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ระดับแอนตี้ทอกซินต่อบาดทะยักภายหลังจากฉีดวัคซีนปฐมภูมิครบในขวบปีแรก

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บทคัดย่อ

เด็ก 184 คน อายุ 3-19 ปี ได้เข้าศึกษาหาระดับของแอนตี้ทอกซินต่อบาดทะยัก โดยแบ่งเด็กเป็น 2 กลุ่ม กลุ่มแรก (94คน) เข้ากลุ่มศึกษาโดยเป็นเด็กที่ได้รับวัคซีนบาดทะยักปฐมภูมิครบในขวบปีแรกเท่านั้น นอกนั้นเป็นกลุ่มควบคุม (90 คน) ซึ่งมีประวัติการฉีดวัคซีนป้องกันบาดทะยักไม่ชัดเจน บางคนเคยได้รับวัคซีนบาดทะยักฉีดกระตุ้น แต่บางคนก็ได้วัคซีนปฐมภูมิไม่ครบ ซึ่งจัดเป็นกลุ่มประชากรทั่วไปของเชียงใหม่ดังต่อไปนี้

ในกลุ่มศึกษา 96.81% ($^{91}/_{94}$) มีระดับแอนตี้ทอกซินบาดทะยักเพียงพอต่อการป้องกันโรค (>0.01 U/ml.) ในกลุ่มควบคุมมีเพียง 80% ($^{72}/_{90}$) ที่สามารถป้องกันโรคได้ ในกลุ่มอายุ 4-9 ปี ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติของระดับแอนตี้ทอกซิน ระหว่างกลุ่มศึกษาและกลุ่มควบคุม ในกลุ่มอายุ 10-14 ปี กลุ่มศึกษามีระดับแอนตี้ทอกซินมากกว่ากลุ่มควบคุมอย่างมีนัยสำคัญ (P=0.010) เช่นเดียวกับกลุ่มอายุ 15-19 ปี ซึ่งกลุ่มศึกษามีระดับแอนตี้ทอกซินมากกว่ากลุ่มควบคุมอย่างมีนัยสำคัญ ทางสถิติ (P=0.0006)

คณะผู้รายงานเสนอว่า ถ้าเด็กได้รับวัคซีนบาดทะยักปฐมภูมิครบภายในอายุขวบปีแรก จะป้องกันโรคได้มากกว่า 10 ปี คณะผู้รายงานหวังว่าผลการศึกษานี้จะมีประโยชน์ในการวางแผนตารางฉีดวัคซีนป้องกันบาดทะยักให้แก่เด็กชาวไทยได้เหมาะสมยิ่งขึ้น

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Abstract To study the level of tetanus antitoxin by ELISA technique in children, after complete primary tetanus immunizations within the first year of age in Chiang Mai, Thailand. 184 children age between 3 to 19 years old were recruited. These subjects were divided into 2 groups: Group I by the criteria of complete primary tetanus immunizations only and Group II by the criteria of uncertainly about tetanus immunization, some had tetanus boosters and some had not completed primary tetanus immunization, saidly, the general population in Chiang Mai.

In the first group, the Study group, 96.81 % (91/94) had preventable tetanus antitoxin (> 0.01 U/ml.)

In the second group, the Control group, only 80% (72/90) can prevent tetanus.

In the subgroup, 5-9 years old, either Study or Control no statistical difference in tetanus antitoxin level. (P = 0.0960).

In the 10-14 years old sub group, the Study group had more tetanus antitoxin statistical significance than the Control group (P = 0.010).

The Same was true of the 15-19 years old sub group, with the Study group having more tetanus antitoxin than the Control group (P = 0.0006).

We suggest that, if the child has completed his primary tetanus immunizations within the first year of age, he can prevent tetanus for more than 10 years. We hope this study will be useful in planning tetanus immunization for Thai children on a reasonable basis.

Introduction :

Tetanus, one of the common infectious diseases ; its manifestations include neurological involvement, such as severe twitching of muscles.

