

ORIGINAL ARTICLE

## Investigation on Immunoglobulin Fortification in Preventing Infections in the Newborn

by

HANS ELDIH MONINTJA

*(From the Department of Child Health Medical School University of Indonesia, Jakarta)*

### Abstract

*Observations in neonatal sepsis revealed that the IgG concentrations in septic newborns is significantly lower than in non septic infants. This condition lead the author to investigate the role of fortification of IgG in infants with intrapartum infections. For this purpose a prospective study was carried out, 35 newborn infants with intrapartum infections were treated with IgG Cutter 0,6 mg per Kg BW per week and 35 other infants with similar criteria served as control group. The result of the trial showed that IgG administration could help in prevention of minor infections.*

### Introduction

In developing countries including Indonesia infection is one of the main cause of neonatal mortality (Perera and Khing, 1984). This is understandable due to the socioeconomic condition in those countries. Systemic infections in the neonate in developed countries remained a major cause of infant mortality despite the development of broad spectrum antimicrobial agents and technological advance in life support therapy. Yoder and Polin (1986) stated that the incidence of neonatal septicemia changed only a little within this past 50 years but the mortality did decline. The mortality rate of sepsis in the low birth weight infants has not exhibited the same trend as in the full term infant and remain ten fold greater than that of infants with higher birth weights.

Hobbs and Davies (1967) demonstrated that there is a linear relationship between the logarithm of the gammaglobulin levels at birth and gestational age. Yeung and Hobbs (1968) confirmed the findings of Hobbs and Davies and further more showed that also in small for date and postmature babies the gammaglobulin levels is lower compared to normal newborns.

Our own observations and later on supported by Budiningsih et al. (1984) revealed that in neonatal Salmonella infections the IgG concentration is much lower compared with control group. Further prospective observations revealed that in other gram negative infections the IgG levels showed the same picture.

### Materials and methods

This was a prospective study covering the period from March 1 to July 31, 1987. All babies delivered with intra partum infection for this purpose were nursed in a

special care unit at the Neonatal ward, Dept. of Child Health. Medicine School University of Indonesia, Jakarta. All babies received standard antibiotic treat-

ment with ampicillin and gentamycin for three days for prevention of infection. The infants were divided into two groups i.e

trial group which received gammastan (IgG CUTTER) 0.6 ml per kg bw per week and the other group served as control group. The treatment and observations lasted for two weeks. The sampling were done randomly. Besides the IgG therapy all received the same nursing and management. Infants with clearcut infection were excluded from this study except those who contract it during the study period. Infants with morphological and functional con-

genital anomalies were also not included in the study.

The population of infants within the groups matched properly, the difference were not significant. The infants were matched on birthweight and gestational period as well as on possibility of intra partum infections. Most of the infants were low birth weight and the gestational period were within the range of 32 to 37 weeks. Intra partrum infection is considered present if the membrane ruptured 24 hours before delivery, or the amniotic fluid being infected and if there is a septic delivery.

These observations created a speculation whether or not fortification of gamma-globulin could have a role in increasing the ability of the newborn in preventing infections. Several methods have been mentioned in the past regarding immuno therapy against neonatal infections.

1. Exchange transfusion which started in 1970s by Prodhom et al. (1974) and Tollner et al. (1977). The rational is to remove bacterial endotoxins, improve circulation and to enhance cellular and humoral immunities. Vain et al. (1980) reported that exchange transfusion immediately improved clinical status and increment of IgM and IgA but not IgG concentrations. Because of the serious adverse effect of exchange transfusion one must consider carefully the benefit of the procedure before making the decision.
2. Granulocyte transfusion also had been advocated as an adjunct immunologic therapy in neonatal sepsis with neutropenia.
3. Immunoglobulin transfusion.

Previous trials on this kind of treatment in managing neonatal infections has been carried out abroad by several authors (Amer et al., 1963; Steen, 1960). Chirico et al. (1987) recently published their work on intravenous IgG therapy as prophylaxis on high risk infants and reported that this method of treatment is safe and effective in preventing infections in the newborn.

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### Results

Table 1 : *The effect of IgG administration on prevention of septicemia*

Groups	No. of babies with sepsis	No. of babies without sepsis	N
IgG	1*	35	35
Control	2	33	35

\*  $p > 0.05$  compared with control group.

Table 1 shows that the administration of IgG did not prevent the occurrence of sepsis. This observation also doubt the value of

antibiotic prevention of septicemia. All cases of septicemia in this series were due to gram negative bacteria.

