ISSN: 0975 -8542

Journal of Global Pharma Technology

Available Online at: www.jgpt.co.in

RESEARCH ARTICLE

# Tetanus Combined Immunization with Tetraxim and Pentaxim in Children from 3 Months to 4 Years

**Alla Philippova*, Elena Gorozhanina, Vadim Samusenkov**

*Sechenov First Moscow State Medical University (Sechenov University), Russian Federation.*

***Corresponding Author: Alla Philippova**

## Abstract

The causative organism of tetanus is the Clostridium tetani. Immunization is one of the effective methods of disease prevention, which is carried out from the first 2 months of life. Further vaccination continues, in combination with the measles vaccine. Thus, tetanus in modern medicine is one of the elements of the combined vaccinations. 300 children were vaccinated hosted by the Department of Infectious Diseases of the Hospital № 2 in Moscow (Russian Federation) during the first six months of 2017. The age interval of children is from 3 months to 4 years. 2100 vaccinations were carried out, 1810 of which were vaccinations with Pentaxim, and the rest with Tetraxim. 255 children (85% of all), immunization program with Tetraxim was prolonged after the Pentaxim vaccinations. This is due to the fact that the first immunization occurs in half of a year. The reasons for this are in the social incompetency of the most parents as they begin immunization from 6 months, not from 3. The proposed drugs showed high-potency in children of different age groups and in state of health. Tetraxim and Pentaxim are applicable for children with allergies, as well as with CNS involvement. Moreover, they can be included in combination vaccines against such diseases as whooping cough, diphtheria, tetanus, poliomyelitis, Haemophilus influenzae b. It is due to the same components used, namely DTwP, IPV.

## Introduction

Prevention of infectious diseases with vaccines is one of the most effective methods in modern medicine. There is a need to create new vaccines because of the constantly growing prevalence of the diseases and the mortality of them. These trends are reflected in the World Health Organization recommendations [1, 3]. According to the recommendations, the greatest numbers of vaccinations falls on the age of 1 year and include vaccinations against hepatitis B, BCG, as well as whooping cough, diphtheria, tetanus, poliomyelitis, Neisseria meningitidis, influenza, and others.

Subsequently, vaccination against measles is carried out in 2 years. If you use these vaccines as a single drug, then vaccination against all diseases will not work, which is due to the huge total amount of vaccinations per a child. On the matter above, the majority of vaccines being developed today are based on the DTP complex. Tetanus is an acute disease with the only cause by a highly potent neurotoxin (tetanospasmin) produced by Clostridium tetani.

Symptoms of tetanus are convulsions and muscle tension caused by bacterial growth and tetanospasmin development in the contaminated wound. Tetanus is diagnosed in people of all ages, and often ends in death. Infection can occur during labour in both birthing mothers and newly-born babies, as well as in other population groups because of injuries. Most cases of tetanus are recorded in countries of tropical climate zone. Out of 200 thousand cases of tetanus, about 30 thousand are cases of maternal tetanus (occur during labour), and the rest are cases of neonatal tetanus.

There are two approaches associated with the prevention of tetanus. The first is the active immunization (administration of the vaccine), the second is the passive immunization (administration of tetanus immunoglobulin). Modification of tetanospasmin causes the production of protective antitoxins in the body. Tetanus antitoxin is transferred from the immunized mother to the fetus through the placenta.

There are several types of tetanus vaccine, which are based on a combined effect against tetanus, diphtheria, whooping cough (DT, DTwP, DTaP, dTaP, and others). The principle of vaccination determines the age at which it is carried out. The combination vaccine against tetanus and diphtheria is made up to 7 years, the vaccine with diphtheria toxoid - after 7 years.

This article studies the effectiveness of the Combination Vaccines of Pentaxim and Tetraxim for children from 3 months to 4 years. The goal is to analyze the proposed drugs tolerance for children of this age group.

## Material and Methods

Three types of Combination Vaccines are used in the Russian Federation. These are Pentaxim (LSR 005-121/06), Tetraxim (LP000548-120511) and Infanrix-Hexa (LP000877-181011). The composition of the first vaccine is DTwP (diphtheria-tetanus-whole cell pertussis vaccine, DTP in the international nomenclature), IPV (inactivated polio vaccine), HIB (Haemophilus influenzae b vaccine), the second-DTwP and IPV, and finally the third - DTwP, IPV, HIB and hepatitis B vaccine. Thus, PENTAXIM and TETRAXIM contain DTwP and IPV vaccines that make it possible to combine them when vaccinating children of different ages (Table 1).

