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Sandra Burkinshaw

Brigham Young University, sandiburkin@gmail.com

Janelle L. B. Macintosh

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A Literature Review of Barriers to Immunization in Preterm, Low-Birth-Weight and
Very-Low Birth Weight Infants

Sandra Burkinshaw

An evidence based scholarly paper submitted to the faculty of
Brigham Young University
In partial fulfillment of the requirements for the degree of Masters of
Science

Janelle Macintosh, Chair

College of Nursing
Brigham Young University

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ABSTRACT

A Literature Review of Barriers to Immunization in Preterm, Low-Birth-Weight and Very-Low Birth Weight Infants

Sandra Burkinshaw College of Nursing
BYU Master of
Science

Approximately 500,000 infants are born each year prior to 37 weeks gestation in the United States. Despite the increased immunologic risk for infants born pre-term (PT), low birth weight (LBW), or very low birth weight (VLBW), infants in the neonatal intensive care unit are often under immunized, if they are immunized at all. Factors that have been identified to inhibit immunization uptake in the NICU population include: immunization effectiveness, safety and adverse events, provider belief, and policy guidelines regarding vaccination in this population. Providers caring for these vulnerable infants can increase the immunization rates by implementing evidenced based education, developing policy for PT and LBW and VLBW immunizations, and researching steroid administration.

Keywords: literature review, preterm infant, NICU, immunization, barriers



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Introduction

Approximately 500,000 infants are born each year prior to 37 weeks gestation in the United States (The Centers for Disease Control and Prevention [CDC], 2013). Being born even three weeks early puts an infant at increased risk for disease due to an immature immune system. Transition immunoglobulin G (IgG) is the major element of newborn immunity. Because an infant's transition IgG is received via maternal-fetal transfer in the third trimester, the amount of IgG present in an infant's system correlates to their gestational age (Gad & Shaw, 2007). Therefore, infants born early do not have the same level of immunity as full term infants and are at an increased risk for severe complications from vaccine preventable diseases.

The American Academy of Pediatrics (AAP) recommends immunization on the same schedule as full term infants for medically stable preterm (PT), low birth weight (LBW) and very low birth weight (VLBW) infants (Saari, & the Committee on Infectious Diseases, 2003). An exception to vaccinating VLBW infants on the same schedule as other infants is the hepatitis B vaccine. The AAP recommends that providers postpone the hepatitis B vaccine in infants weighing less than 2000 grams and born to hepatitis B negative mothers until 2 months of age or until they reach 2000 grams in weight, due to reduced seroconversion and thus, lower hepatitis B antibody concentrations (Saari, & the Committee on Infectious Diseases, 2003). Also during infancy, immunizations are safe and well tolerated by PT, LBW, and VLBW infants (Esposito, Serra, Gualtieri, Cesati, and Principi, 2009).

Despite the increased immunologic risk associated with the PT and LBW and VLBW, infants in the neonatal intensive care unit (NICU) are often under immunized, if immunized at all (Navar-Boggan, Halsey, Escobar, Golden & Klein, 2012). Navar-Boggan et al. (2012) found

that while 73% of NICU infants had at least one immunization before discharge, only 51% of the infants were up to date on immunizations upon discharge from the NICU.

These results demonstrate that although it is imperative that PT, LBW, and VLBW infants are immunized in the NICU, this is not always happening. It becomes important to understand what barriers may be preventing appropriate immunizations to allow health care providers to encourage immunizations for these vulnerable populations. Additionally, overcoming barriers can have a positive effect on future childhood immunizations. Infants that leave the NICU not immunized or under immunized often continue to be underimmunized during the first year of life (Langkamp, Hoshaw-Woodard, Boye, & Lemeshow, 2001). Batra, et al. (2009) found that infants behind on immunizations upon discharge from the NICU had lower immunization compliance at 2, 4, and 6 months of age. The purpose of this paper is to review current literature about NICU immunizations rates and to discuss barriers to immunization if NICU graduates. Based on the findings, recommendations will be made as to strategies that may minimize or eliminate barriers.