Table 2 : *The effect of IgG administration on prevention of enteritis*

Groups	No. of babies with enteritis	No. of babies without enteritis	N
IgG	1*	35	35
Control	6	29	35

\*  $p < 0.05$  compared with control group.

In cases of enteritis IgG administration seems to have a positive effect. However it is our opinion that hygienic measures are still the best one in preventing enteritis. It is the kind and virulency of bacteria that could determine the effectivity of IgG

administration not the kind of pathology.

Table 3 shows that in URTI (upper respiratory tract infection) the administration of IgG has a positive effect. On culture, most of the URTI were due to gram positive bacteria.

Table 3 : *The effect of IgG administration on prevention of upper respiratory tract infection (URTI)*

Groups	No. of babies with URTI	No. of babies without URTI	N
IgG	1*	34	35
Control	10	25	35

\*  $p < 0.05$  compared with control group.

Table 4 : *The effect of IgG administration on prevention of neonatal skin infections*

Groups	No. of babies with skin infections	No. of babies without skin infections	N
IgG	0*	35	35
Control	1	34	35

\*  $p > 0.05$  compared with control group.

Table 5 : *The effect of IgG administration on prevention overall infections*

Groups	No. of babies with infections	No. of babies without infections	N
IgG	2*	33	35
Control	22	13	35

\*  $p < 0.05$  compared with control group.

In overall infections IgG administration do has a positive effect in preventing infections. The results of this study showed that in the newborn with intrapartum infection

concomitant administration of IgG with antibiotics could help in prevention of overall infection in the newborn but not in severe infections.

## Discussions

The immune respons of the neonate according to Miller (1978) is as follows :

1. The modulating factors which derives from the presence within the newborn circulation of humoral and cellular factors derived from the mother during gestational period.
2. Active antibody production.
3. Passive immunity.
4. Cellular immune response and
5. T Cell function, which will not be elaborated in this discussion.

Passively acquired maternal IgG antibodies confer protection upon the newborn against a wide variety of microorganisms. Antibodies against gram negative organisms such as *E. coli* and *Salmonella* usually covered by IgM class which can not cross the placenta. There are, however, some IgG antibodies against somatic antigens of gram negative organisms thereby affording some degree of protection.

The IgM is synthesized rapidly after birth. The levels rise rapidly during 4 to 7 days of life. In our experience of neonatal salmonellosis (Budiningsih et al., 1984) there were a considerable elevated levels of IgM and IgA. This information could serve as early diagnostic clue of this infection.

The aspects of passive immunity greatly attract our interest since new development in immunology provides us with information that fortification of this mechanism could play a role in preventing neonatal infections.

The findings of Budiningsih et al. (1984) which later on reconfirmed by our own observations raise some speculations as to whether the lowering of IgG in gram negative infections could have a therapeutic impact. Based on this speculation we were encouraged to try the IgG first as a

preventive measure and later on as therapeutic measure. In our trial IgG was given only once a week compared to antibiotic prophylaxis which was given 3 to 4 times a day for 3 to 5 days. So the difference in cost is indeed considerable indicating that IgG is practically cheaper than antibiotics.

The results of the investigation showed that IgG do play a role in preventing infections in the newborn. One of the most dreadful preliminary infections is enteritis which in our unit is mostly due to gram negatives such as Salmonellosis (Monintja et al., 1982) and at present is *Pseudomonas* (Monintja and Faizah 1987). These gram negative enteritis oftenly preceed septicemia since actually they attacked submucosal tissue which then spread through circulation leading to septicemia. So by preventing this kind of infection in the primordial state we can save a lot of money, time, energy and lives.

During the study there was no observable clinical side effects, abnormalities in peripheral blood examinations and liver function test. It is our present opinion that this kind of treatment could be used as an ajuvant treatment of neonatal septicemia besides antibiotics.

Amer et al. (1963) reported that the administration of IgG intramuscularly in preterm infants could prevent minor infections in the newborn. Meanwhile Chirico et al. (1987) gave intravenous IgG for this purpose and claimed that it is a save and an effective prophylaxis against infections in preterm and low birthweight babies. According to Chirico et al. (1987) the unsatisfactory results of Amer et al. (1963) and Steen (1960) were due to the route of administration which was intramuscular.

Since the development of the intravenous IgG they concluded that if it was given intravenously the results would be better. Our results compared to Chirico et al. is not so satisfactory especially in preventing septicemia. However, even though in low

doses and even in intramuscular route because of the unavailability of intravenous IgG, the results of our trial is very promising. In the future to face high risk of infection the dosage of IgG has to be increased and given intravenously.

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