**Table 1: Vaccination depending on the age with Tetraxim and Pentaxim**

| The month of the first vaccination | The first vaccination | Revaccination | The third vaccination | Revaccination, if necessary |
|---|---|---|---|---|
| 3 | PENTAXIM | PENTAXIM | PENTAXIM | PENTAXIM |
| 4,5 | PENTAXIM | PENTAXIM | PENTAXIM | PENTAXIM |
| 6 | PENTAXIM | PENTAXIM | PENTAXIM | PENTAXIM |
| 7 | PENTAXIM | PENTAXIM | TETRAXIM | PENTAXIM |
| 8 | PENTAXIM | PENTAXIM | TETRAXIM | PENTAXIM |
| 9 | PENTAXIM | PENTAXIM | TETRAXIM | PENTAXIM |
| 10 | PENTAXIM | PENTAXIM | TETRAXIM | PENTAXIM |
| 11 | PENTAXIM | PENTAXIM | TETRAXIM | PENTAXIM |
| 12 (1 year) | PENTAXIM | TETRAXIM | TETRAXIM | TETRAXIM |
| 13 | PENTAXIM | TETRAXIM | TETRAXIM | TETRAXIM |
| 14 | PENTAXIM | TETRAXIM | TETRAXIM | TETRAXIM |
| 15 | PENTAXIM | TETRAXIM | TETRAXIM | TETRAXIM |
| 16 | PENTAXIM | TETRAXIM | TETRAXIM | TETRAXIM |
| 17 | PENTAXIM | TETRAXIM | TETRAXIM | TETRAXIM |
| 18 | PENTAXIM | TETRAXIM | TETRAXIM | TETRAXIM |
| 19 | PENTAXIM | TETRAXIM | TETRAXIM | TETRAXIM |
| 20 | PENTAXIM | TETRAXIM | TETRAXIM | TETRAXIM |
| 21 | PENTAXIM | TETRAXIM | TETRAXIM | TETRAXIM |
| 22 | PENTAXIM | TETRAXIM | TETRAXIM | TETRAXIM |
| 23 | PENTAXIM | TETRAXIM | TETRAXIM | TETRAXIM |
| 24 (2 years and more) | PENTAXIM | TETRAXIM | TETRAXIM | TETRAXIM |

300 children were vaccinated hosted by the Department of Infectious Diseases of the Hospital No.2 in Moscow city (Russian Federation) during the first six months of 2017. The age interval of children is from 3 months to 4 years. 2100 vaccinations were carried out, 1810 of which were vaccinations with Pentaxim, and the rest with Tetraxim.

Agreement with the parents was made in writing in the case of each vaccination, according to international legal norms. Reactogenicity of Pentaxim as separate study was not conducted due to existing data (Kharit, 2009). According to the study of Tetraxim reactogenicity, the following age group distribution was obtained: out of 300 children, 1) 3 to 4 years - 40 children; 2) 2 to 3 years-45; 3) a year to 2 years - 165 children; 4) 6 months to a year - 28; 5) 3 months to 6 months - 22. Parents were obliged to notify by telephone about the state of health of the child, if necessary - to visit a pediatrician within 3 days after vaccination. Afterward, within 6-8 weeks after vaccination, a medical examination was carried out before making a decision about the subsequent vaccination.

## Results

Tetraxim was used in approximately 1/6 (15%) of cases from the total number of patients in the age range of 3 months to 4 years.

 

The use of the drug covered the entireprogram of vaccinations, if necessary, the addition of Pentaxim was used, from the first vaccination up to revaccination (Table 2).

**Table 2: Different organism responses associated with the duration of Tetraxim vaccination**

| Number of patients vaccinated with Tetraxim | | Systemic reaction, alone with temperature rise, more than 38.5°C | Organism response, local (erythema and other) | Flu, throughout a month after the vaccination |
|---|---|---|---|---|
| The first vaccination | 21 | - | - | - |
| Revaccination | 79 | - | 28.0% | 15.0% |
| The third vaccination | 95 | - | 10.0% | 25.0% |
| Revaccination, if necessary | 60 | 20.0% | 17.0% | - |
| Total | 255 | 20.0% | 55.0% | 40.0% |

The first vaccination was carried out after parent's agreement for 50 children under 1 year according to the drug instructions. Accordingly, in this case Tetraxim was vaccinated at the age it should be vaccinated. 150 children were vaccinated in order to continue the program of vaccination with Pentaxim. 45 children were also vaccinated with Tetraxim, after vaccination with other combination vaccines (DTP, Infanrix-Hexa).

