

ASPIRIN FOR ENDOMETRIAL PREPARATION IN PATIENTS UNDERGOING IVF: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ALI MOURAD¹, WAEL JAMAL^{1,3}, OBEY AL BAINI², ROLAND ANTAKI^{1,3}

DEPARTMENT OF OBSTETRICS AND GYNECOLOGY, FACULTY OF MEDICINE, UNIVERSITY OF MONTREAL,QC, CANADA. 2DEPARTMENT OF RESEARCH, GILBERT AND ROSE-MARIE CHAGOURY SCHOOL OF MEDICINE, LEBANESE AMERICAN UNIVERSITY, BEIRUT, LEBANON. 3 CLINIQUE OVO (OVO FERTILITÉ), MONTRÉAL, QC, CANADA.

INTRODUCTION

The effect of aspirin on the endometrium seems to be favorable, as demonstrated by significantly decreasing the resistance of endometrial and uterine artery blood flow in patients with recurrent pregnancy loss. However, aspirin seems to have a possible negative effect on oocyte and embryo quality by decreasing the oocyte maturation rate and increasing the number of poor quality embryos. Hence, there is a need to evaluate the possible benefit of using aspirin exclusively for endometrial preparation, eliminating its effect at the level of oocyte/embryo by analyzing reports using this medication for recipients of oocyte donation, for frozen embryo transfer (FET), and in fresh transfer in stimulated IVF cycles starting aspirin after oocyte retrieval.

OBJECTIVE

To investigate the role of aspirin as an adjuvant treatment for endometrial preparation on IVF success rates.

METHODS

No approval from an institutional review board was needed to conduct this study, since it is a systematic review and meta-analysis. Relevant reports published were comprehensively selected using PubMed, Medline, Embase and the Cochrane Central Register of Controlled Trials (CENTRAL) until November 15 2020. Randomized controlled trials and retrospective cohorts that used aspirin as an adjuvant treatment for endometrial preparation and reported subsequent pregnancy outcomes, were included. The study protocol was registered with PROSPERO: International Prospective Register of Systematic Reviews (CRD42020218724). The systematic review was conducted and reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

DATA EXTRACTION AND SYNTHESIS

This is a systematic review and meta-analysis including a total of seven studies, involving a total of 15,417 Women. Risk of bias assessment was based on the methodology and categories listed in the Cochrane Collaboration Handbook for the randomized controlled trials and the Newcastle-Ottawa scale for the retrospective studies. The primary outcome was live birth rate. The summary measures were reported as odds ratios with 95% confidence interval. There was a significant evidence that aspirin intake can improve the live birth rate (OR=1.52; 95% Cl=1.15–2.00). No effect of aspirin was noted on the clinical pregnancy rate (OR=1.37; 95% Cl=1.00–1.87); however, in the subgroup analysis of patients receiving oocyte donation (OR=2.53; 95% Cl=1.30–4.92) and in the sensitivity analysis (OR=1.3; 95% Cl=1.02–1.66), a significant effect in favor of aspirin was obtained. No effect of aspirin on the implantation rate (OR=1.31; 95% Cl=0.51–3.36) and the miscarriage rate (OR=0.41; 95% Cl=0.02–7.42) was detected.

CONCLUSION

These findings support a beneficial effect of aspirin on IVF success rates and mainly on live birth rate, if it is given only for endometrial preparation while excluding its effect on ovarian stimulation.

