

Table 2. Included articles

Author Year, Country	Study design	Study duration	Study Groups; Intervention vs. control	Patients (n)	Mean age	Outcome
Badawy, 2008, Egypt	RCT	2003.02- 2006.01	LMWH vs. Placebo	340	27.4	Live birth
Christiansen, 1994, Denmark	Double-blind placebo-controlled trial	1987.10- not reported	Paternal immunisation vs. Placebo	66	29.6	Live birth Complications
Christiansen, 2015, Denmark	Double-blind placebo-controlled trial	2008.08- 2014.04	IvIg vs. Placebo	82	34.3	Live birth Complications
Coomarasamy, 2015, UK	Double-blind, placebo-controlled, randomised trial	2010.06- 2013.10	400 mg x 2 vaginal progesterone vs. Placebo	836	32.7	Live birth
Dolitzky, 2006, Israel	Randomised cohort study	2001-2004	LMWH vs ASA	104	30.0	Live birth, Ongoing pregnancy
El-Zibdeh, 2005, Jordan	RCT	1994.01- 2000.12	Dydrogesteron vs. hCG vs. None	180	26.0	Live birth Complications
Elmahashi 2014, Lybia	Randomised cohort study	2009.01- 2010.12	ASA/LMWH vs. ASA	150	27.3 vs. 26.5	Live birth Complications
Fawzy, 2008, Egypt	Single-blind randomised placebo- controlled trial	2004.01- 2007.05	LMWH vs. Prednisolon/ASA/Progesteron vs Placebo	160	29.1	Live birth Complications
Gatenby, 1993, Australia	RCT	Not reported	Paternal immunisation Placebo	41	32.7	Live birth
The German RSA/IVIG group, 1994, Germany	Double-blinded, randomised, placebo-controlled trial	1989.12- 1991.03	IvIg vs. Placebo	65	28.5	Live birth Complications
Illeny, 1994, Italy	Double-blinded, randomised, placebo-controlled trial	1988.06- 1991.03	Immunotherapy vs. None	44	26 <34 18 >34	Live birth Complications
Jablonowska, 1999, Sweden	Double-blind placebo-controlled trial	1993.11- 1997.04	IvIg Placebo	41	31.8	Live birth Complications
Kumar, 2014, India	RCT	2010.05- 2013.04	Dydrogesterone vs. Placebo vs.	440	25.2	Live birth, Ongoing

			No treatment			pregnancy
Perino, 1997, Italy	Double-blind RCT	1992.01- 1995.07	IvIg Placebo	46	29.6	Live birth Complications
Pandey, 2004, India	Double-blind RCT	Not reported	Paternal immunisation vs. Autologous immunisation vs. Unrelated male lymphocytes vs.Saline	124	26.6	Live birth Complications
Stephenson, 2010, USA/Canada	Multicentered, randomised, double- blinded placebo-controlled trial	1999.11- 2008.02	IvIg vs. Placebo	82	35.5	Live birth Complications

Abbreviations: RCT: Randomised controlled trial, LMWH:low molecular weight heparin, ASA: Acetylsalicyl acid, IvIg: Intravenous immunoglobulin, vs.: versus

Table 3. Outcome: Live birth

Author, year, country	Design	Number of patients	Result	Directness*	Limitations*	Precision*
Acetylsalicylic acid						
Dolitzky, 2006, Israel	RCT	107 randomised N = 104 I = 50 C = 54	I = ASA, 42/50 (84%), C = LMWH (Klexane), 4/54 did not receive allocated treatment 44/54 (82%) RR 0.92 95% CI (0.58-1.46) p = 0.936	?	?	-
Low molecular weight heparin						
Fawzy, 2008, Egypt	RCT 3 arms	N = 170 I = 60 C1 = 60 C2 = 50	I = LMWH, 46/57 (81%) C1= combination of ASA/progesteron/prednisolon, 45/53 (85%) C2= undefined placebo, 24/50 (48%) p = 0.741 compared to C1 p <0.05 compared to C2	-	?	-
Badawy, 2008, Egypt	RCT Open	N = 350 I = 174 C = 176	I = LMWH (folic acid to gestational week 13), 161/170 (95%) C = (folic acid to gestational week 13), 151/170 (89%) p = 0.076	-	?	?
Elmahashi 2014, Lybia	RCT open	N = 150 I = 75 C = 75	I = ASA/LMWH 53/75 (71%) C = ASA 32/75 (42%) p = <0.001	-	?	-
Progesterone						
El-Zibdeh, 2005, Jordan	RCT	N = 180 I = 82 C1 = 50 C2 = 48	I = Dydrogesterone, 71/82 (87%) C1 = hCG 5000IU every 4 days, 41/50 (82%) C2 = No treatment, 34/48 (71%) p = 0.644 compared to C1 p = 0.049 compared to C2	?	-	-