Methods

An electronic search was conducted to identify studies published between 1990-2015. A broad range of dates was chosen due to limited information on this subject. The following databases were searched: CINAHL MEDLINE, PubMed, and Psych Info. Search terms used were “immunize”, “vaccine”, “NICU”, and “intensive care units, neonatal”. Only English articles were included. The initial query resulted in 107 articles (see figure 1). Nineteen articles were eliminated due to discussion of caretaker immunization instead of infant immunization. Nineteen articles discussed disease exposure and nosocomial infections of NICU infants and were eliminated. Eleven articles were eliminated due to discussing specific vaccination effects on PT

or LBW or VLBW infants. Forty-three articles were eliminated because they did not discuss immunizations. Nine further relevant references were retrieved from reference lists. Twenty-seven articles were found to contain information pertinent to this review of literature. Additionally, one seminal article from 1986 by Vohr and Oh examining policy adherence regarding NICU immunizations was included.

Results

Factors that have been identified to inhibit immunization uptake in the NICU population include: immunization effectiveness, safety and adverse events, provider belief, and policy guidelines regarding vaccination in this population. Each of these will be discussed.

Immunization effectiveness

Immune response of PT, LBW or VLBW infants is of concern to both providers and parents. The concern is that these infants will have a lackluster immune response that renders immunizations ineffective and so may question the efficacy of having them immunized. However, evidence suggests a lower response rate still provides adequate protection. A blood sample can be obtained to assess the level of geometric mean titer (GMT) to assess the protection the infant has from a disease.

Titer levels- initial immune response. An appropriate immune response to an immunization is considered to be a four-fold increase in IgG titer. PT, LBW and VLBW have lower levels of antibody production; although titer levels following immunization can be lower in PT, LBW and VLBW infants than their full-term cohorts, a four-fold rise in titer is considered protective (Slack, et al., 2003). Esposito et al. (2009) concluded that the immune response that is invoked in PT, LBW, and VLBW infants is sufficient to induce a “valid immune memory” (p.

S44) and therefore it is effective to immunize PT, LBW, and VLBW infants at recommended chronological age.

Titer levels- continuing immune response. Additionally, PT, LBW and VLBW infants produce a long term immune response that will protect them from diseases they are being immunized against. Khalak, Pichichero, and D'Angio, (1998) found extremely preterm infants who had titer levels drawn at three to four years of age, had similar antibody levels as 3-4 year olds who were full-term infants. Additionally, Kirmani, Lofthus, Pichichero, Voloshen, and D'Angio, (2002) reported that although extremely preterm children had lower titers than their full term cohorts, in a seven year follow up study, titer levels were still deemed protective.

Safety and Adverse Events

Along with immunization effectiveness, safety is a concern for both providers and parents. Common physical conditions that may result in safety concerns and delay immunization include: “intraventricular hemorrhage, antenatal or postnatal steroids, recent surgery, family history of seizure disorder, prematurity and low birth weight” (p. 2 McCrossan, McCafferty, Murphy, & Murphy, 2015). The most commonly reported adverse events found in the literature that PT, LBW or VLBW infants experience after immunization are apnea and fever, which can require a septic workup. Despite these adverse events, they are generally considered non-emergent in nature and do not alter the course of hospitalization.

Apnea. Cardiorespiratory events are of great concern to providers administering immunizations to PT, LBW and VLBW infants. Due to an immature respiratory system PT infants often experience a condition known as apnea of prematurity (Cooper et al., 2008). Pfister, Aeschbach, Stuber, Martin and Siegrist, (2004) found that following immunization, VLBW infants might experience a transient episode of apnea, bradycardia, and/or desaturation. The

authors reported that infants who are higher acuity at the time of immunization were at higher risk for cardiorespiratory events. Although there is an increased risk of cardiorespiratory events with administration of the first dose of a vaccine, a PT infant that experiences an apneic event following the administration of a first dose of an immunization does not have an increased risk of further apneic episode following the administration of the second dose of an immunization (McCrossan, et al. 2015).

