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Original Article

Pain Response Comparison Between Two Different Vaccinations

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Abstract We aimed to determine the effect of the order of 2 different intramuscular vaccine injection 13-valent pneumococcal conjugate (PCV-13) vaccine and diphtheria and tetanus toxoids, acellular pertussis, inactivated poliovirus and *Haemophilus influenzae* type b (Hib) (DTaP-IPV-Hib) conjugate vaccine by using Modified Behaviour Pain Scale (MBPS) at the same visit. The 72 infants at the 4th and 54 infants at the 6 months of age were injected either PCV-13 first or DTaP-IPV-Hib first followed by the other vaccine/vaccines. After first vaccine, she was recorded the crying time and pain score according to the MBPS. Mean cry duration time after injection was significantly shorter when DTaP-IPV-Hib vaccine was administered first compared with PCV-13 vaccine ($p<0.001$). If DTaP-IPV-Hib vaccine was done first, total MBPS score was significantly lower than if PCV-13 vaccine was done first ($p<0.001$). When multipl vaccines are injected at the same visit, they should be administred in order of increasing painfulness.

Key words 13-valent pneumococcal conjugate vaccine; Diphtheria and tetanus toxoids, acellular pertussis, inactivated poliovirus and *Haemophilus influenzae* type b (Hib) conjugate vaccine; Pain; Vaccination

Introduction

Vaccinations administered by needle injections are some of the most common causes of iatrogenic pain during infancy and childhood.[1-3] During routine infant immunisations, multiple pain-causing injections are administered. According to Turkey's immunisation schedule, 1-3 vaccinations are administered in a single visit;[4] therefore, more efforts are being made to reduce pain while administering vaccination injections.[5] Previous studies have focused on the physiology, assessment, and management of pain, including the use of pharmacological, physical, and psychological strategies.[6-8] Moreover, some recent studies have demonstrated that certain vaccinations are more painful than others.[9,10]

In this study, we conducted a randomised clinical trial with healthy infants that ranged in age from 4 to 6 months. Our goal was to use the Modified Behaviour Pain Scale (MBPS)[1] to determine whether the 13-valent pneumococcal conjugate (PCV-13) vaccination was more painful than the diphtheria and tetanus toxoids, acellular pertussis, inactivated poliovirus, and *Haemophilus influenzae* type b (DTaP-IPV-Hib) conjugate vaccination administered during the same visit.

Methods

This randomised controlled clinical trial was conducted

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during routine vaccination appointments in a family healthcare centre. A total of 150 infants receiving their regular vaccinations at 4 and 6 months old were enrolled in this study, which took place from November 2015 through January 2016. Healthy infants who were born at 37-42 weeks gestation with birth weights greater than 2,500 g participated in this study. Those infants with acute or chronic illnesses, congenital abnormalities, taking medications, and being treated with topical or systemic analgesics within 24 hours before the vaccination appointment were excluded from the study. All of the infants were awake and quiet before the vaccinations were administered, and they had been breastfed or given formula at least 30 minutes before the vaccinations. If an infant was crying and could not be calmed down, he or she was not included in the study (Figure 1). Overall, 126 healthy infants were included in the analysis.

This study received approval from the Ethics Board of the Ankara Child Health and Diseases Hematology-Oncology Research and Training Hospital in Turkey (2015-076/07.12.2015). Informed consent was obtained from all of the parents.

Seventy-two 4-month-old infants and 54 6-month-old infants were administered either the PCV-13 vaccination (Prevnar 13; Pfizer, Philadelphia, PA, USA) first or the DTaP-IPV-Hib conjugate vaccination (Pentaxim; Sanofi Pasteur, Lyon, France) first, followed by the other vaccination(s). The second vaccination was administered 2 minutes after the first vaccination during the same visit. In addition to the PCV-13 and DTaP-IPV-Hib vaccinations, hepatitis B and oral polio vaccinations were given to the 6-month-old infants during the same visit.

