

Therapeutic Effect of intravenous Pentaglobulin In Treatment of neonatal sepsis

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Abstract

Neonatal sepsis is the leading cause of morbidity and mortality in neonates in developing countries, intervention trials showed that using Pentaglobin in neonatal sepsis decrease morbidity and mortality.

Patients and Methods:-

The study included 100 patients sustained neonatal sepsis, (age 0-30 days), fifty patients were treated with antibiotics only, and the remaining 50 patients were treated with antibiotics and pentaglobin as an adjuvant therapy.

Results:-

The study showed that improvement occurred when treatment included (Pentaglobin) in 74% compared to 38% in case of treatment with plain (antibiotics) with a relative risk of 1.95.

Conclusions:-

Pentaglobin is useful in the management of neonatal sepsis.

Recommendations:-

Pentaglobin may be added to the (antibiotics) in the management of neonatal sepsis further studies are required to determine the cost effectiveness.

Introduction

Infections are frequent and important cause of neonatal and infant morbidity and mortality. As many as 2% of fetuses are infected in the uterus, and up to 10% of infants have infections in the first month of life¹.

Neonatal sepsis is a clinical syndrome characterized by systemic signs of bacteremia in the first month of life, Sepsis occurring in the first 72 hours of life is defined as early-onset sepsis (EOS) and that occurring beyond 72 hours as late-onset sepsis (LOS). Neonatal early onset sepsis is defined by Centers for Disease Control and prevention (CDC) as blood or cerebrospinal fluid culture proven infection occurring in the newborn younger than seven days of age. Neonatal late onset sepsis is usually defined as culture proven infection in an infant between seven days and three months of age²⁻⁴.

Neonatal sepsis should be suspected in neonate when he has lethargy, seizures, feeding intolerance, skin infection, hypotonia, metabolic acidosis, and pneumonia⁵.

Bacterial neonatal sepsis diagnosed by blood culture, CBP, CSF culture, urine culture, GUE, GSE, stool culture, and C-reactive protein positive¹.

Bacterial neonatal sepsis treated by⁴⁻⁷;

- Wide spectrum antibiotics, (amoxicillin, and gentamycin) for at least 7-10 days.
- Intravenous fluid if needed.
- Oxygen if needed.
- The use of intravenous Pentaglobin has been shown to decrease mortality in patient with sepsis when used as an adjuvant therapy¹.

Pentaglobin preparation is the only approved intravenous immunoglobulin for treating bacterial infections and

contains anti-bacterial, anti-inflammatory and immunomodulatory antibodies from the immunoglobulin⁸⁻⁹.

To date, there are no studies conducted in Baghdad assessing the efficacy of Pentaglobulin preparations in pediatric wards. In this framework, the objective of this trial was to assess the efficacy of an IgM preparation as adjuvant therapy in the treatment of neonates with sepsis in Baghdad. We hypothesized that administration of the IgM preparation in combination with standard-of-care antibiotics would increase the overall survival rate in septic patients admitted to NICU⁹.

Aim of the study

The aim of this study is to determine the role of (pentaglobin) therapy in treatment of neonatal sepsis.

Patients and Methods

A prospective clinical trial in neonates 0-30 day of age designed to see the effectiveness of supplying (immunoglobulin) during neonatal sepsis episodes on the course and outcome of the illness.

100 children with a presenting symptom of neonatal sepsis admitted to the neonatal unit in Al-Elwea teaching hospital between Jan. 1st 2016 and Jan. 1st 2017.

Inclusion and exclusion criteria

The study included all neonates aged 0-30 days presented with signs and symptoms of sepsis (lethargy, poor feeding, poor reflexes, hypotonea, vomiting, or other signs of sepsis).

Children who had one or more of the following criteria were excluded:

1. If the neonate discharged against medical advice.

2. Examination revealed syndromes of genetic diseases.

3. Lab. Investigations revealed negative C - reactive protein.

A prepared questionnaire form was proposed for every child included in the study, the questionnaires involved age, sex, weight, type of feeding, and the outcome at discharge.