Tetanus is caused by Clostridium tetani, contaminating and infecting a wound. The organism has 2 toxins: First Tetanospasmin, a watersoluble toxin which produces the disease. The second, Tetanolysin, which can hemolysis red blood cell in vitro, but had never yet been seen in the human being.(1) Tetanus prevention includes appropriate cleaning of wounds and vaccination.

Trends of tetanus decrease are seen in many countries. In Thailand too, reports of epidemiology from the Ministry of Public Health, said that in the year 1978 more than two thousand cases of tetanus were reported (excluding tetanus neonatorum); and in

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the year 1984, only 913 cases of tetanus were reported[2] (excluding tetanus neonatorum). The decrease of cases was seen in every age group.

This decreasing of tetanus cases may have been influenced by the EPI (Expanded Program on Immunization), which The Ministry of Public health started in 1977. Nowadays, in Thailand, immunization programs include 6 basic vaccines (BCG, DPT, OPV and Measles vaccines) as follows:

Immunization schdule[3]

Age	Immunization	For Prevention of	Dosage Number
Newborn-1 month	BCG	Tuberculosis	
2-3 months	DPT	Diptheria, Pertussis, Tetanus	1
	OPV	Poliomyelitis	1
4-5 months	DPT	Diptheria, Pertussis, Tetanus	2
	OPV	Poliomyelitis	2
6-7 months	DPT	Diptheria, Pertussis, Tetanus	3
	OPV	Poliomyelitis	3
9-12 months	Measles (or MMR)	Measles (or Measles, Mumps and Rubella	-
1½-2 years	DPT	Diptheria, Pertussis, Tetanus	4(Booster)
	OPV	Poliomyelitis.	4(Booster)
4-7 years	DPT(DT)	Diptheria, Pertussis, Tetanus	5(Booster)
	OPV	Poliomyelitis	5(Booster)
	BCG	Tuberculosis	Booster
	Typhoid	Typhoid fever	
11-14 years	dT	Diptheria, Tetanus	Booster
	Typhoid	Typhoid fever	
	Rubella	Rubella	
	(For girls who never recieved Rubella vaccine)		
Pregnant			
First seen	T	Tetanus neonatorum	1
1-2 months later	T	Tetanus neonatorum	2

Abbreviation :

BCG = Bacillus Calmette-Guerin vaccine
DPT = Diptheria-Pertussis-Tetanus vaccines
OPV = Oral Polio Virus vaccine
MMR = Measles, Mumps, and Rubella vaccines
dT = Diptheria-Tetanus vaccines
DT = Pediatric Diptheria-Tetanus vaccines
T = Tetanus toxoid

Primary immunization[3] for tetanus including diptheria and pertussis (DPT vaccines) consists of a 0.5 ml. intramuscular injection at the outer-midthigh or deltoid muscle, 3 times in total 2 months apart each. The first dose should start at age of 2-3 months.

Booster or Reinforcing dose[3]; recommend injection of DPT at doses of 0.5 ml. intramuscularly (after complete primary

immunization) at age of 1½-2 years, and again at the age 4-7 years old, then injection of 0.5 ml. of dT or T intramusculary every 5-10 years there after.

Tetanus antitoxin can be detected as early as 2 weeks after the first dose of vaccine. After 3 doses,the antitoxin will be 16 times higher, and after 4 doses, 150 times higher than the preventable level. And if 4 doses of tetanus vaccines are injected, the child would have more than 10 years of tetanus prevention[4].

Antitoxin of tetanus by neutralization and ELISA technique that can prevent the disease must more than 0.01 U/ml. (5,6,7).

From the EPI report, only 21 % of children below 1 year old recieved the complete 3 doses of DPT (Target was 70 %) in 1982 ; increasing to 69 % in 1986 (Target 80 %)[8]. The aim of the 6th Issue Developing Plan of Public Health (1987-1991) is to have at least 90 % of children under 1 year old recieve complete primary immunization, with an increase in the school children booster doses of dT from 46.8 % in 1982 to 75.6% in the year 1985.