Septic Work up. Unlike apnea, elevated temperature is an expected response following immunization. Approximately one in fifteen children develops a fever after receiving an immunization (CDC, 2013). In the NICU setting, a new onset of fever can be cause for alarm. Infection must be ruled out by completing a septic workup, including a complete blood count (CBC), blood culture, and lumbar puncture (Simonsen, Anderson-Berry, Delair, & Davies, 2014). A septic evaluation is a lengthy work up that often leads to delayed discharge of the infant from the NICU.

Navar-Boggan, et al. (2010) studied 490 infants who were immunized in the NICU. The authors reported increased rates of apnea and fevers; however, the researchers did not find an increase in septic evaluations. The researchers determined the lack of septic evaluations may be the result of two things: 1) providers are immunizing infants when they are at their healthiest and/or 2) providers are declining to collect blood cultures after immunization using the rationale that the fever may be an expected side effect of the immunization rather than a sign of infection. However, McCrossan, et al. (2015) studied 344 infants and reported no documented adverse reactions to immunizations and theorized that the only true contraindication to immunizations is a confirmed previous anaphylactic reaction to a vaccine.

Provider belief

Because of expected and unexpected side effects, providers may hesitate to immunize PT, LBW and VLBW infants. Batra et al. (2009) found that despite CDC and AAP recommendations, many health care providers believe that factors such as birth weight, current weight and degree of prematurity should determine the decision to immunize NICU infants. Health care workers also cite illnesses of the infant as a barrier to vaccination (Batra et al., 2009). Health care workers hold these beliefs despite national recommendations and scientific data to the contrary.

At times, health care providers may not see immunizations as a high priority with these infants or depend on the primary care provider to immunize the infant after discharge. Navar-Boggan et al. (2012) suggested that providers in the healthcare system may not place high priority on immunizations in infants that will be followed closely by a primary care provider after discharge. Yet providers' initial lack of prioritization of immunizations in PT, LBW and VLBW often leads to immunizations being delayed in the following years (Navar-Boggan et al., 2012).

Policy and guidelines

Other problems with immunizations are that hospital policies regarding immunizations are not always followed nor are national guidelines adhered to. Vohr & Oh (1986) examined 30 NICUs across the United States and found that only 15 of those hospitals had an immunization policy that followed the current AAP guidelines. Of the 30 NICUs studied, only 3 (1%) enforced adherence to the policy (Vohr & Oh, 1986). No more recent studies about NICU immunization policies were found in the literature.

Implications for Practice

Navar-Boggan et al. (2012) recommend that to reduce hospital readmission, immunizations should be given to infants before discharge to allow time for monitoring for immunization related events. The researchers found that providers could be assured that aligning hospital policy with current immunization guidelines will not prolong the length of stay for infants in NICU due to increased rates of sepsis evaluation. Researchers also recommend that blood cultures be deferred in the first 24 hours after immunization if the infant shows no signs of infection besides fever (Navar-Boggan et al., 2010). DeMeo et al. (2015) recommend that medical providers increase the threshold for sepsis evaluations in infants who were healthy prior to immunization and present with fever following immunization.

There is room for improvement to safeguard PT and LBW and VLBW infants from vaccine preventable diseases. Providers caring for these vulnerable infants can increase the immunization rates of PT and LBW and VLBW infants by implementing evidenced based education, developing policy for PT and LBW and VLBW immunizations, and researching steroid administration.

Education

Gaps exist between recommendations of AAP and CDC and provider belief regarding PT, LBW and VLBW immunizations. Education for health care workers who care for these infants can provide knowledge as to the importance of immunizations and dispel common concerns. NICUs should provide mandatory in-services for providers. Information in the form of a researched based pamphlet-describing PT, LBW and VLBW immune response to vaccination should be provided. It is important to emphasize that all infants should be immunized on the

same schedule regardless of gestational age or birth weight. Offer ample time to address questions and concerns. This same education should be given to new hires upon employment in a NICU.