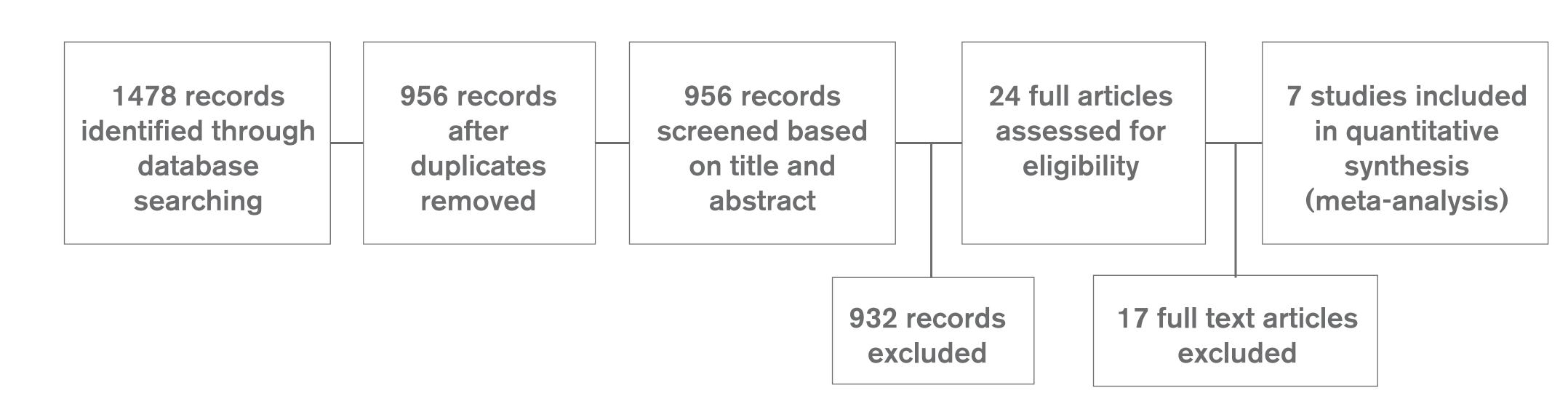


Figure 1. Forest plot of comparison: Low-dose aspirin versus placebo or no treatment, outcome:

a. clinical pregnancy rate, b. clinical pregnancy rate for recipients of oocyte donation subgroup, c. clinical pregnancy rate for FET subgroup, d. clinical pregnancy rate for Fresh ET in sIVF subgroup

Figure a. Clinical pregnancy rate

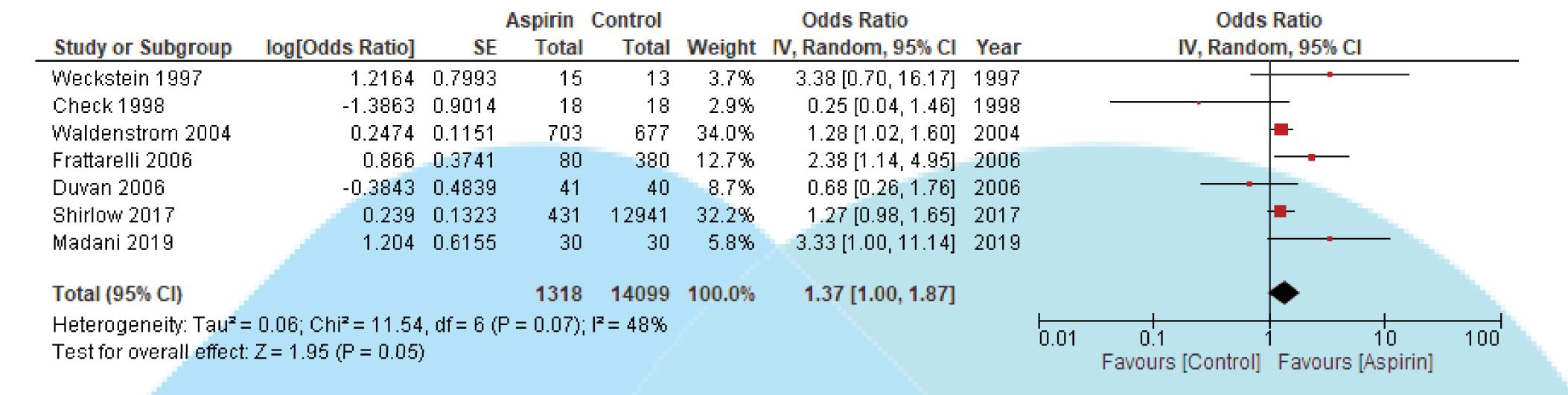


Figure b. Clinical pregnancy rate for recipients of oocyte donation subgroup

			Aspirin	Control		Odds Ratio		Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Weckstein 1997	1.2164	0.7993	15	13	18.0%	3.38 [0.70, 16.17]	1997	
Frattarelli 2006	0.866	0.3741	80	380	82.0%	2.38 [1.14, 4.95]	2006	
Total (95% CI)			95	393	100.0%	2.53 [1.30, 4.92]		
Heterogeneity: Tau² = Test for overall effect:	•		0.01 0.1 1 10 100 Favours [Control] Favours [Aspirin]					