During the visit, each infant's age, sex, weight, height, and head circumference were recorded, and the participating parents were asked questions about their educational and socioeconomic levels. The education level was classified as primary education (less than 8 years), secondary education (more than 8 years), or university

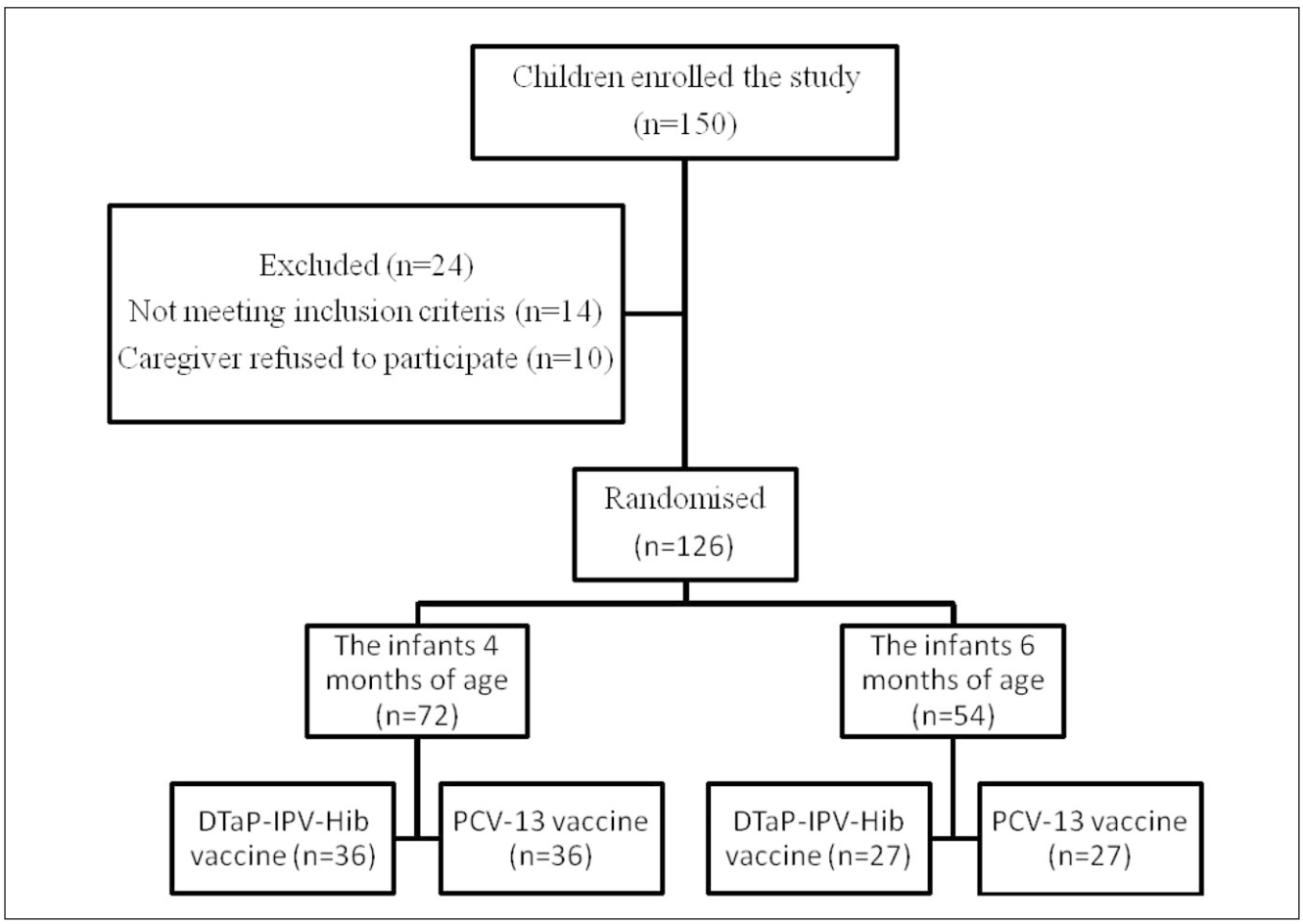

Figure 1 Flow diagram of patient recruitment.

education. The socioeconomic status (SES) was classified according to the monthly household income and the 2015 official poverty thresholds of the Turkish Statistical Institute as a poor, middle, or high income level.[11] In addition, the infants were divided into 2 groups according to their feeding styles: breastfeeding (exclusive or full breastfeeding with or without formula and/or complementary feeding) and nonbreastfeeding (formula with or without complementary feeding).