And secondary exclusion involved the following conditions

1. When the patient failed to receive the medication.

2. If received medications other than the decided regimen such as frusamide.

3. If further investigations diagnose congenital heart disease, in born error of metabolism, congenital TORCH infection, or other causes of neonatal morbidity.

Final reassessment intentionally included 50 children treated with antibiotics only and other 50 treated with antibiotics plus pentaglobin therapy.

Clinical intervention

Patients were randomly divided into two equal groups 50 children were treated with fluid, amoxicillin, gentamycin, O₂ if needed with doses calculated according to WHO regimen⁽¹⁾ alone, while the remaining 50 children were treated with the same doses plus pentaglobin intravenously, administration of IGM preparation was started on the day of sepsis diagnosis at a volume of 5ml/kg body weight per day and was infused over six hours for three consecutive days¹.

Improvement was considered when c reactive protein changed to negative after three days therapy².

The safety and efficacy of adding pentaglobin were tested and proved by previous studies such as New Delhi, and North Indian studies^(10,11).

Data Analysis

Data analysis was performed Using:-

A) Descriptive statistics (frequency and percentage).

B) Inferential statistics (X² test) were $P < 0.05$ considered statistically significant.

Results

One hundred children presented with neonatal sepsis admitted to the neonatal care unit in AL-Elwea teaching hospital were included in the study sample analysis. 50 of them were treated with pentaglobin and standard sepsis therapy, the range of their age was (0-30 days), and the mean of their ages was 13.3 days, mean weight 3.3kg.

The other 50 children were treated with standard sepsis therapy alone, the range of their ages was (0-30 days), and the mean of their age was 13.1days, mean of weight 3.2 Kg.

The percentage of improvement after 72 hours in neonates who were treated with pentaglobin was 74%, while for those who didn't receive pentaglobin was 38%, and hence the relative risk was 1.95 (those who were included in the first arm of the study had 1.95 time better chance of improvement than those who were included in the second arm) (tab. 1).

The difference between results of treatment in both groups was statically significant (X² test $P=0.0005$).

Analysis of the results regarding the age of the children (children aged < 7 days compared to children aged > 7

days) showed improvement of both age groups (tab.2) .

Both sexes showed improvement in the outcome when pentaglobin was added to the treatment (tab. 3)

Considering type of feeding it was showed that improvement of outcome in case of adding pentaglobin whatever

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the type of feeding, but the relative risk compared to bottle feeding(tab.4,5,6).
was more in case of breast feeding

Table (1) the outcome of treatment of neonatal sepsis with pentaglobulin

Type of treatment	No. improved neonates	No. of improved neonates	Total	percentage of improvement
Pentaglobin +antibiotic	37	13	50	74%
antibiotic only	19	31	50	38%
Total	56	44	100	56%

P=0.0005 relative risk= 1.95

Table (2) the outcome of treatment of neonatal sepsis in relation to age.

Age	Type of treatment	No. of improved children	No. of non-improved children	Total	percentage of improvement	P value (X2 test)	Relative risk
>7days (n=49)	Pentaglobin+ antibiotic	18	7	25	72%	0.032	1.73
	antibiotic only	10	14	24	41.7%		
	Total	28	21	49	57.14%		
=< 7 days (n=51)	Pentaglobin+ antibiotic	18	7	25	72%	0.032	1.87
	antibiotic only	10	16	26	38.46%		
	Total	28	23	51	54.9%		

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Table (3): The outcome of treatment of neonatal sepsis in relation to sex

Sex	Type of treatment	No. of improved neonates	No. of non-improved neonates	Total	Percentage of improvement	P value (X2 test)	Relative risk
Male (n.=48)	Pentaglobin + antibiotic	18	7	25	72%	0.032	1.66
	antibiotic only	10	13	23	43.48%		
	Total	28	20	48	58.3%		
Female (n.= 52)	pentaglobin + antibiotic	18	7	25	72%	0.016%	1.94
	antibiotic only	10	17	27	37.04%		
	Total	28	24	52	53.85%		

Table (4): Percentages of improvement of breast fed neonates treated with pentaglobin.

