	01	02	03	04	06
Maximum	03	08	12	10	14
Median	02	03	06	06	08

Adverse effects

Five babies developed fever within one week of vaccination. They were assessed by a consultant Paediatrician. Fever was due to sepsis in three of them. In other two, fever was due to dehydration resulting from failure in establishing breast feeding. No baby had fever attributable to BCG. None had BCG adenitis or abscess. No other side effects were detected or reported by the parents, which could

be attributed to BCG. Two babies excluded due to uncertainties of vaccination procedure also developed a scar and did not have any complications.

Discussion

Scar formation is indicative of successful BCG vaccination. A scar does not occur in all BCG recipients [4-7]. This may be due to a personal idiosyncrasy, faulty vaccination technique or inefficacy of the vaccine. In this study cold chain was maintained and correct technique was employed during vaccination. One objective of this study was to find out whether cleaning the vaccination site with 70% alcohol inactivate the vaccine. As all babies in this study developed a scar we can conclude, cleaning the vaccination site with alcohol does not inactivate the vaccine. The present practice of not cleaning the vaccination site risking cellulitis and abscess formation is unfounded.

Results of this study confirm that BCG is a safe vaccine, provided the correct technique is employed during vaccination. In immune competent individuals local adverse reaction rate such as injection site abscess and lymphadenitis occur in less than 1% [11], and disseminated BCG disease is extremely rare [12]. Results of this study indicate correct technique of vaccination and cleaning the site prior to vaccination reduces complications further.

Sepsis and dehydration cause fever in neonates. Attributing fever to BCG vaccine results in delayed presentation of neonates with fever to medical attention. Common belief of BCG vaccination causing fever has not been scientifically tested before. Fever is reported with BCG treatment of bladder cancer [13], but not with routine BCG vaccination. In our study none of the babies developed fever attributable to BCG vaccine, rejecting the common belief. Bathing after BCG is considered contraindicated by Sri Lankan public. Avoiding bathing results in skin sepsis, leading to septicaemia. Effects of bathing after BCG are also not studied before. In our study all babies were bathed within 24 hours of vaccination. This had no effect on potency or side effects of the vaccine.

Present practice of early discharge of babies from the hospital reduces overcrowding in postnatal wards and better bonding between mother & the baby. Often discharges are delayed because BCG is given only in the morning. We could not find any previous studies in medical literature which assessed whether timing of BCG vaccination has any effect on efficacy and complications. In our study BCG vaccination was carried out at different times of the day, including evenings. Some babies were given BCG within 4 hours of birth to facilitate early discharge. Results of this study confirm timing of vaccination has no bearing on safety of efficacy.

Delay in reaction to BCG vaccination often cause concern to parents. Previous studies provide information on types of reactions, but detailed description is not given [8]. This study provides a detailed description of reactions taking place after BCG vaccination. Induration and mild discolouration is the first sign to appear around one week. Maximum duration taken to produce a reaction was six weeks. By 14 weeks all babies had a visible BCG scar. Though some studies have shown scar formation may take more than six months [8] initial stages of reaction would appear well before this. Accordingly, the present practice of waiting six months to revaccinate a child without a reaction is questionable. We propose, a child with no reaction after four months of vaccination can be revaccinated along with other vaccines given at that time, provided inactivated polio vaccine is used. However, as simultaneous administration of BCG and oral polio vaccine reduces the efficacy of BCG [14], timing of BCG revaccination should be decided considering all these facts.

Conclusions

Duration taken for BCG scar formation varies from 6 -14 weeks. BCG is a safe vaccine provided correct technique of administration is employed. Cleaning the vaccination site with 70% alcohol, bathing after vaccination and timing of vaccination has no effect on side effects or efficacy of the vaccine. BCG vaccine is not a cause for fever in neonates.

Conflict of interest

All the authors declare that they have no conflict of interest.

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