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Compliance with aspirin in pediatric congenital heart disease post percutaneous transcatheter occlusion: A cross-sectional study

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DECLARATIONS

Ethics approval and consent to participate

Ethical approval of the study was obtained from the Ethical Review Board of Hunan Children's Hospital (approval number: HCHLL-2016-32).

Consent for publication

Not applicable

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

QqS, LhZ, OyC, JML initiated the study and were responsible for the study protocol and design of the study. QqS, ZrX, ZC, JcM contributed to the data acquisition. QqS, CZ and JML performed the analysis. All authors were involved in the data interpretation. QqS, YbX and JML drafted the first manuscript and substantively revised it. All authors approved the submitted version after substantially modified previous versions. All authors, QqS, LZ, OyC, ZrX, ZC, YbX, JcM, CZ, JML, agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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ABSTRACT

Background: Predictors of compliance with aspirin in children following cardiac catheterization have not been identified. The aim of this study is to identify the caregivers' knowledge, compliance with aspirin medication, and predictors of compliance with aspirin in children with congenital heart disease (CHD) post percutaneous transcatheter occlusion.

Methods: A cross-sectional explorative design was adopted using a self-administered questionnaire and conducted between May 2017 and May 2018. Recruited were 220 caregivers of children with CHD post percutaneous transcatheter occlusion. Questionnaires included child and caregivers' characteristics, a self-designed and tested knowledge about aspirin scale (scoring scale 0-2), and the 8-item Morisky Medication Adherence Scale (scoring scale 0-8). Data were analyzed using multivariate binary logistic regression analysis to identify predictors of compliance with aspirin.

Results: Of the 220 eligible children and caregivers, 210 (95.5%) responded and 209 surveys were included in the analysis. The mean score of knowledge was 7.25 (SD 2.27). The mean score of compliance was 5.65 (SD 1.36). Child's age, length of aspirin use, health insurance policies, relationship to child, monthly income, and knowledge about aspirin of caregivers were independent predictors of compliance with aspirin ($p<0.05$).

Conclusion: Caregivers of children with CHD had an adequate level of knowledge about aspirin. Compliance to aspirin medication reported by caregivers, was low. Predictors of medium to high compliance with aspirin were related to the child's age and socio-economic reasons. Further studies are needed to identify effective strategies to improve knowledge, compliance with medication and long-term outcomes of children with congenital heart disease.

KEY WORDS: Congenital Heart Disease; Percutaneous Transcatheter Occlusion; Medication; Adherence; Compliance; Aspirin

INTRODUCTION

Congenital heart disease (CHD) is a general term of cardiovascular malformation caused by incomplete development of cardiac structure during embryonic period.[1] It is one of the most common congenital diseases in newborns. Hoffman and others have found that the incidence of congenital heart disease in newborns is about 1‰, and this ratio is even higher in death fetal or abortion.[2,3] Children with congenital heart disease often have a series of physiological, psychological and social problems due to repeated infections and long treatment.[4-7] The two most common types of CHD are ventricular septal defect (VSD) and atrial septal defect (ASD), which accounts for 31.49% and 20.20% of CHD respectively.[8,9]

With the develpment of medical technology, medical devices and surgical treatment of CHD, minimally invasive procedures are becoming more common in pediatric cardiology. Since the introduction of the Amplatzer occlusion device at the end of the last century, which had a positive effect on the treatment of left-to-right shunt congenital heart disease, interventional therapy has gradually developed into the first choice of treatment for some forms of CHD.[10-12] Although guidelines and quality control standards exist for interventional catherization therapy, the prognosis and complications vary among children with CHD. Studies have shown that patients post percutanous closure continue to have changes in the aggregation and activation of platelets.[13,14] A statement from the American Heart Association addresses that cardiac catherization remain associated with complications such as device embolism, marker band embolism (located at the tip of the sheath), and cerebral embolism.[15] Krumsdorf and colleagues documented that thrombus formation was found in the left atrium, right atrium, or both in five of the 407 (1.2%) children with ASD and 15 of the 593 (2.5%) children with VSD.[16] Therefore, in these groups of children, long-term oral anti-platelet aggregation medication are recommended.

