Association of Environmental Tobacco Smoke Exposure with Carotid Intima Media Thickness in Healthy Children: a Systematic Review and Meta-Analysis

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1. Background and Aim

- Environmental tobacco smoke exposure (ETS) on the severity of paediatric lung diseases is well known
- Beginning to understand the long-term effects of ETS on the paediatric antecedents of adult cardiovascular diseases
- Atherosclerosis (AS) is the underlying cause of the majority of cardiovascular diseases, and thicker carotid intima media thickness (CIMT) is proved to be a predictor of AS development
- In adults a clear association between ETS and thickening of CIMT, however such association has not been systematically reviewed in paediatric population
- Aim to determine the association between ETS exposure and CIMT in healthy children and adolescents

2. Methodology

- **1) Search strategy:** ① 6 electronic database: MEDLINE (Ovid), Pubmed, Embase, CINAHL, Web of Science, Scopus; ② Further scanned reference lists of retrieved articles
- **2) Keywords:** ‘(environmental tobacco smoke exposure OR second hand smoke OR passive smoke OR involuntary smoke) AND (atherosclerosis OR carotid intima media thickness OR tunica Intima)’
- **3) Inclusion criteria:** ① Studies investigated the association between ETS and CIMT; ② Full-text English articles with subjects under 18 years old; ③ Healthy subjects without traditional risk factors of cardiovascular disease
- **4) Exclusion criteria:** ① Investigated acute effect of ETS exposure; ② Active smoke exposure; ③ Review study, guideline, consensus statement, letter and conference abstract; ④ Data was not published; ⑤ Repeated or ongoing research
- **5) Statistical analysis of meta:** Review Manager 5.3

3. Results

- 331 articles retrieved and screened, 4 articles included, studies are heterogeneous in methodologies
- **1) Association between postnatal ETS and CIMT:** all 4 studies investigated, 3 studies found a statistically significant positive association while 1 reported negative results
- **2) Association between prenatal maternal smoke and CIMT:** 3 studies investigated, 2 studies found a statistically significant positive association while 1 reported no significant association
- **3) Association between postnatal maternal smoke and CIMT:** 2 studies investigated, 1 found a statistically significant positive association
- **4) Dose-response relationship:** the 2 studies using serum cotinine measurement demonstrated potential dose-response relationship between ETS exposure and CIMT

4. Conclusion

- ☐ Up to now, only few studies addressed associations between ETS and childhood AS risk, our review results might add to the knowledge that cardiovascular effects of tobacco smoke exposure could begin in childhood, long before clinical cardiovascular disease is evident
- ☐ Our study could enhance the evidence for policy makers and parents to take the action for the no smoke environment generation for the paediatric population

Bibliography

1. Katariina Kallio et al. *Circa Cardiovasc Qual Outcomes*. 2010

2. Caroline C. Geerts et al. *PEDIATRICS*. 2012

3. Bo Yang et al., *Journal of the Renin-Angiotensin- Aldosterone System*. 2012

4. Julian G. Ayer et al. *European Heart Journal*. 2011

3.1 Search Results

Figure 1. Flow diagram of the study selection process

3.2 Study characteristics

Study	Country	Title	Study design, N, Age, Male%	ETS Measurement	CIMT Measurement	ETS grouping	Main Results
Katarina Kallio et al.	Finland	Arterial Intima-Media Thickness, Endothelial Function, and Apolipoproteins in Adolescents Frequently Exposed to Tobacco Smoke	Prospective	Prenatal maternal: Delivery records (yes OR no);	High-resolution ultrasound	Prenatal maternal- 3 groups: 5/160; 7/171; 10/163	Prenatal maternal: Single determinant regression coefficient: pregnancy maternal smoke: -0.004 ± 0.013, p= 0.77
			494		Maximal CIMT		
			13.0	Postnatal: serum cotinine level		Postnatal - 3 groups: low (n=160), intermediate (n=171), high (n=163); By averaged serum cotinine (ng/mL*): 0.28 (0.27- 0.29), 0.52 (0.51- 0.53), 1.05 (1.00- 1.11)	Postnatal all: Adolescents with higher longitudinal exposure to tobacco smoke had increased CIMT (exposure groups [mean ± SD] (crude data): low, 0.502 ± 0.079 mm; intermediate, 0.525 ± 0.070 mm; high, 0.535 ± 0.066 mm; P<0.001) Low vs inter: 0.013; low vs high: <0.001; inter with high 0.57, no difference after adjustment
Caroline C. Geerts et al.	The Netherlands	Parental Smoking and Vascular Damage in Their 5-year-old Children	Prospective	Prenatal : Questionnaire (yes OR no)	High-resolution ultrasound	Prenatal maternal- 2 groups: Yes (n=15), No (n=244)	Prenatal- Children of mothers who had smoked throughout pregnancy (n=244) had 0.0188 mm thicker CIMT (95% confidence interval [CI] 1.1, 36.5, P =0.04)
			259		Maximal CIMT	Prenatal both- 2 groups: Yes (n=6), No (253)	The associations were strongest if both parents had smoked during pregnancy, with 0.0277 mm thicker CIMT (95% CI 0.002, 0.0553) Coefficient: crude: 0.0154 (-0.02, 0.0329), p= 0.08
			5.4 ± 0.3	Postnatal parental: Questionnaire		Postnatal any- 2 groups: Yes (n=49), No (n= 210)	
Bo Yang et al.	China	Deterioration of endothelial function and carotid intima-media thickness in Tibetan male adolescents exposed to second-hand smoke	Cross-sectional	Prenatal: Data not found yet	High-resolution B-mode ultrasonography	3 groups: 205 boys, intermediate cotinine group (Intermediate Group) with 210 boys, and low cotinine group (Low Group) with 209 boys	Postnatal- The CIMT had deteriorated in the High Group compared with the Low Group (p<0.001).
			624				
			16.0	Postnatal: serum cotinine level	Maximal CIMT	Averaged serum cotinine (ng/ml)- low: 0.26-0.57 (0.39±0.09); intermediate: 0.58-0.89 (0.74±0.11); high: 0.90-1.14 (1.00±0.08)	Mean IMT (mm): 0.62±0.08; 0.66±0.09; 0.69±0.11; p1 <0.001, p2<0.001, p3>0.0024 (p1: compared between Low Group and Intermediate Group; p 2: compared between Low Group and High Group; p 3: compared between Intermediate Group and High Group)
Julian G. Ayer et al.	Australia	Maternal cigarette smoking is associated with reduced high-density lipoprotein cholesterol in healthy 8-year-old children	Prospective	Prenatal maternal: Questionnaire (yes OR no)	High-resolution B-mode ultrasound	Prenatal maternal - 2 groups: Exposed (n=93), Non-exposed (n=312)	Prenatal- Smoking in pregnancy: n=93, mean CIMT (mm): 0.59±0.06; No smoking in pregnancy, n= 312, mean CIMT (mm): 0.66±0.06, p= 0.31; Difference (mm): 0.008 (0.007- 0.02), p= 0.31
			405	Prenatal other: questionnaire	Maximal CIMT		
			8.0	Postnatal maternal: home visit interview or phone call		Postnatal maternal: Sample number not found yet	Postnatal maternal: 0.59/0.60, difference: 0.01 (-0.02 to 0.03); p=0.8 Neither smoking in pregnancy nor postnatal ETS exposure was associated with alterations of carotid artery wall thickness
			49.6%				