Therefore, the vaccination with Tetraxim was caused by the human factor in 1/6 cases-namely, the parents' wish to avoid the use of HIB vaccine and, as a result to reduce the number of vaccinations for the child. More than 25% of the surveyed parents didn't want to vaccinate children against this infection in the first 3 months. The remaining cases (74.4%) are caused by the need of revaccination after the course of Pentaxim, thus vaccination of this group of children began at the age of six months.

The studies also indicate that most parents don't consider vaccination from 3 months good, despite the justification according to the instructions. For the minority of cases (about 11%), the main reason for vaccination after six months is the opinion of the parents about the risk of so many vaccinations .The remaining cases are the result of consultations with pediatricians who diagnosed children with CNS involvement (45.5% of cases), various forms of dermatitis (15%), ARVI (15%) and other diseases.

However, all of the above-mentioned conditions of the body are part of the false contraindications to immunization. Therefore, the incompetence of doctors in the matter of immunization period may ultimately leads to tetanus and whooping cough vulnerability of children aged 1-2 years. This is confirmed by the Rosprirodnadzor (Federal Service for Supervision of Natural Resource Usage) data, according to which unvaccinated children under 1 year old are at high risk of developing whooping cough.

## Discussion

### The Causative Organism and Course of the Disease

The causative organism of tetanus is the bacterium Clostridium tetani. Spores of this anaerobic bacterium are quite common, especially in tropical areas where they are found in the soil. The usual mode of entry is through dirty or infected wound. Then, under anaerobic conditions, these bacteria begin growing, simultaneously producing a dangerous neurotoxin-tetanospasmin.

Tetanospasmin effects the central nervous system and blockage its neurotransmitters, that is expressed by generalized muscular rigidity with subsequent spasms. Tetanus is characterized by a relatively short latent period, 1 week on average. Mortality from tetanus varies from 9-75%. The death risk factors include a) age, b) immune status, and c) timeliness of treatment.

Mortality can reach up to 100% in case of no treatment and this applies primarily to the elderly and young people. Mortality is reduced to almost 15% in the case of forehanded care. Pentaxim and Tetraxim vaccines proposed in this study are safe. The earlier study, on the sample of 200 people vaccinated at the age of 1.5-3.5 years, showed that the majority (80%) had no side effects to these drugs. Only 2% (on the edge of a statistical error) temperature rise was observed down from norms (up to 38.7 °C).

Every fourth child who has allergies or CNS involvement and every tenth healthy child were noted with allergic skin reactions such as erythema and swelling up to 5 cm in diameter [4].

 

The study also showed an asymptomatic period after vaccination of Tetraxim, with approximately the same rate of local reactions (up to 4%) and fever (2%). Children had no local erythema and swelling during the first days after vaccination (see Table 2). Thus, such reactions occurred with the second and subsequent vaccinations.

This does not contradict the data of other scholars [5, 7]. Thereof, Tetraxim is a complex drug, which can be also used for children with various diseases and state of health. Mortality from tetanus among birthing mothers and newly-born babies is high. Adult mortality rates of up to 52% are registered in Asia and Africa [8, 14].

Mortality caused by neonatal tetanus is even higher, from 3% to 88% in these regions [15, 18]. Most cases of tetanus are found in the countryside areas. Mortality is higher among patients not admitted to hospital, and delayed hospitalization is associated with worse outcomes for neonatal tetanus [19].

Admitting birthing mothers and newly-born babies to ventilation and intensive care rooms help to improve the final outcomes. However, cardiovascular and other respiratory complications develop, with improved respiratory support [20]. The worse outcome for neonatal tetanus is associated with low birth weight (especially <2.5 kg), infection at early age, fever, generalized muscular rigidity and risus sardonicus [15].

A meta-analysis of 4535 cases [21] of neonatal tetanus (based on studies published from 1974 to 2011) showed that low birth weight and infection at early age were the most important prognostic factors. Moreover, the combination of low birth weight (less than 5 kg) and infection at early age (less than 6 days) are the most significant. The rapid progression (short latent and onset periods), the internal entry site and the underlying disease are important worse outcome factors for maternal tetanus [12]. The full recovery from tetanus may take 6-8 weeks, while spasms often lasting 2-3 weeks [22, 24].