When an infant was presented for his or her vaccination appointment, the same nurse randomly assigned the infant to an odd or even group according to his or her registration number. If the infant's registration number was odd, the DTaP-IPV-Hib vaccination was administered first. If the number was even, the PCV-13 vaccination was administered first. The immunisation procedures and the vaccination conditions were standardised, and the vaccinations were administered by the same nurse. Each infant's crying time and pain score, based on the MBPS, were recorded by the same nurse, which constituted one limitation of our study. This clinical nurse was not involved in any other part of our study.

One dose of the vaccine (0.5 ml) was drawn up into an auto-disable syringe with a 23-gauge 1.5-cm needle using an aseptic technique, and the vaccination was administered intramuscularly in the middle third of the anterolateral thigh at a 90° angle to the skin. The needle length was the same for all of the vaccinations administered throughout the study. In those infants who did not cry, the second vaccination was administered 2 minutes after the first one. In those infants who cried after the first vaccination, the second vaccination was administered 2 minutes after the crying stopped. If an infant was enrolled in the study at 4 months of age, he or she was not enrolled again for his or her 6-month vaccinations. After the vaccination, the infant was given to the mother who had the laid the infant in a supine position in her lap. The infant was observed in the vaccination room for 15 minutes after the vaccination administration without toys or videos, breastfeeding, sweet-tasting solutions, or a pacifier.

After the first vaccination, the nurse recorded the crying time and MBPS pain score. The crying latency was defined as "did not cry" or "cried immediately." The total crying duration (in seconds) was measured from the time at which the infant started to cry until he or she stopped. In order to assess the vaccination pain according to the MBPS, the infant's facial expressions, crying, and body movements were each assigned a behaviour score (Table 1). The MBPS, which was validated previously in children, has a total score ranging from 0 to 10. The facial expression and body movement scores range from 0 to 3, and the crying score ranges from 0 to 4.[1,10]

Table 1 Modified Behaviour Pain Scale (MBPS)[1]

Parameter	Finding	Points
Facial expression	Positive expressions (smiling)	0
	Neutral expression	1
	Slightly negative expression (grimace)	2
	Definite negative expression (furrowed brow, eyes closed tightly)	3
Cry	Laughing or giggling	0
	Not crying	1
	Moaning quite vocalising gentle or whimpering cry	2
	Full lunged cry or sobbing	3
	Full lunged cry more than baseline cry	4
Movements	Usual movements and activity	0
	Resting and relaxed	0
	Partial movement (squirming, arching limb, tensing, clenching)	2
	Attempt to avoid pain by withdrawing the limb where puncture is done	2
	Agitation with complex/generalised movements involving the head torso or other limbs	3
	Rigidity	3

Data Analysis

All of the statistical analyses were performed using the Statistical Package for the Social Sciences for Windows (version 17.0; SPSS Inc., Chicago, IL, USA). The data were expressed as the mean ± standard deviation or the number and percentage. The Student's t test was used to compare the continuous variables and the chi squared test was used to compare the categorical variables between two or more groups. If the groups did not exhibit a normal distribution, they were analysed using the Mann-Whitney U test or Kruskal-Wallis test, as appropriate. The factors most predictive of the crying duration and the total MBPS score were determined using a multivariate linear regression analysis. Those variables with p values of <0.10 in the univariate analysis were included in the multivariate linear regression model as potential risk factors. The regression coefficient and 95% confidence interval (CI) were calculated for each variable. A logarithmic transformation was performed for the regression analysis, because the crying duration data and total MBPS scores were not normally distributed. Finally, a p value of <0.05 was considered to be statistically significant.

Results

A total 126 infants were randomised into 2 vaccine groups, and there were no significant differences in the demographic variables between the groups (Table 2).

The median crying duration after the injection was significantly shorter when the DTaP-IPV-Hib vaccination was administered first, when compared with the PCV-13 vaccination being administered first. However, there were no differences with regard to the age, gender, mother's educational level (MEL), SES, or feeding style (Table 3).