From the above data, it is evident that many of children had not completed primary immunizations and that a lot of children had not recieved their booster dose of tetanus vaccine. There have many papers studying the prophylactic of tetanus in different groups. Sangpetchsong et al[9], 1980, in a study of Thai adults aged 15-55 years old, found that the tetanus antitoxin will decrease as the years of age go by. In the 15-24 years old group, only 13.9% had antitoxin >o.o1 U/ml.

Pichichero et al[10], in a study of 33 children aged 18 months, who had completed 3 doses of DPT. At Rochester N.Y., found that every child had tetanus antitoxin > 0.01 U/ml.

In 1981, Simonsen et al[11], studied samples of people who had completed their primary immunizations and never recieved tetanus vaccination booster. They found 98.42 % (125/127) of samples had tetanus antitoxin > 0.01 U/ml. by passive hemagglutination and Neutralization Technique. And those who had received the tetanus vaccine booster, 247 from 261 (94.64 %) had tetanus antitoxin > 0.01 U/ml. In the last group, 61 samples had received boosters of tetanus vaccine more than 22.5 years earlier.

Simonsen et al, rechecked the tetanus antitoxin after boosters with a single dose of tetanus vaccine in the above 412 samples (who had been complete their primary immunization in 25-30 years ago.) All had significant increased in tetanus antitoxin level. They suggest that, after complete primary immunization, only one dose of tetanus booster before 20 years of age is enough.

Reports from the USA 1965-1966[12], found 8 tetanus cases. who had recieved complete primary immunization within the preceding 10 years, and five cases of tetanus who had completed primary immunization and had received a tetanus booster within the ten preceding years. But these patients did not look for tetanus antitoxin at first seen. As only 3 cases of tetanus were younger than 10 years of age, (equal to 3.8/100,000,000/year) Laforce et al suggested it is better to give a tetanus booster every 10 years after complete primary immunization, including administration to adults.

Sangpetchsŏng et al[9] found only 13.9 % of samples in the age 15-24 years group had enough tetanus antitoxin, but they did not studied in those who complete primary immunization, and how long from the last doses of vaccination.

In the year 1987, WHO had a campaign "Immunization: A chance for every child." We would like to study of tetanus antitoxin after complete their primary immunization within one year of life, and no other tetanus toxoid booster in Chiang Mai province and give them booster with dT vaccines.

Subjects & Study group :

1. Children who completed their primary immunization within 1 years of age from the "4C" (Comprehensive child care clinic, faculty of Medicine, Chiang Mai University) and never recieved tetanus booster.
2. Pupils/students from school/college in Chiang Mai Province who completed their primary immunization within 1 year of age and never recieved tetanus booster.

There are 94 children in this group.

Control group :

Children in Chiang Mai,for whom a history of tetanus immunization was not clearly known. We gathered 90 children in this group.

Both groups age between 3-19 years old. The study was conducted between June 88 and March 89.

Method :

1. Select Study Group from 4C's health and immunization records.
2. Select Studying Group from the health and immunization records of pupils/student from schools or colleges in Chiang Mai.
3. Select Control Group, from pupils/students in Chiang Mai,for whom history of tetanus immunizations was not clearly known.
4. Use 2 way communication letters to make appointment, if they and their parents want to join this study.
5. We interviewed both child/and parents with our questionairs to confirmed only primary immunizations of tetanus vaccine in our Study group.
6. Health education about immunization and tetanus, was given to the children and their parents. And let them knew about the aim of our study.
7. A physical examination was conducted by researcher.
8. Children who were not in the good health, or whose parents did not want to join our study were excluded.
9. 2 ml. of blood were collected by venopuncture from all children,both Study and Control Group. Then all blood samples were taken to the laboratory.
10. All children received 0.5 ml. of dT intramuscularly into the deltoid muscle, and not remenber to record this vaccines in their health/immunization records.
11. Result of tetanus antitoxin by ElISA technique from laboratory will be gather for statistical analysis by means of chi-sqcare test and one way analysis of variane.