Aspirin is usually been prescribed for 6 months after ASD or VSD closure via cardiac catherization.[17,18] The recommended aspirin dose is 3-5mg/day to avoid cardiac thrombosis and prevent post-interventional systemic embolism.[13,19] Therefore, maintaining good compliance to aspirin medication is imperative to successful treatment and reducing complication rates in children with congenital heart disease after percutaneous closure. To our knowledge, there is currently no evidence describing predictors of compliance with aspirin in children following cardiac catheterization. Therefore, the aim of our study is to explore the compliance with aspirin of children with CHD post percutaneous transcatheter occlusion as reported by the child' caregivers. Specifically, the objectives of our study are: 1) To identify the caregivers' knowledge about aspirin in children with CHD; 2) to describe the compliance with aspirin intake in children after percutaneous transcatheter occlusion; 3) to identify predictors of compliance with aspirin medication in children after percutaneous transcatheter occlusion.

METHODS

Design

The study adopted a cross-sectional explorative survey design. The study was conducted over a 12-month period; May 2017 to May 2018. Ethical approval of the study was obtained from the Ethical Review Board of Hunan Children's Hospital (approval number: HCHLL-2017-43). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies has been used for reporting the study.[20] Specifically, the STROBE checklist for cross-sectional studies was used.

Setting

The study was performed at Hunan Children's Hospital in Changsha, Hunan Province, China. The cardiology department is a tertiary center serving children with cardiac diseases within Hunan Province with a population of 67 million. The department includes the interventional pediatric cardiology unit with a catheterization laboratory performing over 1500 interventional therapies or cardiac catheterization. Of these, around 900 percutaneous transcatheter occlusion interventions are carried out in children with ASD or VSD.

Participants

Children who underwent successful atrial septal defect or ventricular septal defect percutaneous transcatheter occlusion and their parents.

Sample size

A cluster sampling method was adopted for the study. According to the single population proportion formula $n=Z^2_{1-\alpha/2}\, p(1-p)/d^2$ where n is a desired sample size for population over than 10,000; $Z_{1-\alpha/2}$ is standard normal distribution usually set as 1.96 (which corresponds to 95% confidence level); p means that we use estimated Omega-3 Polyunsaturated Fatty Acid Supplementation average adherence rate at 0.85[21], to maximize sample size; negative prevalence =1− 0.85=0.15; d is the degree of accuracy desired (marginal error is 0.05); then the sample size is $n=1.96^2*0.85\ (1-0.85)/0.05^2=196$. Adding a 10% contingency, the final sample size is 216.

Inclusion and exclusion criteria

Included were: Children with ventricular septal defect or atrial septal defect post successful percutaneous transcatheter occlusion treatment and have been prescribed oral aspirin for six month for anticoagulant therapy; Children with oral aspirin for more than one month; Children aged below nine years of age; Caregivers responsible for providing aspirin to the child; Caregivers able to read Chinese and complete the questionnaire; Caregivers able to sign the written consent form.

Excluded were: Children with other complicated congenital malformations, such as complex congenital heart disease requiring surgery, congenital esophageal fistula and other surgical treatments; Children with other serious chronic diseases requiring long-term oral medication, such as epilepsy or asthma.

Instruments

A 3-part survey was employed to measure (1) basic characteristics of children and caregivers, (2) aspirin-related-knowledge, and (3) compliance with medication. The first part included characteristics of children and caretakers: gender; age; disease type; length of aspirin use; relationship to child; childcare experience; marital status; education level; occupation; monthly income; health insurance policies.

The second part of the survey was aspirin-related knowledge post percutaneous transcatheter occlusion and was developed by the pediatric cardiovascular interventional therapy specialist group with six doctors and 10 nurses after a three-round Delphi method. A pretest of this survey was performed among 10 caregivers of children in March 2017. The feedback of the caregivers was reviewed, and the survey was modified. The final version of the aspirin-related knowledge survey included six questions related to: major role of low-dose aspirin; reasons for taking aspirin after catheter interventional closure; dosage of aspirin intake; length of aspirin intake after interventional closure; proceedings of how to take aspirin; common side effects of aspirin. The survey used a 5-point scoring scale. If the question was answered correctly, the item received a score of 2; when the multiple-choice answers were partly correct, the item received a score of 1; if the answer was incorrect or the option 'unclear' was used, a score of 0 was given. The total score of this survey was 12 points; the higher the score, the higher the aspirin-related-knowledge. As we did not have any reference of this new survey, we defined a score of ≥ 6 as having an adequate level of knowledge about aspirin and < 6 as insufficient knowledge. The internal consistency of the survey resulted in a Cronbach's α of 0.70. The content validity ratio was 0.71.