The crying onset latency showed no significant differences with regard to the age or gender (p=0.622 and p=0.571, respectively), but the crying onset occurred sooner in the PCV-13 first vaccination group (69.4%) than in the DTaP-IPV-Hib first vaccination group (30.6%) (p<0.001) (Table 4). Based on the age, gender, and MEL, there were no statistically significant differences between the groups with regard to the MBPS scores (Table 5); however, if the DTaP-IPV-Hib vaccination was administered first, the total MBPS score was significantly lower (3.76± 2.36) than when the PCV-13 vaccination was administered

Table 2 Demographic characteristics of the vaccination groups

	PCV-13* vaccine group Mean±SD	DTaP-IPV-Hib† vaccine group Mean±SD	p
Gender (n/%)			
Male	31 (49.2)	33 (52.4)	0.722
Female	32 (50.8)	30 (47.6)	
Age (n/%)			
4-month-aged	36 (57.1)	36 (57.1)	1.00
6-month-aged	27 (42.9)	27 (42.9)	
Birth weight (gr)	3261.9±435.53	3316.67±423.84	0.476
Weight (gr)	7445.83±955.46	7150.81±929.80	0.141
Height (cm)	65.14±3.39	64.89±2.90	0.829
Head circumference (cm)	41.74±1.53	41.56±1.37	0.796
Breastfeeding (n/%)	40 (63.5)	35 (55.6)	0.364
Pacifier use (n/%)	34 (54)	28 (44.4)	0.285
Mother's age (year)	29.23±4.73	30.04±4.37	0.321
Mother's education level (n/%)			
Primary education	11 (17.5)	9 (14.3)	0.094
Secondary education	18 (28.6)	9 (14.3)	
University education	34 (54)	45 (71.4)	

*PCV-13: 13-valent pneumococcal conjugate vaccine

†DTaP-IPV-Hib: Diphtheria and tetanus toxoids, acellular pertussis, inactivated poliovirus and *Haemophilus influenzae* type b (Hib) conjugate vaccine

Table 3 Median cry duration time

n (%)	Cry duration* (seconds)	p
Gender		
Male [64 (50.8)]	12.5 (0-300)	0.905
Female [62 (49.2)]	10 (0-360)	
Months of age		
4 months [72 (57.1)]	15 (0-300)	0.851
6 months [54 (42.9)]	10 (0-360)	
Vaccine		
DTaP-IPV-Hib† [63 (50)]	0 (0-360)	<0.001
PCV-13‡ [63 (50)]	60 (0-300)	
Mothers' Education Level		
Primary education [20 (15.9)]	10 (0-180)	0.105
Secondary education [27 (21.4)]	60 (0-300)	
University education [79 (62.7)]	10 (0-360)	
Socioeconomic status		
Poor-Middle income [86 (68.3)]	10 (0-360)	0.770
High income [40 (31.7)]	12.5 (0-300)	
Feeding sytle		
Breastfeeding [75 (59.5)]	10 (0-300)	0.325
Non-breastfeeding [51 (40.5)]	20 (0-360)	

**All values was given median (Min-Max)*

†DTaP-IPV-Hib: Diphtheria and tetanus toxoids, acellular pertussis, inactivated poliovirus and *Haemophilus influenzae* type b (Hib) conjugate vaccine

‡PCV-13: 13-valent pneumococcal conjugate vaccine

Table 4 Latency of onset of cry evaluation according to age, gender and first vaccination of infants

	Latency of onset of cry		
	Not cried n (%)	Immediately cried n (%)	p
Age (months)			
4-	29 (53.7)	43 (59.7)	0.622
6-	25 (46.3)	29 (40.3)	
Gender			
Male	29 (53.7)	35 (48.6)	0.571
Female	25 (46.3)	37 (51.4)	
Vaccine			
PCV-13*	13 (24.1)	50 (69.4)	<0.001
DTaP-IPV-Hib†	41 (75.9)	22 (30.6)	

*PCV-13: 13-valent pneumococcal conjugate vaccine

†DTaP-IPV-Hib: Diphtheria and tetanus toxoids, acellular pertussis, inactivated poliovirus and *Haemophilus influenzae* type b (Hib) conjugate vaccine

first (5.93±2.13) (p<0.001) (Table 6).