Both adults and newly-born babies may need ventilation for several weeks (average 23 days 17-60 in the range) and intensive care for even longer period [24]. There are few studies on long-term effects. 8.6% of the survived patients from northwestern Tanzania were dismissed from hospital with total permanent disability, namely persistent vegetative state, limb amputations and gait disturbances [12]. Neurological disorders associated with generalized muscular rigidity and memory loss were registered among patients from Bangladesh, where three out of 75 patients were dismissed from hospital with total permanent disability [9].

All 45 survived patients after discharge suffered from muscular rigidity in a study carried out in Thailand [25]. There are a few studies that examined the effects of neonatal tetanus, but the frequency of complications is likely to be even higher. 20-40% of survived newly-born babies were noted with symptoms of brain damage, manifested with microcephaly and mild neurological disorders associated with development or behavior [26].

Cerebral palsy complications, cognitive developmental delay and deafness were registered in 20% of survived patients in one series of cases in Nigerian [19]. These complications can be caused by hypoxia and hypoglycemia, usually detected during a clinical course. The first vaccination does not provide complete protection and implies the subsequent ones. The concentrations of antitoxins necessary for immunization appear during repeated vaccination, and the third vaccination provides practically 100% immunization.

The time interval between tetanus vaccinations should be at least 1 month in this case. If increasing the intervals, then, the duration of the immune response will increase, accordingly. Such vaccinations are effective in more than 80% of cases, which is confirmed by already conducted studies. Tetanus vaccination in the 40 years of the last century in the United States caused a decrease in the morbidity of tetanus by an order. The newborns did not suffer from tetanus after two- or three-times vaccination compared with the control group that was not vaccinated according to data received in Columbia. Thus, tetanus vaccination is a prerequisite for the prevention of this dangerous disease.

## Conclusion

According to present research, a misunderstanding of timely vaccination is present not only among parents, but also among pediatricians and other specialists

 

who give medical withdrawals from vaccination starting from 3 months. This is aggravated by the fact that the proposed vaccines have a complex effect not only on tetanus, but also on whooping cough, diphtheria, HIB. HIB is the main reason for the parents refusing the vaccination. The advantage of Pentaxim and Tetraxim is that they can be used in the case of allergies or CNS involvement in children. These are combination vaccines therefore they can prevent not only tetanus, but other diseases, and may be applicable from the earliest age of vaccination (3 months) to 4 years.