			p = 0.287 C2 compared to C1			
Kumar, A, 2014, India	RCT	N = 540 I = 180 C1 = 180 C2 = 180	I = Dydrogesterone 20mg, 163/175 (93%) C1 = placebo tablet 10 mg lactose, 144/173 (83%) C2 = no treatment, 168/174 (97%) p = 0.004 I compared to C1 p = 0.0001 C2 compared to C1	?	+	?
Coomarasamy, 2015, UK/ the Netherlands	RCT	N = 836 I = 404 C = 432	I = Progesterone vagitorium, 262/398 (65.8%) C = 271/428 (63.3%) RR 1.04 95% CI (0.94-1.15)	?	+	+
Intravenous immunoglobulin						
Jablonowska, 1999, Sweden	RCT	N = 41 I = 22 C = 19	I = IvIg, 17/22 (77%) C = Placebo (Saline), 15/19 (79%) p = 0.803	?	?	-
Perino, 1997, Italy	RCT Double blind	N = 46 I = 22 C = 24	I = IvIg, 16/22 (73%) C = Placebo (Albumin), 19/24 (79%) p = 0.869	+	+	-
Stephenson, 2010, USA/Canada	RCT	N = 47 I = 23 C = 24	I = IvIg, 16/23 (70%) C = Placebo (Saline), 15/24 (63%) p = 0.760	+	+	-
The German RSA/IVIG Group, 1994, Germany	RCT Double blind	N= 64 I= 33 C= 31	I= IvIg, 20/27 (74%) C= Placebo (Albumin), 21/30 (70%) p = 0.963	+	+	-
Christiansen, 2015, Denmark	RCT Double blind	N = 171 I = 42 C = 40	I = IvIg, 22/42 (55%) C = Placebo (albumin), 19/40 (48%) p = 0.67	+	?	?

Leucocyte immunisation						
Christiansen, 1994, Denmark	RCT	75 randomised N = 66 I= 43 C= 23	I = Paternal immunisation, 29/43 (67%) C = Autolog immunisation, 10/23 (43%) p = 0.003	+	?	-
Gatenby, 1993, Australia	RCT	N = 41 I = 19 C= 19	I = Paternal immunisation, 13/19 (68%) C = Autolog immunisation, 9/19 (47%) p = 0.1	-	?	-
Illeni, 1994, Italy	RCT	N= 44 I= 16 C= 14	I = Paternal immunisation, 10/16 (63%) C = Expectant management, 11/14 (79%) p = 0.576	+	?	-
Pandey, 2004, India	RCT Double blind	N = 110 I = 32 C1 = 28 C2 = 31 C3 = 19	I = Paternal immunisation, 21/25 (84%) C1 = Autolog immunisation, 4/12 (33%) C2 = Unrelated male lymphocytes, 6/19 (32%) C3 = Saline C1 p =0.007 C2 p =0.001 C3 p =0.007	?	?	-

Abbreviations

RCT: Randomised controlled trial, LMWH:low molecular weight heparin, ASA: Acetylsalicyl acid, IvIg: Intravenous immunoglobulin,

N: number included, I: intervention, C: control, p: p-value

*(Atkins et al.,SBU)

Table 4. Outcome: Complications

Author, year, country	Design	Number of patients	Result	Comments
Acetylsalicylic acid				
Dolitzky, 2006, Israel	RCT	N = 107 I = 50 C = 54	I = ASA Complications: anomaly 1, neonatal complications 2, preterm birth 5, preeclampsia 3 C = LMWH Complications: anomaly 1, IUGR 1, preterm birth 5	Surprisingly few side effects.
Low molecular weight heparin				
Fawzy, 2008, Egypt	RCT	N = 170 I = 57 C1 = 53 C2 = 50	I = LMWH Complications: preterm birth 1, IUGR 1, bleeding 1, thrombocytopenia 1 C1 = Combination of ASA/progesterone/prednisolone Complications: preterm birth 1, IUGR 1, anomaly 1, bleeding 1, gestational diabetes 1. C2 = Placebo Complications: anomalies 2, preterm birth 2, IUGR 2, IUFD 1, preeclampsia 1	Side effects on mother as hemorrhage and allergic reaction were a second outcome. Neonatal side effects registered as congenital anomalies.
Badawy, 2008, Egypt	RCT open	N = 350 I = 174 C = 176	I = LMWH Complications: bleeding 37, bleeding at delivery 10, thrombocytopenia 6, local reaction 51, 5DVT 4, congenital abnormality 2 C= Placebo (folic acid tablets) Complications: bleeding in first trimester 23, bleeding at delivery 9, DVT 4	No significant difference in side effects between the two groups. Not blinded.
Elmahashi 2014, Lybia	RCT open	N = 150 I = 75 C = 75	I = ASA/LMWH Complications: thromboembolism 0, thrombocytopenia 0, mild local reaction. C = ASA	-