According to our results, there was a statistically significant relationship between the crying length increment and formula feeding (95% CI=0.010-1.661, p=0.047).

Discussion

Vaccinations are some of the most painful medical procedures that infants and children undergo.[12] These early painful experiences can affect a child's future responses with regard to procedural anxiety, analgesia, and needle fears, and they can have an influence on the mother-infant relationship.[12-14] It is important to reduce pain during the administration of vaccinations because some parents have reported that they want to delay their children's immunisations because they make their children cry. For this same reason, some parents do not want all of the injections to be given at one time, and some parents are even unwilling to have their children immunised.[12]

Vaccination pain management strategies include physical, psychological, and pharmacological interventions.[12,13] However, the results of previous studies have shown that distraction is most effective for decreasing pain in younger children.[15] Some distractions involving music and parental verbal behaviour have been found to be effective methods for decreasing vaccination-induced pain and distress.[16] Moreover, some previous studies have shown that breastfeeding reduces pain during intramuscular vaccinations.[17] In one review, it was reported that pacifier use and kangaroo care reduced the pain response, while touching, rocking, and holding did not reduce the pain.[18] In our study, the crying duration predictive factors were evaluated using a multivariate linear regression model. Breastfeed infants had shorter crying duration than those formula fed but the differences was not statistically significant. This can be attributed to the decreased stress hormone levels and increased anti-stress hormone levels seen in breastfed infants due to the skin-to-skin contact between the mother and the infant.[14]

The assessment of vaccination pain in infants is difficult to measure because it is difficult to quantify. In infants and children, physiological measures, such as the heart rate, respiration, and sweating can be used to assess vaccination pain.[19] In addition, several pain scales, such as the MBPS, Children's Hospital of Eastern Ontario Pain Scale, visual analogue scale, and Neonatal Infant Pain Scale, can

be used.[6,19,20] In our study, we used the MBPS, and based on those results, the age, gender, MEL, SES, and feeding style did not differ significantly differ between the infants. However, the infants who were vaccinated with the PCV-13 vaccination first started to cry instantly, their crying durations were longer, and they had significantly higher MBPS scores. In many studies, the first crying duration was shown to be a marker of the pain severity that is both easy to measure and reliable.[17]

The age, gender, and developmental level can all have effects on a child's immunisation pain response. In general, younger children tend to show more distress and pain than older children. Although female adults and adolescents exhibit greater pain responses than male adults and adolescents, there is no sex difference in the pain responses of infants and children.[12] In our study, we did not find any differences in the age and gender with regard to the MBPS score and the crying duration. One of the factors that does affect the pain response during vaccinations is the application method, and intramuscular vaccinations tend to be more painful than subcutaneous vaccinations.[13] In our study, both of the vaccinations were administered via intramuscular injections.

One previous study showed that the vaccination order can affect the infant pain response.[21] Because some vaccinations are more painful than others, when multiple vaccinations are injected during the same appointment, previous authors have recommended that the most painful vaccination should be administered last.[12] However, it is known that the pain increases after the first injection, regardless of the order in which the vaccinations are administered.[9] Unfortunately, there are no recommendations for the time interval between the vaccinations given during the same visit. One previous study reported a 2-minute interval,[13] while another reported a 1-minute interval[21] between the vaccinations administered during the same visit.

Although one recent study reported that intramuscular injections using longer needles caused less pain,[15] another study showed that the needle length did not

Table 5 Pain evaluation according to age, gender and mothers' education levels of infants with the MBPS (Mean±SD)