Type of treatment	No. of improved neonates	No. of non-improved neonates	Total	percentage of improvement
pentaglobin +antibiotic	13	2	15	86.7%
antibiotic only	8	10	18	44.4%
Total	21	12	33	63.64%

Relative risk = 1.95

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Table (5) Incidence of improvement in bottle fed neonates treated with pentaglobin.

Type of treatment	No. of improved children	No. of non-improved children	Total	Percentage of improvement
Pentaglobin +antibiotic	10	9	19	52.6%
antibiotic only	9	14	23	39.1%
Total	19	23	42	45.2%

Relative risk = 1.35

Table (6) Incidence of improvement in mixed feed neonates treated with pentaglobin

Type of treatment	No. of improved children	No. of non-improved children	Total	percentage of improvement
pentaglobin + antibiotic	10	6	16	62.5%
antibiotic only	4	5	9	44.4%
Total	14	11	25	56%

Relative risk = 1.41

Discussion

Our study shows that the percentage of improvement in neonates who were treated with pentaglobin plus antibiotics is better than those treated with antibiotics only.

The percentage of improvement in the group treated with pentaglobin plus antibiotics, and in those treated with antibiotics only, and the relative risk were (74%, 38%, 1.95) respectively (table 1), compared to (65%, 39%, 1.67) respectively obtained in similar

study in Iran ⁽¹²⁾, and (70%, 42%, 1.67) in Cairo ⁽¹³⁾, and (66%, 38%, 1.73) in Syria⁽¹⁴⁾.

The somewhat better results observed in our study compared to the other studies is probably resulted from the exclusion criteria applied in this work including congenital heart diseases, in born errors of metabolism, TORCH infections and congenital nephrotic syndrome.

In our study less than 7 days old improved slightly better than older

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neonates, with relative risks of 1.87 Vs 1.73 respectively, this deference may be related to the immaturity of the immunity of neonates aged below seven days that resulted in more improvement once pentaglobin therapy started. A comparable difference was also found in a study performed in North India⁽¹¹⁾ with relative risks of 1.62, Vs 1.55. When compared to the South India study⁽¹⁵⁾, our study showed more impressive of adding Pentaglobin in both age groups, this difference may be related to the exclusion of preterm infants in our study.

Adding Pentaglobin was beneficial in both genders but it was more beneficial in females than in males this related to the fact that RDS more common and severe in males.

A single study performed in Pakistan⁽¹⁶⁾ showed better improvement in females compared to males.

Considering the type of pre-morbid feeding; it was shown that breast fed children showed better improvement than bottle fed children (86.7%, Vs 52.6% respectively), while children on mixed feeding improved in 62.5% of the cases .

The relative risk of improvement of breast fed babies was (1.12), and in bottle fed ones was (1.35) and in mixed fed babies was (1.41) (tab.4,5,6),.we are unaware about a comparable study to compare these results with them in relation to type of feeding .

The impact of adding Pentaglobin in the management of neonatal sepsis was more impressive in breast fed children compared to bottle fed ones, this may be attributable to the role of breast milk in neonatal immunity, and this is in

addition to the other known benefits of breast milk, regarding physiological composition and the sterility.

Conclusions

- Addition of Pentaglobin in the management of neonatal sepsis is useful in decreasing severity and duration of illness.
- Pentaglobin is effective in the management of neonatal sepsis in early and late sepsis and in both males and females.
- Adding Pentaglobin to the treatment is more beneficial in breast fed babies than in mixed fed and bottle fed babies.

Recommendations

Further studies are required to answer the following questions

- The cost-effect relationship of adding Pentaglobin to the management of neonatal sepsis.
- To study side effects of pentaglobin in neonates.
- Assessing the effect of adding Pentaglobin to the therapy in certain infections such as E-coli, lesteria monocytogenus, and streptococcus infections.
- Study pentaglobin therapy and side effects in preterm related to full term neonates.

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