

**Seto A et al. Pregnancy outcome following first trimester exposure to antihistamines: meta-analysis. *Am J Perinatol* 14, 119-24, 1997**

Type of study	<p>Meta-analysis:            Studies: 109 identified            24 included (criteria for inclusion: human subjects, maternal exposure to studied drugs in pregnancy, nonexposed control group, outcome-malformation, presentation of exposed and nonexposed rates of outcome):</p> <ul style="list-style-type: none"> <li>- Bunde CA, Bowles DM. <i>Curr Ther Res</i> 5, 245-8, 1963</li> <li>- General Practitioner Clinical Trials. <i>Practitioner</i> 191, 775-80, 1963</li> <li>- Mellin G, Katzenstein M. <i>Br Med J</i> 26, 222-3, 1963</li> <li>- Nora J, Nora A, Sommerville R et al. <i>JAMA</i> 1967</li> <li>- Nelson M, Forfar J. <i>Br Med J</i> 1, 523-7, 1971</li> <li>- Ayd FJ. <i>Dis Nerv Syst</i> 33, 459-69, 1972</li> <li>- Kullander S, Kallen B. <i>Acta Obstet Gynecol Scand</i> 55, 105-11, 1976</li> <li>- Miklovich L, Van den Berg B. <i>Am J Obstet Gynecol</i> 125, 244-8, 1976</li> <li>- Greenberg G, Inman WHW, Weatherall JAC et al. <i>Br Med J</i> 2, 853-6, 1977</li> <li>- Heinonen OP, Slone D, Shapiro S. <i>Birth defects and drugs in pregnancy.</i> Littleton MA: PSG Publishing; 1977</li> <li>- Newman NM, Correy JF, Dudgeon GI. <i>Aust NZ J Gynaecol</i> 17, 156-9, 1977</li> <li>- Smithells RW, Sheppard S. <i>Teratology</i> 17, 31-6, 1978</li> <li>- Rothman KJ, Fyler DC, Goldblatt A et al. <i>Am J Epidemiol</i> 109, 433-9, 1979</li> <li>- Fleming DM, Knox JDE, Crombie DL. <i>Br Med J</i> 283, 99-101, 1981</li> <li>- Gibson GT, Colley DP, McMichael AJ et al. <i>Med J Aust</i> 1, 410-14, 1981</li> <li>- Jick H, Holmes LB, Hunter JR et al. <i>JAMA</i> 246, 343-6, 1981</li> <li>- Eskenazi B, Bracken M. <i>Am J Obstet Gynecol</i> 144, 919-24, 1982</li> <li>- Morelock S, Hingson R, Kayne H et al. <i>Am J Obstet Gynecol</i> 142, 209-13, 1982</li> <li>- Aselton PJ, Jick H. <i>JAMA</i> 250, 33-4, 1983</li> <li>- Golding J, Vivian S, Baldwin JA. <i>Hum Toxicol</i> 2, 63-73, 1983</li> <li>- Michaelis J, Michaelis H, Gluck E et al. <i>Teratology</i> 27, 57-64, 1983</li> <li>- Zierler S, Rothman KJ. <i>NEJM</i> 313, 347-52, 1985</li> <li>- Seto A, Einarson T, Koren G. <i>Reprod Toxicol</i> 7, 393-5, 1993</li> </ul> <p>85 excluded: (criteria for exclusion: animal studies, stillbirths/abortions as outcome measure, case reports, review articles, editorial comments, obstetric aspects, duplicate or irrelevant articles)            References indicated in the meta-analysis</p>
When	1960-1991
Characteristics of the recruited patients	Newborns exposed to the studied drugs with and without major malformations; newborns non-exposed to the studied drugs with and without major malformations
Characteristics of the treated diseases	Not indicated
Exposure definition	Intake during the first trimester of pregnancy: antihistamines (H <sub>1</sub> blockers) defined as any compound with H <sub>1</sub> receptor antagonist action as its principal intended effect (any compound indicated for the treatment of allergies, nausea, vomiting, cough, cold, respiratory disorders)
Ascertainment of drug exposure	Not indicated
Size of the studies included for meta-analysis	29,603 exposed; 144,965 non-exposed newborns
Malformations definition	Not indicated
Malformations ascertainment	Not indicated
Analysis	<ul style="list-style-type: none"> <li>- Pooled OR calculated using the Mantel- Haenszel method</li> <li>- Homogeneity calculated using Mantel-Haenszel Chi-square: <math>c^2=512</math> (df=23, <math>p&lt;0.01</math>)</li> </ul>

Strengths	<ul style="list-style-type: none"> <li>- Ability of the meta-analysis to increase the sample size and the statistical power</li> <li>- Two reviewers independently reviewed the retrieved articles</li> </ul>
Weaknesses	<ul style="list-style-type: none"> <li>- Combination of well-designed studies with poorly designed ones</li> <li>- Negative studies more likely not published and not identified</li> <li>- No description of observed birth defects</li> <li>- No information about ascertainment of drugs exposure, malformations definition/ascertainment, other reproductive end points</li> <li>- Possibility of confounding by indication</li> </ul>
Main outcomes	<p>The summary OR of major malformations associated with antihistamines taken during the first trimester was 0.76 (95% CI 0.6-0.9). This analysis indicates that H<sub>1</sub> blockers used mainly for morning sickness during the first trimester do not increase the teratogenic risk in humans and may be associated with a protective effect</p>