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A Retrospective Study of Intrathechal vs. Intramuscular Administration of Human Tetanus Immunoglobulin in Pediatric Tetanus

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Abstract

Aim: To evaluate the effect of intrathecal vs. intramuscular tetanus immunoglobulin therapy on hospital stay and mortality in pediatric tetanus patients admitted to a tertiary care hospital. *Methods and Material:* Retrospective analysis of hospital records of tetanus cases to the pediatric ward during two year period between 2012 and 2014 was done. All patients were managed as per pre-existing unit protocol. Group A received Human tetanus immunoglobulin (TIG) 250 unit a via the Intrathecal route preceded by IV ketamine (1 mg/kg) for proper relaxation to ease the procedure and the group B was given TIG 750 unit via intramuscular route. Whether to give TIG by Intrathecal or intramuscular route was decided according to the treating unit's protocol. Information regarding–sex, age, immunization status, mode of infection, grade of tetanus, out-come and hospital stay was recorded in the two groups. *Statistical Analysis:* Fisher's exact test, Chi square test, Unpaired t test. *Results:* There were total 40 patients with tetanus aged between 1 to 12 years during the two year study period. Neonatal tetanus cases were excluded. Out of 40, 15 patients were included in group A (intrathecal route) and 25 in group B (intramuscular route). Mortality and hospital stay was found to be less in group A (26.67%; 12.4 ±2.25days) as compared to group B (28%:15.4 ± 1.69 days). *Conclusion:* We found no significant difference between intrathecal immunoglobulin and intramuscular immunoglobulin therapy in management of pediatric tetanus in terms of mortality and hospital stay.

Keywords: Tetanus; Immunoglobulin; Intrathecal.

Introduction

Tetanus is an acute, spastic paralytic illness historically called lockjaw that is caused by the neurotoxin produced by *Clostridium tetani,* a motile, gram-positive, spore-forming obligate anaerobe whose natural habitat worldwide is soil, dust, and the alimentary tracts of various animals [1]. Mortality and morbidity caused by tetanus is significant in spite of all available treatments. It is the only vaccine preventable disease that is infectious but not contagious from person to person. In spite of simple preventive measures available, tetanus remains a major cause of mortality in the developing countries.

Treatment of tetanus consists of administration of tetanus immunoglobulin to neutralize the toxin, drugs to control spasms, antibiotics to eradicate organisms and supportive care. Although textbooks do not recommend intrathecal tetanus immunoglobulin, there have been several reports for this route of administration although with variable dosages in the management of tetanus [1-4]. Intramuscular route is widely accepted and requires less skill while Intrathecal administration requires a skill with full aseptic precaution and proper sedation. The toxin produced by Cl. Tetani binds at the neuromuscular junction then gets transported to the alpha motor neuron by retrograde axonal transporter. The toxin exit the motor neuron in the spinal cord

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and enters the adjacent inhibitory neurons where it prevents the release of the neurotransmitter GABA [1]. Once the toxin has begun its axonal ascent, it cannot be arrested by systemic administration of TIG. Studies show that antitetanus immunoglobulin by intrathecal route has better clinical progression than by intramuscular route in mild and moderate tetanus [5,6].

This study aims to compare outcome of tetanus patients on the basis of hospital stay and mortality treated with intrathecal and intramuscular tetanus immunoglobulin therapy.

Subjects and Methods

The cases of tetanus admitted to pediatric ward, Sir. T. hospital, Bhavnagar from 1 month to12 years of age admitted between December 2012 and December 2014 were evaluated retrospectively. Neonatal tetanus was excluded from our study. Tetanus was diagnosed on the basis of a history of localized or generalized spasms in a child along with clinical findings of trismus, risus sardonicus and/ or provoked or unprovoked generalized spasms [1]. All patients were managed as per treating unit's established protocol. Group A received Human tetanus immunoglobulin (TIG) 250 unit administered via the Intrathecal route preceded by IV ketamine (1 mg/kg) for proper relaxation to ease the procedure and group B were given intramuscular TIG 750 unit [7]. Decision to give TIG either by Intrathecal route or intramuscular route depended upon unit's protocol. Patients received penicillin G (100,000 U/kg/day divided every 4-6 hours IV for 10-14 days) along with metronidazole (10 mg/kg/dose every 8 hourly IV) for 10-14 days. All patients received diazepam both for relaxation and seizure control (dose and route depending on severity). We followed the modified Patel and Joag criteria [8] (Table 1).