			Complications: thromboembolia 0.	
Progesterone				
El-Zibdeh, 2005, Jordan	RCT	N = 180 I = 82 C1 = 50 C2 = 48	<p>I = Dydrogesterone Obstetric complications 19/82=antepartum hemorrhage 4, preterm birth 5, IUGR 3, preeclampsia 5, congenital malformations 2. Delivery complications 7/82 = fetal distress 3, post partum hemorrhage 2, perinatal death 2. Urinary tract infection 2. C1 = hCG Obstetric complications 13/50=antepartum hemorrhage 4, preterm birth 4, IUGR 2, preeclampsia 2, congenital malformations 1. Delivery complications 5/41 = fetal distress 2, post partum hemorrhage 1, perinatal death 2. C2 = No treatment Obstetric complications 12/48= antepartum hemorrhage 3, preterm birth 3, IUGR 3, preeclampsia 2, congenital malformations 1. Delivery complications 4/34 = fetal distress 2, post partum hemorrhage 1, perinatal death 1. Urinary tract infection 1.</p>	The authors did not report any adverse effects during treatment with dydrogesterone or hCG.
Intravenous immunoglobulin				
Jablonowska, 1999, Sweden	RCT	N = 41 I = 22 C = 19	<p>I = IvIg 7/22 Complications: preterm birth 1, rash, itching, fever, flush, bleeding total 6 C = Placebo = NaCl 2/19 Complications: itching and bleeding 2</p>	The majority of complications reported is maternal, possibly associated with IVIG.
Stephenson, 2010, USA/Canada	RCT	N = 47 I = 23 C = 24	<p>I = IvIg 12/23 Complications: preterm 1, biochemical miscarriage 3, anembryonic 2,</p>	Stopped due to slow recruitment.

			yolk sac 1, fetal miscarriages 1, rash 3, headache 1 C= placebo= NaCl 16/24 Complications: IUGR 1, Down syndrome 1, Klinefelter 1, preterm 2, biochemical miscarriage 4, anembryonic 4, fetal miscarriages 1, gastrointestinal 2	
The German RSA/IVIG Group, 1994, Germany	RCT Double blind	N = 64 I = 31 C = 34	I = IvIg 3/31 Complications: headache, nausea and temperature rise 1, preterm 1, preeclampsia 1 C= Placebo= Albumin 5% Complications: headache, nausea and temperature rise 5, preterm 1	Study stopped at interim analysis since it was estimated that the study could not meet the criteria for statistical significance based on the power calculation.
Perino, 1997, Italy	RCT Double blind	N = 46 I = 22 C = 24	I = IvIg 20/22 Complications: rash 1, erythema 1, preterm 1, IUGR 1, mola 1, radius ameli 1, miscarriage < v 12 5, miscarriage > v.15 1. C = Placebo/Albumin 5%7/24 (29%) Complications: miscarriage < v12 4, preterm gw 24 1, oligohydramnion 1, preeclampsia 1.	
Christiansen, 2015, Denmark	RCT Double blind	N = 171 I = 42 C = 40	I = IvIg 22/42 Complications: skinrash17/42, headache 22/42 C = placebo = Albumin19/40 Complications: skinrash 8/40, headache 12/40 p = 0.04 I compared to C	
Leucocyte immunisation				
Pandey, 2004, India	RCT	N = 110 I = 32 C1 = 28 C2 = 31 C3 = 19 C4 = 14	I = Immunisation paternal No adverse side effects after 1,5 years follow up C1= Immunisation autolog No adverse side effects after 1,5 years follow up	Only those who gave birth were followed up for adverse events.

Christiansen, 1994, Denmark	RCT	N = 66 I = 43 C = 23	I = Immunisation paternal Complications: shunt 1, sepsis with psychomotor retardation 1, diaphragma hemisphere 1, C = Immunisation autologous Complications: inguinal hernia 2, intestinal invagination 1, pyloric stenosis 1, Salmonella infection 1, epilepsia and psychomotoric retardation 1	Maternal complications not reported. Complications were evaluated as not related to the given treatment.
Illeni M.T, 1994, Italy	RCT	N = 44 I = 16 C = 14	I = Paternal immunisation, 10/16 C = Expectant management, 11/14 p = 0.576 No complications were noted	

Abbreviations

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N: number included, I: intervention, C: control, p: p-value