After initial education, continuing educational efforts, with the most current evidenced based information, will be necessary. Trainings should focus on reminding providers of AAP and CDC recommendations, reviewing hospital policy on PT, LBW and VLBW infant immunization guidelines, and assessing if providers recognize the importance of adhering to AAP and CDC recommendations. Educators can further help healthcare workers by engaging in open dialogue with providers with time to answer questions or concerns. Signs placed in the NICU that display AAP and CDC recommendations as well as the immune response to those immunizations can serve as a reminder to providers and parents to immunize infants while in the NICU.

Policy

Along with education, policy development and enforcement could impact immunization rates of PT, LBW, and VLBW infants. Hospitals should develop policies that follow AAP and CDC recommendations. In order to align with AAP and CDC guidelines, policies should state that clinically stable PT and LBW and VLBW infants should receive immunizations on the same schedule and receive the same dose as full-term infants.

In order to decrease readmissions following immunizations, policies should include the requirement that immunizations are given at least 48 hours prior to expected discharge from the NICU to monitor for adverse events. Accordingly, in the event of an elevated temperature following immunization, septic evaluation should be deferred for a minimum of 48 hours if the infant shows no other sign of infection besides a fever.

Along with policy creation and implementation, enforcement is a critical element for successful policy adoption. In order to enforce an immunization policy, strict adherence to documentation will be needed. This documentation needs to include the following information about all immunizations: date, time, dose, lot number, site, and adverse events. If an immunization is not given, documentation along with the reason for immunization refusal will be required. Chart audits by individual units, hospitals and state agencies should be done to help enforce immunization policies.

Follow Up Care

PT, LBW or VLBW infants often require frequent follow up care in a pediatric clinic or neonatal follow up clinic. Creating a nursing position that acts as a liaison between the hospital and outpatient setting can increase the chances that NICU infants who are not immunized in the hospital can be immunized on schedule in the outpatient setting. Job responsibilities may include creating flow sheets that show immunizations infants received in the hospital setting and what immunizations are needed in the outpatient setting. The liaison's responsibility would be to ensure PT, LBW and VLBW infants are receiving needed immunizations and follow up care on schedule. Creating NICU follow-up clinics could help meet this need by providing a specialized environment for parents to take their infants for follow up care and immunizations. A NICU follow-up clinic would provide a multi-disciplinary clinic including a pediatrician, neonatologist, physical therapy, occupational therapy, and immunization specialist where providers are specialists at providing care for PT and LBW and VLBW infants.

Steroid Administration

Throughout the literature, there is an anecdotal evidence that administration of steroids, during either the antenatal or postnatal period, affects immune response in PT, LBW and VLBW

infants (McCrossan, et al 2015). Common provider assumptions are that PT, LBW and VLBW infants receiving steroids will have a lackluster immune response to immunizations, rendering the immunization ineffective. However, researchers have found that neither antenatal nor postnatal steroid administration is a contraindication to immunization (McCrossan, et al 2015). More research needs to be conducted on steroid administration to determine if steroids affect PT, LBW and VLBW infant's immune response to immunizations.

Conclusion

Despite AAP and CDC recommendations that PT, LBW and VLBW infants be immunized on the same schedule as their full term cohorts, many infants are not fully immunized. A pattern of under or non-immunization continues throughout a child's life. Immunizations are safe and produce appropriate antibodies in PT, LBW, and VLBW infants. Although adverse events have been documented with initial immunizations, observation for 48 hours can offset provider and parental concerns.

Educating providers regarding AAP and CDC recommendations of immunizing PT, LBW and VLBW infants on the same schedule as full term infants along with the immune response of these infants can increase the rate at which NICU infants are immunized. Developing, implementing, and enforcing hospital policy for NICU immunizations will protect PT, LBW and VLBW infants from vaccine preventable diseases. Immunizations are safe and effective for preventing disease in PT, LBW and VLBW infants.