The third part of the survey included the 8-item Morisky Medication Adherence Scale (MMAS-8).[22] The Chinese version of the scale was used in our study.[23] The answer options of the first seven items were Yes and No (yes=0 and no=1). The scale of the last items was a 5-point Likert scale: never, occasionally, sometimes, frequently, all time, with the scores 1, 0.75, 0.50, 0.25, and 0 points respectively. The total score of the MMAS-8 is 8; a score <6 indicates low compliance with medication, 6~7 medium compliance with medication and 8 high compliance with medication. The scale has been used among children with asthma and the results indicated a Cronbach's α coefficient of 0.90.[24]

Recruitment and Data Collection

Recruitment of eligible children and caregivers was performed at the follow-up clinic one month after hospital discharge. A specialist nurse from our department always contacts the caregivers for a follow-up appointment. During this phone call, the specialist nurse provided a brief information about the study and informed the caregivers that they would receive a study invitation during the follow-up clinic. Once the children and caregivers visited the follow-up clinic, they received an invitation letter including the study objectives, information about the survey, assurance of confidentiality, and their right to withdraw at any time. After signed consent was obtained, the anonymous survey was distributed to the caregivers for completion while they visited the follow-up clinic. The doctors at the follow-up clinic were informed about the study.

Statistical Analysis

Data were entered into IBM SPSS Statistics for Windows, Version 20.0 (Armonk, NY: IBM Corp.). Descriptive statistics including frequency, mean, percentage, standard deviation was used to summarize baseline data and evaluate distribution of responses. Univariate analysis was performed to analyze the association between compliance with medication and independent variables. All variables with $p<0.05$ in the univariate

analysis were included in the multivariate binary logistic regression analysis, which was performed to identify potential predictors of compliance. Confidence interval (95%) was reported in each logistic regression analysis. P value < 0.05 was considered as statistically significant.

RESULTS

Of the 220 eligible children and caregivers, 210 (95.5%) responded. Of these, 209 questionnaires were valid to be included in the analysis.

Characteristic of children and caregivers

The characteristics of the children and caregivers are presented in Table 1. The mean age of the children was 4.2 years (SD 2.70). The questionnaires were mostly completed by mothers or fathers (66.9%). Of the 209 respondents, 103 (49.3%) had no previous parenting experience.

Aspirin related knowledge

The knowledge about aspirin mean scores of the caregivers was 7.25 (SD 2.27; min 2, max 10). 134 respondents had an overall score of ⩾6, representing 64.1% of the respondents having an adequate level of aspirin knowledge. Detailed scores of the six individual questions of the knowledge about aspirin survey are presented in Table 2.

Compliance with aspirin

The maximum score of the MMAS-8 reported by 209 caregivers was 8, the minimum score was 2.5, with an overall mean score of 5.65 (SD 1.36). Of the 209 respondents, 101 (48.3%) had a low compliance score (<6) and 108 (51.7%) respondents had a medium to high compliance score (6-8). Notably, only five respondents complete the MMAS-8 with a maximum score of 8.

Univariate analysis of characteristics and compliance with aspirin

The analysis revealed several predictive factors related to compliance with aspirin. Significant differences were observed between compliance with aspirin medication and the predictive factors child's age, length of aspirin use, health insurance policies, relationship to child, education of caregivers, monthly income, and knowledge about aspirin of caregivers (Table 3).

Multivariate binary logistic regression analysis of compliance with aspirin

Based on the results of univariate binary logistic regression analysis, the variables child's age, length of aspirin use, health insurance policies, relationship to child, education of caregivers, monthly income, and aspirin knowledge of caregivers were included in the multivariate binary logistic regression analysis. The results showed that child's age, aspirin use, and knowledge about aspirin were significantly associated with aspirin compliance (Table 4). The variable relationship to child showed that only the father and mother were significantly associated with aspirin compliance. Having health insurance policies and a monthly income of caregivers over 5000 CNY were also significant predictors of compliance with aspirin.