Results

Total of 184 subjects age between 3 to 19 years old, 94 were in Study group and another 90 were in Control group.

age group (years) / Antitoxin U/ml.	3-4	5-9	10-14	15-19	
< 0.01	-	1	2	-	(3)
0.01-0.05	4	4	7	5	(20)
0.051-0.099	1	6	6	-	(13)
> 0.1	5	44	7	2	(58)
	(10)	(55)	(22)	(7)	94

Table 1

Study group were divided by age groups and antitoxin level.

Table 2

Show the distribution of control group accordingly to tetanus antitoxin levels and age group.

age group (years) / Antitoxin U/ml.	5-9	10-14	15-19	
< 0.01	-	16	2	(18)
0.01-0.05	2	21	7	(30)
0.051-0.099	2	8	6	(16)
> 0.1	8	11	7	(26)
	(12)	(56)	(22)	90

In Study group (table I)

Most of samples age more than 5 years old. 10 cases were under five years old, and all of them had preventable tetanus antitoxin.

Only 3 of 94 (3.19%) who had tetanus antitoxin lower than 0.01 U/ml.

In Control group (table 2), all of the samples are older than 5 years old. 20.0% (18/90) had tetanus antitoxin lower than 0.01 U/ml.

To Compare with table 2 (Control group), we revised table I by excluding 10 cases of under 5 years old, as in table 3.

age group (years) / Antitoxin U/ml.	5-9	10-14	15-19	
< 0.01	1	2	-	(3)
0.01-0.05	4	7	5	(16)
0.051-0.099	6	6	-	(12)
> 0.1	44	7	2	(53)
	(55)	(22)	(7)	84

Table 3 (Revised from table 1) Study group after excluding under five years old cases.

After exclude under five years old, we obtaind 84 subjects in Study group (Table3). In this table, 3 case (3.57%) of 84 subjecs had lower than 0.01 U/ml. of tetanus antitoxin. Or we can said that 96.43 % (81/84) had enough tetanus antitoxin.

Three cases of not enough tetanus antitoxin, one belonged to 5-9 years old group, and others two were in 10-14 years old group.

3.57% (3/84) of study group as compared to 20.0% (18/90), of control group there was highly statistical significance different. ($p < 0.001$) in cases of not enough tetanus antitoxin.

Discussion

3 cases of complete primary immunization whom tetanus antitoxin not enough to prevent the disease, one case age 6 years old and others two age 13 years old. That is only 1 case and 2 cases of studying subjects had not enough tetanus antitoxin after 5 and 12 years from complete primary immunization.

20.0% (18/90) in Control group had tetanus antitoxin below 0.01 U/ml. 16 cases were in 10-14 years old group and 2 in 15-19 years old group. Nevertheless 80% of control group had preventable tetanus antitoxin more than Sangpetchsong et al.[9] had studied in 1980, in which only 13.9% of 15-24 years old group had enough tetanus antitoxin. Effect of naturally acquires of tetanus may be interfere in those who did not complete tetanus immunization and had last long tetanus antitoxin, same as Ehrengert et al reported.[13]

Problems in this study were included young age group (1-4 years old) were hard to find if only primary vaccination were recieved, this may be the effectiveness of EPI.

Samples in this study were small amount of cases, because of most of children were recieved booster of dT or DT or tetanus toxoid else where. Some recieved from primary school health care, and a lot of cases recieved when they had seen doctor after accidents. Even in "4C" group, we send 190 two ways letters communication. Only 80 letters were return, a few returned to senders because of they moved to another place, somes had anothers tetanus booster already. We had 43 cases of "4C" in Study group.

At first, Control group, we would have volunteers who complete primary and had tetanus booster appropriate to their age (as in immunization schdule). But we got less than 10 cases, so we summaried them with general population whose tetanus immunization were uncertained or forgotten.

There were no statistical significance at $\alpha = 0.05$ ($p=0.0969$) in tetanus antitoxin in 67 cases of 5-9 years old group between Study and Control group.