Doses of the sedatives (administered by nasogastric tube) were as follows:

Mild Grade

Diazepam -20 mg/kg/day divided in 2 hourly doses;

Moderate Grade

Diazepam - 40 mg/kg/day divided in 2 hourly doses, and Chlorpromazine (CPZ) - 0.5 mg/kg/dose, 4 times a day; and

Severe Grade

Diazepam-60 mg/kg/day divided in 2 hourly doses, Chlorpromazine (CPZ) - 0.5 mg/kg/dose, 4 times a day, and Phenobarbitone (PB) - 5 mg/kg/day in 2 divided doses. Additional dose of diazepam (0.2 mg/kg/dose) was given for individual spasms as required. The quantity of diazepam was increased if spasms persisted.

Supportive therapy included IV fluids, oral suction and relative isolation in a quiet corner of the general ward. After the first 48-72 hours, Ryle's tube feeds were initiated with calorie-dense feeds. IV Diazepam was substituted with oral Diazepam in the same dose once good control of spasms was achieved.

Information including sex, age, immunization status, mode of infection (otogenic/ post-injury/ unknown), and grade of tetanus, outcome and hospital stay were recorded in the two groups.

Results

From December 2012 to December 2014 we

Table 1: Modified Patel and Joag Criteria for Grading Tetanus

Sign(s) /Symptoms(s)	Points
Rigidity	
Neck	1
Abdomen	1
Limb	1
Trismus	1
Spasms	
Less than 1/hour	2
More than 1/hour	4
Continuous/Laryngeal	6
Vital Parameters	
Temperature >38°C	2
Pulse >120/min	2
Respiratory rate >40/min	2

Grade– Mild: 3; Moderate: 4-10; Severe : >10

analyzed 40 patients admitted with tetanus excluding neonatal tetanus.15 children received TIG by intrathecal route and 25 by intramuscular route. Baseline characteristics about sex, age, immunization, portal of entry and severity of tetanus were compared between two groups (Table 2).

Mortality (Fisher's Exact Test, P=0.7159) and mean

Table 2: Epidemiological characteristic between the two groups

Characteristic	Group A Intrathecal N=15	Group B Intramuscular N=25	P Value
Sex			
Male	10	19	0.7162*
Female	5	6	
Age			
Mean age	6.33	6.21	0.8828**
Immunization Status			
Unvaccinated	14	23	0.6924#
Partially vaccinated	0	1	
Fully vaccinated	1	1	
Mode of infection			
Traumatic	11	19	1.000*
Otogenic	4	6	
Severity			
Mild	1	2	1.0000*
Moderate	9	17	0.7356*
Severe	5	6	1.3890*

*Fisher's exact test **Unpaired t test #Chi square test

Table 3: Outcome and mean hospital stay in the study groups N(%)

Parameter	Group A N=15	Group B N=25	P Value
Expired	4 (26.67)	7 (28)	1.000*
Discharged	11	18	
Hospital stay			
Mean days	12.4	15.4	0.3213**

*Chi square test **Unpaired t test

days of hospitalization (Unpaired T test, P=1.017 with 38 degree of freedom) were less in intrathecal group which was not statistically significant (Table 3).

Discussion

Studies showed that human tetanus immunoglobulin by intrathecal route had better clinical progression, fewer complications particularly respiratory ones, needed less intervention and had a shorter duration of spasms than treated by intramuscular route [2-4,6,7]. We found no statistically significant difference in route of administration of TIG based on mortality and mean hospital stay.Intrathecal TIG probably acts at motor neuron in the spinal cordwhere it inhibit ascent of toxin [7].

Mortality in tetanus patients depend on many factors. Early tracheostomy, elective paralysis and mechanical ventilation might be required to reduce mortality and morbidity in patients with severe tetanus; meticulous nursing care and sedation might be effective enough in mild to moderate cases if administered in time with proper aseptic precautions.

Single center, small numbers of subjects, absence of study other parameters like mechanical ventilation, tracheostomy, other drugs required for control of spasms, other complications are major limitation of our study.

Conclusion

In our study we found that in the pediatric tetanus patient the route of administration of TIG does *not significantly* affect patient outcome in terms of hospital stay and mortality; although both were found to be less in the intrathecal group.

Recommendations

In order to substantiate the results of this study, multicentric trials with a larger sample size, and comparative treatment protocols, barring only the mode of administration of TIG, need to be conducted. Appropriate sedation and nursing care with timely life saving measures whenever indicated appear to be more fruitful for improving clinical outcome.

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