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Figure 1- Search and selection

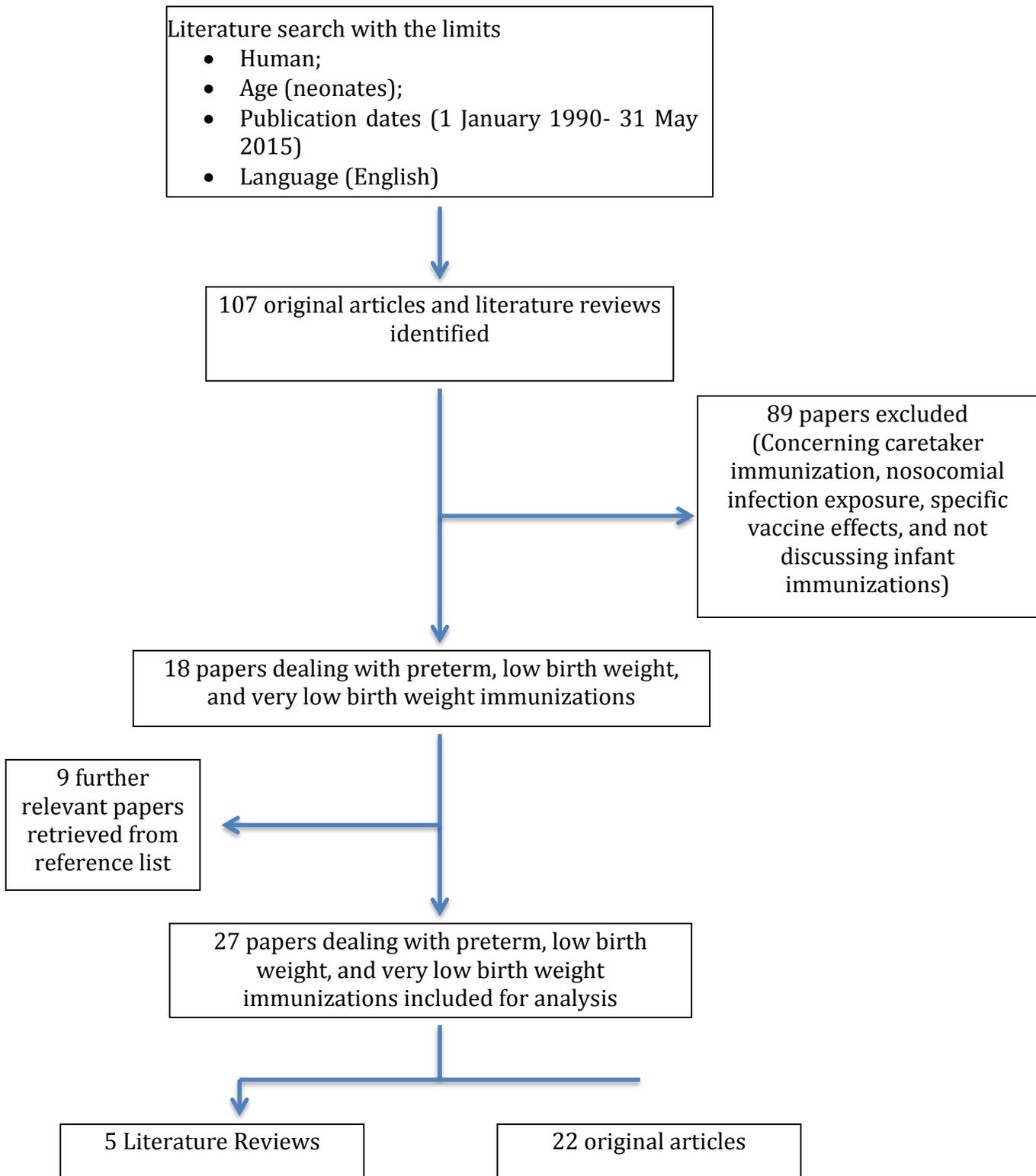


Figure 2

Clinical Implications

- Focus education, both initial and continuing, on the AAP recommendation that PT and LBW infants be immunized at chronological age and on the same schedule as full term infants.
- Develop and implement policy that follows AAP and CDC recommendations for immunization. Policy should state that PT and LBW and VLBW infants be immunized at least 48 hours prior to expected discharge from NICU to monitor for adverse events.
- Follow up care in pediatric clinic or NICU follow up clinic to ensure infants not immunized in the NICU can be placed on a catch up schedule for immunizations.
- Further research on steroid administration effecting immune response needs to be done.