## References


1. General Recommendations on Immunization (2011) Recommendations of the Advisory Committee on Immunization Practices (ACIP). Morbidity and Mortality Weekly Report, 60(2): 1-61.
2. Recommendations for Routine Immunization Summary of WHO Position Papers (2012) http://www.who.int/immunization/documents/positionpapers/
3. Recommended Immunization Schedule for Persons 0 through 6 Years of Age (2012) http://www.cdc.gov/vaccines/recs/schedules/downloads/child/0-6yrs-schedule-pr.pdf
4. Harit SM, Tchernyaeva TV, Nacharova EP, Vasileva GA, Ruleva AA (2009) The estimation of safety booster vaccination children is more senior than 1,5 years against diphtheria, whooping cough, tetanus, poliomyelitis and Haemophilus influenzae type B with PENTAXIM. Journal Infectiology, 1(2, 3): 73-78.
5. Rennels MB (2003) Extensive swelling reactions occurring after booster doses of diphtheria-tetanus-acellular pertussis vaccines. Pediatric Infectious Diseases, 14: 196-198.
6. Woo EJ, Burwen DR, Gatumu SN, Ball R, Vaccine Adverse Event Reporting System (VAERS) Working Group (2003) Extensive limb swelling after immunization: reports to the Vaccine Adverse Event Reporting System. Clinical infectious diseases, 37(3): 351-358.
7. Bults M, Kemmeren JM, Van der Maas NAT (2007) Adverse events following booster doses of diphtheria-tetanus-inactivated poliovirus and a cellular pertussis vaccines for 4-year-old children in The Netherlands. Vaccine, 25(29): 5272-5277.
8. Ertem M, Çakmak A, Saka G, Ceylan A (2004) Neonatal tetanus in the South-Eastern region of Turkey: changes in prognostic aspects by better health care. Journal of tropical pediatrics, 50(5):297-300.
9. Feroz AHM, Rahman H (2007) A ten-year retrospective study of tetanus at a teaching hospital in Bangladesh. Journal of Bangladesh College of Physicians and Surgeons, 25(2): 62-69.
10. Adekanle O, Ayodeji OO, Olatunde LO (2009) Tetanus in a rural setting of south-western Nigeria: a ten-year retrospective study. Libyan Journal of Medicine, 4(2): 78-80.
11. Amare A, Yami A (2011) Case-fatality of adult tetanus at Jimma University Teaching Hospital, southwest Ethiopia. African health sciences, 11(1): 36-40.
12. Chalya PL, Mabula JB, Dass RM, Mbelenge N, Mshana SE, Gilyoma JM (2011) Ten-year experiences with Tetanus at a Tertiary hospital in Northwestern Tanzania: A retrospective review of 102 cases. World Journal of Emergency Surgery, 6(1): 20.
13. Marulappa VG, Manjunath R, Babu NM, Maligegowda L (2012) A ten year retrospective study on adult tetanus at the Epidemic Disease (ED) Hospital, Mysore in southern India: a review of 512 cases. Journal of Clinical and Diagnostic Research: JCDR, 6(8): 1377.
14. Muteya MM, a Kabey AK, Lubanga TM, Tshamba HM, a Nkoy AMT (2013) Prognosis of tetanus patients in the intensive care unit of Provincial Hospital Jason Sendwe, Lubumbashi, DR Congo. Pan African Medical Journal, 14(1): 93.
15. Basu S, Paul DK, Ganguly S, Chandra PK (2006) Risk factors for mortality from neonatal tetanus: 7 years experience in North Bengal, India. Annals of tropical pediatrics, 26(3): 233-239.
16. Amar-Singh HS (2009) Neonatal tetanus in Malaysia. Med J. Malaysia, 64(1): 1-2.
17. Fetuga BM, Ogunlesi TA, Adekanmbi FA (2010) Risk factors for mortality in


 

neonatal tetanus: a 15-year experience in Sagamu, Nigeria. World Journal of Pediatrics, 6(1): 71-75.

18. Mwaniki MK, Gatakaa HW, Mturi FN, Chesaro CR, Chuma JM, Peshu NM, Berkley JA (2010) An increase in the burden of neonatal admissions to a rural district hospital in Kenya over 19 years. BMC Public Health, 10(1): 591.
19. Ugwu GM, Okolugbo NE (2010) Neonatal tetanus in Warri Niger Delta: a ten year retrospective study. Continental Journal of Medical Research, 4: 3.
20. Gibson K, Uwineza JB, Kiviri W, Parlow J (2009) Tetanus in developing countries: a case series and review. Canadian Journal of Anesthesia/Journal canadien d'anesthésie, 56(4): 307-315.
21. Lambo JA, Anokye EA (2013) Prognostic factors for mortality in neonatal tetanus: a systematic review and meta-analysis. International Journal of Infectious Diseases, 17(12): e1100-e1110.
22. Attygalle D, Rodrigo N (2002) Magnesium as first line therapy in the management of tetanus: a prospective study of 40 patients. Anaesthesia, 57(8): 778-817.
23. Thwaites CL, Yen LM, Loan HT, Thuy TTD, Thwaites GE, Stepniewska K, Farrar JJ (2006) Magnesium sulphate for treatment of severe tetanus: a randomised controlled trial. The Lancet, 368(9545): 1436-1443.
24. Karanikolas M, Velissaris D, Marangos M, Karamouzos V, Fligou F, Filos KS (2010) Prolonged high-dose intravenous magnesium therapy for severe tetanus in the intensive care unit: a case series. Journal of medical case reports, 4(1): 100.
25. Sathirapanya P, Sathirapanya C, Limapichat K, Setthawacharawanich S, Phabphal K (2009) Tetanus: a retrospective study of clinical presentations and outcomes in a medical teaching hospital. Medical journal of the Medical Association of Thailand, 92(3): 315-319.
26. Barlow JL, Mung'Ala- Odera V, Gona J, Newton CRJC (2001) Brain damage after neonatal tetanus in a rural Kenyan hospital. Tropical Medicine & International Health, 6(4): 305-308.

 