DISCUSSION

This study explored the knowledge about aspirin and compliance with aspirin of children post percutaneous transcatheter occlusion as reported by caregivers and predictors of compliance with aspirin were identified. In our study, 209 caregivers participated and the majority (64%) of the caregivers had adequate knowledge of aspirin. Half of the caregivers reported a medium to high compliance with aspirin scores. The main identified predictors affecting compliance with aspirin included child's age, aspirin use, and knowledge about aspirin, and socio-economic factors.

Knowledge about aspirin

Aspirin-related-knowledge was defined as knowledge about complications, administering, duration, dosage, reason, and pharmacological action of aspirin. In our study, the overall parental aspirin knowledge was 7.25 (max scale score 12; participants scores max 10) indicating that parents had possibly an adequate level of aspirin knowledge. A reference or cut-off point has not been identified to determine the minimal level of knowledge for providing optimal medication support to children. Duffy et al reported in their review that knowledge about aspirin and compliance was not optimal ranging between 72-92%.[25] Of the 12 included studies in this review, none of the studies were related to children. Specifically, in children, Lee and colleagues conducted a study among parents of 87 children waiting for organ transplantation. The results showed that if parent have more knowledge about medication the children have better compliance with medication.[26] Therefore, educational interventions are recommended as our study also confirms that aspirin knowledge was a predictor of low aspirin medication intake.

Compliance with medication

Compliance to medication is referred to the compliance level of prescribed medication use. The connotation includes taking the medicine according to the dose and time. Studies have been using the MMAS-8 to explore compliance with medication among patients. Basharat and colleagues identified low compliance with medication (45%) among 310 children with asthma.[27] Another study among 75 children with sickle cell anemia receiving hydroxyurea documented a high compliance with medication of 84%.[28] Both study were related to children with chronic conditions which needed medication to enhance treatment or relieve symptoms. In our study, the compliance with aspirin was low to medium, 48.3%, 49.3% respectively. In our population, the cardiac malformations were corrected by percutaneous transcatheter occlusion. Parents might have believed that aspirin was not necessary to prevent post interventional complications. The results suggest to improve the compliance with aspirin and knowledge of parents. Discharge information interventions might help parents to increase compliance with medication regimes.[29,30]

Predictors of compliance with aspirin

The child's compliance with medication was related to age. The results of this study showed that the medium to high compliance rate of children with congenital heart disease between 1 to 6 years old accounted for 72.4%(n=145) and the medium to high compliance rate of children aged 6~9 years were just 6.2%(n=64).A study among children (n=2860) and adolescents (n=17,179) with acne vulgaris documented differences in compliance with acne medication; adolescent were less likely to adhere

to the medication regime than children.[31] In our study, all patients were under 9 years of age and might have less autonomous behavior ability and rely on the caregivers' responsibility to adhere to the medication regime.[32] Various factors might influence the caregiver's level of knowledge and compliance with aspirin such as advice given by medical and nursing staff or family support strategies.

The length of aspirin use is one of the predictors that can influence negatively compliance with aspirin. Our study documented that aspirin use more than three months showed a decrease in compliance rates. So far, this result has not been confirmed in other studies with children in cardiology. However, a study among children with anxiety disorders documented that treatment adherence was associated with the length of medication usage.[33] Possible reasons for a decline in the compliance with medication over a longer time period could be the lack of continuous or regular health education support.

Social and economic factors have been identified as predictors of compliance with medication. A review of studies on compliance with medication in children with epilepsy identified several environment-related factors influencing compliance with medication.[33,34] For example, three identified studies in the review documented that support form medical and nursing staff was related to better adherence. Three other studies reported that better socio-economic status of the family would predict better compliance with medication. These factors have been confirmed in our study where compliance with aspirin was better when family and caretakers had a higher monthly income.