Figure c. Clinical pregnancy rate for FET subgroup

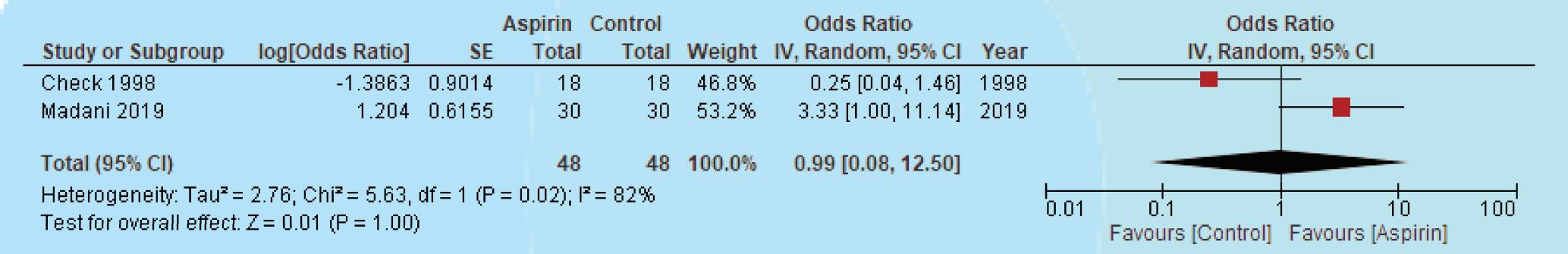


Figure d. Clinical pregnancy rate for Fresh ET in sIVF subgroup

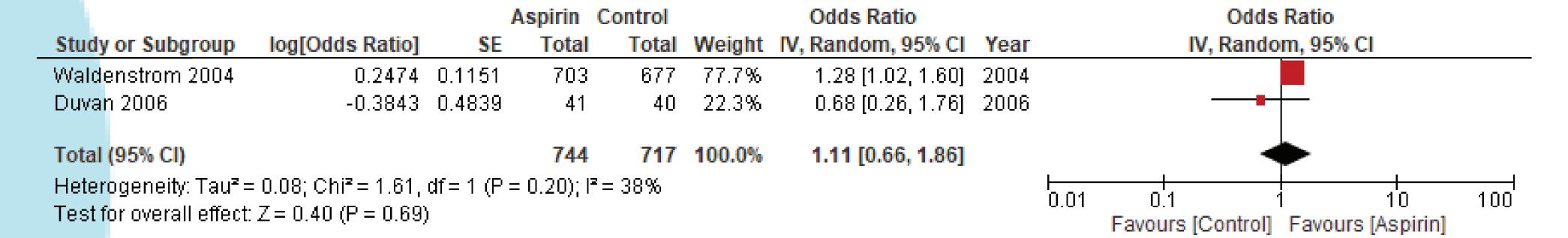


Figure 2. Forest plot of comparison: Low-dose aspirin versus placebo or no treatment, outcome: a. live birth rate, b. live birth rate for recipients of oocyte donation subgroup

Figure a. Live birth rate

			Aspirin (Control		Odds Ratio		Odds Ratio	
Study or Subgroup	log[Odds Ratio]		Total		Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI	
Weckstein 1997	0.6774	0.7931	15	13	3.0%	1.97 [0.42, 9.32]	1997		
Waldenstrom 2004	0.2115	0.1244	703	677	41.2%	1.24 [0.97, 1.58]	2004		
Frattarelli 2006	0.6048	0.2836	80	380	17.7%	1.83 [1.05, 3.19]	2006		
Shirlow 2017	0.392	0.1587	431	12941	34.4%	1.48 [1.08, 2.02]	2017	-	
Madani 2019	1.7918	0.7136	30	30	3.7%	6.00 [1.48, 24.30]	2019	•	
Total (95% CI)			1259	14041	100.0%	1.52 [1.15, 2.00]		•	
Heterogeneity: Tau ² = 0.03; Chi ² = 6.36, df = 4 (P = 0.17); $I^2 = 37\%$									
Test for overall effect:	Z = 2.93 (P = 0.003)			0.0	1 0.1 1 10 100 Favours [control] Favours [Aspirin]			

Figure b. Live birth rate for recipients of oocyte donation subgroup

		Aspirin Control			Odds Ratio				Odds Ratio					
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	Year	r IV, Random, 95% CI						
Weckstein 1997	0.6774	0.7931	15	13	11.3%	1.97 [0.42, 9.32]	1997		-					
Frattarelli 2006	0.6048	0.2836	80	380	88.7%	1.83 [1.05, 3.19]	2006							
Total (95% CI)			95	393	100.0%	1.85 [1.09, 3.12]				•				
Heterogeneity: Tau² = Test for overall effect:		0.01 Fav	0.1 ours [experime	ntal] Favoui	10 s [control]	100								