After that, there were highly significant ($p=0.0006$) different in tetanus antitoxin between Study and Control groups especially in 15-19 years old group. (Mean of tetanus antitoxin in Study group age 15-19 years old=0.0763 U/ml)

From this study, we know that after complete primary immunization, within first year of life they can prevent tetanus for more than 10 years. But in Thailand, children in rural area may not complete 3 doses of DPT., we suggest to booster DPT once again at 4-7 years old by discard 18 months booster. Many children are afraid of doctors and health care workers, also their parents. Because now a day many vaccines are developed and recommend to injected in childhood. These vaccines include hepatitis B vaccines, by which first dose starts early after birth at least 3 doses together. Japanese encephalitis vaccines 2 doses, start at one year old and first booster about one year later,. then every 3-5 years. Others include typhoid, cholera vaccines, and so on.

In the near future, if tetanus cases reports decrease to only small amount, we may postpone tetanus booster program to a long period after completed primary tetanus immunization. We hope children may had good attitute to health care providers from new immunization programs. But we never over look for Diptheria and Pertussis (which are in same preparation, DPT), we may study Dipheria and Pertussis titers whether how long they can prevent the diseases after complete primary immmunization.

References:

1. Tetanus, in Report of the Committee on Infectious disease 19th edition p. 260-263.
2. Report of Survillance, Ministry of Public Health Thailand, 1984.
3. Immunization program-Handbook for practixtioner, Ministry of Public Health, Thailand, 1984.
4. Thomas C Peebles, Leo Levine, Mary C. Edred and Geoffrey Edsall. Tetanus-toxin emergency boosters, A reappraisal, New Eng. J.Med. 280, 575-581, 1969.
5. Giuliano gentili, Carlo Pini and Collotti- = The use of an immunoenzymatic assay for the estimation of tetanus antitoxin in human sera: a comparison with seroneutralization and indirect hemagglutination. J. Biol. stand 1985, Jan: 13(1): P53-9
6. Luis R, Varela Francis L. Black and Cesar A. Mendizabal-Moris., "Tetanus Antitoxin titers in Women of Child baring age from Nine Diverese populations: Journal of Infections disease., Vol 151; No 5, May 1985., p. 850-853.
7. Voller, A., D.E. Bidwell, and A Bartlelt. 1976, Enzyme immunoassays in diagnostic medicine: Theory and practice. Bull. WHO. 53, 55.
8. Weekly Epidemiological Surviellance Report Vol 18, No.14, APRIL 17, 1987. P.157-165.
9. Varanya Sangpetchsong, Phd., Sudapan Kuansathapornthavee, M.Sc., Ashara Vichitanant, B.Sc. and Amonerath Podhipak, M.Sc. "Dermatination of Relative factors and the levels of tetanus antitoxin in adut.": J.Med. Ass. Thailand, Vol. 66; June, 1983.
10. Michail E. Pichichero, MD., Roger M. Barking, MD. and Joel S. Samuelson, MD., "Pediatric diptheria and Tetanus toxicls adsorbed vaccine: Immune response to the first booster following the diptheria and tetanus toxoid vaccine primary series: Pediatric Infection Desease., July-Aug, 1986., Vol.5, No.4, P. 428-430.
11. O. S monsen, K. Kjeldsen and I. Heron. "Immunity against tetanus and effect of revaccination 25-30 year after primary vaccination.,": The Lancet, December, 1984., P.1240-1242.
12. F. Mare La Force, MD. Lawell S. young, MD., and John V. Bennett, MD., "Tetanus in the Unitted States (1965-1966)". The New England Journal of Medincine., Vol 280; No.11, March 13, 1969., P. 569-574.
13. Ehrengut-W; Sarateanu-DE; AgRhaly-A. Koumare-B; Simaya-sy: Diallo-D, "Naturally acquired tetanus in the serum of children and adults in Mali: Immun infekt 1983 Nov; 11(6); P 229-32.