Implication for clinical practice

The attention to predictors of compliance with aspirin in children post percutaneous transcatheter occlusion is warranted by clinicians. Providing targeted support to parents or the primary caregivers might benefit the long-term adherence and reduce complication rates. General strategies to improve compliance with medication can be related to family members but should also include healthcare professionals [30,33]. For parents, support strategies could include education or counseling, information brochures, and reminders. Healthcare professionals need to consider to organize continuous education on compliance with medication, build a stronger child-professional relationship, or developing a multi-disciplinary teams with specific roles in follow-up clinics. Further studies are needed to identify effective aspirin prescriptions in terms of frequency and length of use for children post percutaneous transcatheter occlusion.

Limitations

This study warrants several limitations to be addressed. First, the use of self-reported questionnaires has its limitation because respondents might exaggerate the responses to the survey questions or might be uncomfortable to disclose private details. Therefore, we performed a rigorous method in designing the survey related to the knowledge about aspirin. Second, this was a single center study which might limit the generalizability of the findings. Third, we only recruited children and their caregivers who visited the follow-up clinic. This might have been a bias in the selection procedure. It is unclear what the knowledge and the compliance with aspirin is of the no-show children in the

follow-up clinic. Further investigation is warranted to determine the overall compliance in children post percutaneous transcatheter occlusion.

CONCLUSION

Our study documented that caregivers of children post percutaneous transcatheter occlusion had an adequate level of knowledge about aspirin. However, the knowledge level of the caregivers was correlated with a low compliance with aspirin. Several predictors have been identified that might influence the compliance with medication of the prescribed aspirin regime of six months. The compliance with medication was better in children who were younger and when children had health insurances, higher monthly incomes, better awareness of aspirin and being the father or mother of the child. Further studies are needed to identify the consequences of low compliance with aspirin such a long-term complication rates and effective parental educational interventions.

ABBREVIATIONS

ASD: Atrial Septal Defect
CHD: Congenital Heart Disease
CNY: Chinese Yuan
MMAS-8: 8-item Morisky Medication Adherence Scale
VSD: Ventricular Septal Defect

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Table 1. Characteristics of children and caregivers

Children (n=209)		n	%
Gender	Male	106	50.7%
Age (years)	1-6	145	69.2%
	6-9	64	30.8%
Aspirin use (months)	1-3	138	66.0%
	3-6	71	34.0%
Only child in family	Yes	105	50.2%
	No	104	49.8%
Heart defect	ASD	91	43.5%
	VSD	118	56.5%
Health insurance policies	≥2	64	30.6%
	1	85	40.7%
	None	60	28.7%
Caregivers (n=209)			
Gender (male)	Male	128	61.2%
Age (years)	20-25	14	6.7
	25-40	90	43.1
	41-55	55	26.3
	≥55	50	23.9
Relationship to child	Mother	49	23.4%
	Father	91	43.5%
	Grandparent	47	22.5%
	Others	22	10.5%
Childcare experience	No	103	49.3%
	Yes	106	50.7%
Marital status	Married	137	65.6%
	Divorced or widow	72	34.4%
Education	Junior high school	135	64.6%
	Senior high school	39	18.7%

	Bachelor or higher	35	16.7%
Monthly income (CNY)	<2000	33	15.8%
	2000-4999	98	46.9%
	5000-9999	50	23.9%
	≥10000	28	13.4%

CNY=Chinese Yuan

Table 2. Knowledge about aspirin of caregivers (n=209)

Questions	Score			Knowledge level	
	Min	Max	Mean (SD)	Scores 1 or 2: n (%)	Score 0: n (%)
Complication of aspirin	0	1	0.47 (0.500)	99 (47)	110 (53)
How taking aspirin	0	2	0.83 (0.378)	173 (83)	36 (17)
Length of aspirin intake	0	2	1.72 (0.692)	180 (86)	29 (14)
Dosage of aspirin	0	2	1.97 (0.238)	206 (99)	3 (1)
Why to take aspirin	0	2	1.19 (0.984)	124 (60)	85 (40)
Role of low-dose aspirin	0	2	1.06 (1.001)	110 (53)	99 (47)

SD=Standard Deviation; Score range of the multiple-choice questions were 0-2.