	Age (months) (n)(%)		**p**	**Gender (n)(%)**		**p**	**Mothers' education level (n)(%)**			**p**
	4- (72)(57.1)	**6- (54)(42.9)**		**Male (64)(50.8)**	**Female (62)(49.2)**		**PE (20)(15.9)**	**SE (27)(21.4)**	**UE (79)(62.7)**	
Facial expressions	1.61±0.59	1.62±0.65	0.974	1.56±0.58	1.67±0.64	0.342	1.6±0.59	1.81±0.62	1.57±0.61	0.159
Cry	2.12±0.96	1.98±1.03	0.446	1.96±1.02	2.16±0.96	0.289	2.05±1.05	2.4±0.93	1.91±0.98	0.110
Movements	1.15±1.01	1.20±1.03	0.778	1.14±0.36	1.20±1.01	0.708	1.2±1.00	1.48±1.01	1.06±1.01	0.171
Total MBPS score	4.88±2.48	4.79±2.52	0.934	4.65±2.45	5.04±2.54	0.360	4.85±2.43	5.70±2.49	4.55±2.47	0.084

MBPS=Modified Behaviour Pain Scale; PE=Primary Education: PE; SE=Secondary Education; UE=University Education

Table 6 Pain evaluation according to socioeconomic status, feeding sytle and vaccination of infants with the MBPS (Mean±SD)

	Socioeconomic status (n)(%)		**p**	**Feeding sytle (n)(%)**		**p**	**Vaccine (n)(%)**		**p**
	Poor-Middle income (86)(68.3)	**High income (40)(31.7)**		**Breast-feeding (75)(59.5)**	**Non-breast-feeding (51)(40.5)**		**DTaP-IPV-Hib* (63)(50)**	**PCV-13† (63)(50)**	
Facial expressions	1.62±0.61	1.60±0.63	0.778	1.61±0.61	1.62±0.63	0.927	1.36±0.57	1.87±0.55	<0.001
Cry	2.08±1.00	2.02±0.97	0.743	2.06±0.99	2.05±1.00	0.973	1.65±0.88	2.47±0.93	<0.001
Movements	1.18±1.00	1.15±1.07	0.885	1.16±0.98	1.19±1.07	0.800	0.74±1.01	1.60±0.83	<0.001
Total MBPS score	4.88±2.46	4.77±2.59	0.759	4.82±2.46	4.88±2.55	0.836	3.76±2.36	5.93±2.13	<0.001

MBPS=Modified Behaviour Pain Scale;

*DTaP-IPV-Hib=Diphtheria and tetanus toxoids, acellular pertussis, inactivated poliovirus and *Haemophilus influenzae* type b (Hib) conjugate vaccine;

†PCV-13=13-valent pneumococcal conjugate vaccine

affect the vaccination pain.[16] In our study, we used the same needle length for both vaccinations, which were administered using an intramuscular technique.

Recent studies have shown that the crying duration is a sensitive pain marker.[21] In our study, the crying duration was significantly longer in the PCV-13 vaccination first group, when compared to giving the other vaccination first. However, several studies have suggested that there is no significant relationship between the vaccination-related crying duration and the different vaccination types. Therefore, the crying volume and tone have been hypothesised to better reflect the pain than the duration.[21] An evaluation of the factors predictive for the crying duration revealed that the infants who were fed only formula had significantly longer crying durations when compared to the breastfed infants, which can be attributed to the fact that the breastfed infants may have had better infant-mother contact.

In conclusion, the results of this study showed that if the more painful injection was given first, there was a negative effect on the infant's pain response.[13,22] In addition, we observed that the PCV-13 vaccination was more painful than the DTaP-IPV-Hib conjugate vaccination; therefore, we recommend that if these vaccinations are to be administered during the same visit, the DTaP-IPV-Hib should be administered first.

Declaration of Interest

The authors declare that they have no conflict of interests.