Table 3 Univariate analysis characteristic and compliance with aspirin (n=209)

Characteristics Children (n=209)		Compliance (n, %)			
		Low	Medium to High	χ^2	*P*
Gender	Male	57 (27.3)	48 (23.0)	3.506	0.061
	Female	43 (20.6)	61 (29.2)		
Age (years)	1-6	40 (19.1)	105(50.2)	77.895	<0.001
	6-9	60 (28.7)	4 (2.0)		
Aspirin use (months)	1-3	41 (19.6)	97 (46.4)	53.549	<0.001
	3-6	59 (28.2)	12 (5.8)		
Only child in family	Yes	53 (25.4)	52 (24.9)	0.585	0.445
	No	47(22.5)	57 (27.3)		
Heart defect	ASD	54 (25.8)	65 (31.1)	0.675	0.411
	VSD	46 (22.0)	44 (21.1)		
Health insurance	≥2	14 (6.7)	50 (23.9)	28.492	<0.001
	1	56 (26.8)	29 (13.9)		
	None	30 (14.4)	30 (14.4)		
Characteristics Caregivers (n=209)					
Gender	Male	58 (27.8)	70 (33.5)	1.201	0.273
	Female	43 (20.6)	38 (18.2)		
Age (years)	20-25	6 (2.9)	8 (3.8)	1.395	0.707
	25-40	46 (22.0)	44 (21.1)		
	41-55	28 (13.4)	27 (12.9)		
	⩾55	21 (10.0)	29 (13.9)		
	Mother	38 (18.2)	53 (25.4)		

Relationship to child	Father	39 (18.7)	9 (4.3)	29.518	<0.001
	Grandparent	17 (8.1)	31 (14.8)		
	Others	6 (2.9)	16 (7.7)		
Childcare experience	No	54 (25.8)	49 (23.5)	1.368	0.242
	Yes	47 (22.5)	59 (28.2)		
Marital status	Married	31 (14.8)	41 (19.6)	1.011	0.315
	Divorced or widow	78 (37.3)	85 (40.7)		
Education	Junior high school	87(41.6)	47(22.5)	49.525	<0.001
	Senior high school	12(5.7)	27(12.9)		
	Bachelor or above	1 (0.6)	35 (16.7)		
Monthly income (CNY)	<2000	29 (13.9)	3 (1.5)	62.818	<0.001
	2000-4999	58 (27.8)	40 (19.1)		
	5000-9999	12 (5.7)	38 (18.2)		
	⩾10000	1 (0.5)	28 (13.4)		

CNY=Chinese Yuan

Table 4. Multivariate binary logistic regression analysis of predictors of non-compliance with medication (n=209)

Variable		B	SE	Wald	*p*	OR	OR (95%CI)	
							Min	Max
Age child (years)	6-9		0			1		
	1-6	2.861	0.970	8.697	0.003	17.479	2.611	117.028
Aspirin use (month)	3-6		0			1		
	1-3	3.469	0.966	12.897	<0.001	32.120	4.835	213.374
Education	Bachelor or		0	5.192	0.075	1		
	Junior high	-2.541	1.360	3.489	0.062	0.079	0.005	1.134
	Senior high	-0.543	1.836	0.088	0.767	0.581	0.016	21.225
Relationship to child	Other		0	10.505	0.015	1		
	Mother	-6.191	1.943	10.150	0.001	0.002	0.000	0.092
	Father	-3.724	1.563	5.678	0.017	0.024	0.001	0.516
	Grandparents	-2.087	1.246	2.808	0.094	0.124	0.011	1.425
Health insurance	⩾2		0	6.647	0.036	1		
	1	2.813	1.097	6.579	0.010	16.668	1.942	143.072
	0	1.071	0.841	1.624	0.203	2.919	0.562	15.166
Monthly income	⩾10000		0	10.323	0.016	1		
	5000-9999	-4.026	1.570	6.577	0.010	0.018	0.001	0.387
	2000-4999	-2.475	1.360	3.314	0.069	0.084	0.006	1.209
	<2000	-0.597	1.447	0.170	0.680	0.550	0.032	9.390
Aspirin-knowledge	7.25 ± 2.27	-3.459	0.859	16.204	<0.001	0.031	0.006	0.170
Constant		2.477	1.967	1.586	0.208	11.907		

OR=Odds Ratio; SE=Standard Error; CI=Confidence Interval