References

1. Girish GN, Ravi MD. Vaccination Related Pain: Comparison of Two Injection Techniques. Indian J Pediatr 2014;doi:10.1007/s12098-014-1347-1.
2. Abuelkheir M, Alsourani D, Al-Eyadhy A, Temsah MH, Meo SA, Alzamil F. EMLA (R) cream: a pain-relieving strategy for childhood vaccination. J Int Med Res 2014;42:329-36.
3. Shah V, Taddio A, Rieder MJ; HELPinKIDS Team. Effectiveness and tolerability of pharmacologic and combined interventions for reducing injection pain during routine childhood immunizations: systematic review and meta-analyses. Clin Ther 2009;31 Suppl 2: S104-51.
4. T.C.Sağlık Bakanlığı Çocukluk Dönemi Aşı Takvimi. 2017. https://www.saglik.gov.tr/TR,21088/sagliga-asilanin.html Accessed 25 April 2017
5. Reis EC, Roth EK, Syphan JL, Tarbell SE, Holubkov R. Effective pain reduction for multiple immunization injections in young infants. Arch Pediatr Adolesc Med 2003;157:1115-20.
6. Dilli D, Küçük IG, Dallar Y. Interventions to reduce pain during vaccination in infancy. J Pediatr 2009;154:385-90.
7. Modarres M, Jazayeri A, Rahnama P, Montazeri A. Breastfeeding and pain relief in full-term neonates during immunization injections: a clinical randomized trial. BMC Anesthesiol 2013;13:22.
8. Taddio A, Ilersich AL, Ipp M, Kikuta A, Shah V; HELPinKIDS Team. Physical interventions and injection techniques for reducing injection pain during routine childhood immunizations: systematic review of randomized controlled trials and quasi-randomized controlled trials. Clin Ther 2009;Suppl 2:48-76.
9. Ipp M, Parkin PC, Lear N, Goldbach M, Taddio A. Order of vaccine injection and infant pain response. Arch Pediatr Adolesc Med 2009; 163:469-72.
10. Ipp M, Cohen E, Goldbach M, Macarthur C. Effect of choice of measles-mumps-rubella vaccine on immediate vaccination pain in infants. Arch Pediatr Adolesc Med 2004;158:323-6.
11. Türkiye İstatistik Kurumu http://www.tuik.gov.tr (Accessed 25 April 2017).
12. Taddio A, Chambers CT, Halperin SA, et al. Inadequate pain management during routine childhood immunizations: the nerve of it. Clin Ther 2009;Suppl 2:152-67.
13. Fallah R, Gholami H, Ferdosian F, Binesh F. Evaluation of Vaccines Injection Order on Pain Score of Intramuscular Injection of Diphtheria, Whole Cell Pertussis and Tetanus Vaccine. Indian J Pediatr 2016;83:1405-9.
14. Erkul M, Efe E. Efficacy of Breastfeeding on Babies' Pain During Vaccinations. Breastfeed Med 2017;12:110-5.
15. Schechter NL, Zempsky WT, Cohen LL, McGrath PJ, McMurtry CM, Bright NS. Pain reduction during pediatric immunizations: evidence-based review and recommendations. Pediatrics 2007; 119:e1184-98.
16. Jacobson RM, Swan A, Adegbenro A, Ludington SL, Wollan PC, Poland GA; Vaccine Research Group. Making vaccines more acceptable-methods to prevent and minimize pain and other common adverse events associated with vaccines. Vaccine 2001; 19:2418-27.
17. Gupta NK, Upadhyay A, Dwivedi AK, Agarwal A, Jaiswal V, Singh A. Randomized controlled trial of topical EMLA and vapocoolant spray for reducing pain during wDPT vaccination. World J Pediatr 2017;13:236-41.
18. Pillai Riddell RR, Racine NM, Gennis HG, et al. Non-pharmacological management of infant and young child procedural pain. Cochrane Database Syst 2015;2015: CD006275.
19. Ipp M, Cohen E, Goldbach M, Macarthur C. Pain response to M-M-R vaccination in 4-6 year old children. Can J Clin Pharmacol 2006;13:e296-9.
20. Yilmaz G, Caylan N, Oguz M, Karacan CD. Oral sucrose administration to reduce pain response during immunization in 16-19-month infants: a randomized, placebo-controlled trial. Eur J Pediatr 2014;173:1527-32.
21. Kumar M, Upadhyay A, Singh J, et al. Effect of change in sequence of administration of DTwP and Hepatitis B vaccines on perception of pain in infants: A randomized control trial. Vaccine 2016;34:1816-22.
22. Ravikiran SR, Kumar PM, Meundi AD. Pain response in newborns to the order of injecting BCG and Hepatitis-B vaccines: a randomized trial. Indian J Pediatr 2011;78:693-7.