Efficacy and safety of direct oral anticoagulants during pregnancy

a systematic literature review

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the INTRODUCTION

1 ANTICOAGULATION

Anticoagulation with VKA can cause malformations

Anticoagulation with LMWH may be less safe for the mother

2 DOACS

Direct oral anticoagulants (DOACs) are increasingly used for anticoagulation or prevention of thromboembolic events in conditions that may co-occur with pregnancy

3 Efficacy and Safety

Evidence regarding efficacy and safety during pregnancy is scarce.

the Methods

SEARCH

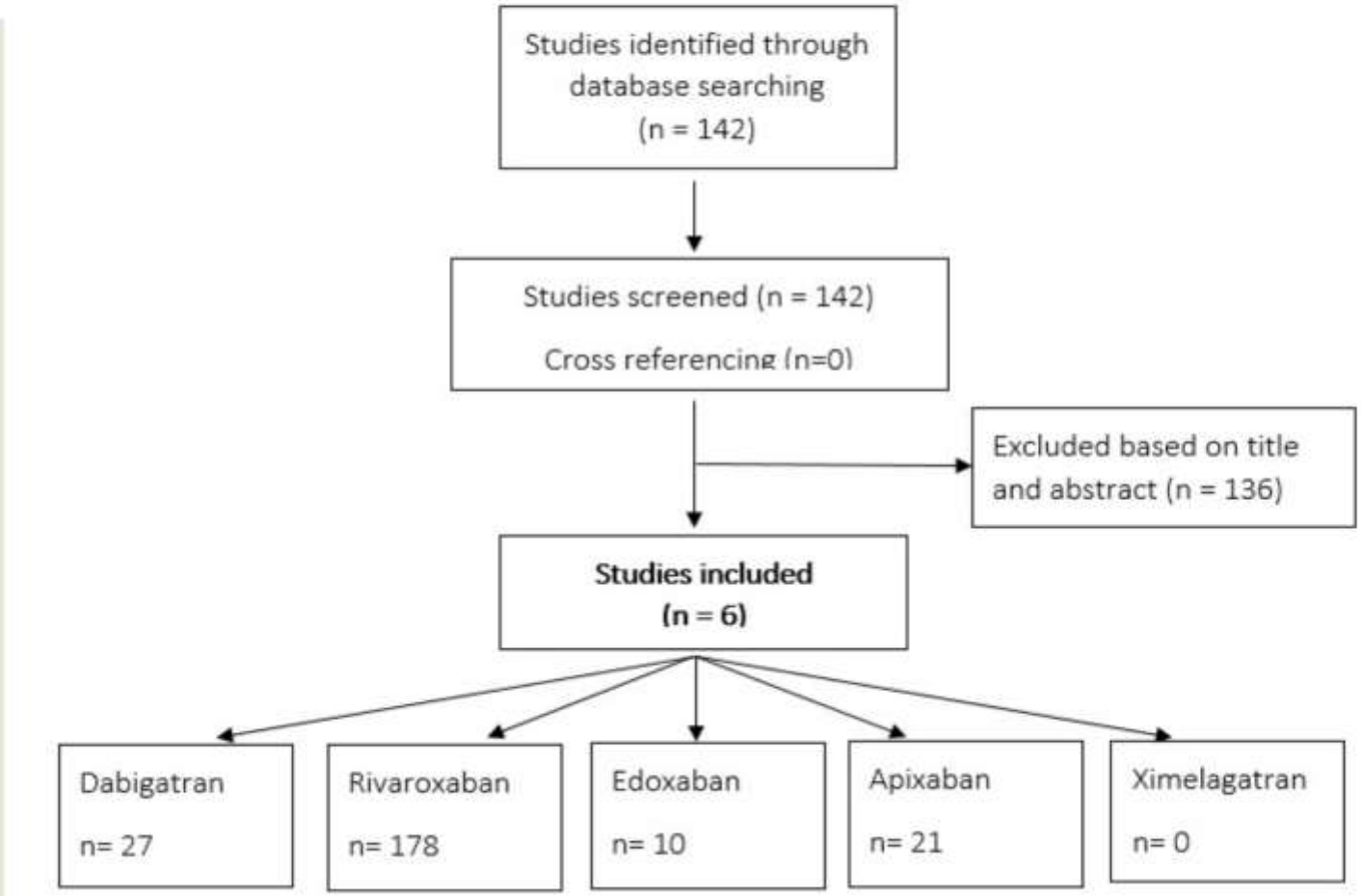
MedLine public database

All studies describing the use of DOACs during pregnancy

Published up to 04-07-2017

the

Results


Studies identified through database searching (n = 142)
Studies screened (n = 142)
Cross referencing (n=0)
Excluded based on title and abstract (n = 136)
Studies included (n = 6)
Dabigatran n= 27
Rivaroxaban n= 178
Edoxaban n= 10
Apixaban n= 21
Ximelagatran n= 0

the

Results

236 cases

Rivaroxaban = most reported (n=178).

DOACs were mostly used for DVT (n=91).

DOACs were discontinued <2 months in 84%

Maximum duration of use = 26 wks

Pregnancy outcome data were available for 140 pregnancies

Occurence/absence of thrombotic/bleeding only reported for 42 pregnancies (18%): PE (n=1), DVT (n=1, 5%), bleeding (n=3, 8%)

the

Results

	All DOACs	Rivaroxaban	Dabigatran	Apixaban	Edoxaban
Pregnancies with sufficient outcome data (n,% of all pregnancies)	140 (59%)	105 (59%)	13(48%)	12 (57%)	10 (100%)
Cases with known duration of exposure (n, %)	73 (52%)	*	*	*	*
Maximum duration of exposure	1 month (n=22) 2 months (n=39) 3 months (n=2) 4 months (n=3) 5 months (n=3) 6 months (n=1)	* 1 week (n=1) 10 weeks (n=36) 15 weeks (n=1) 25 weeks (n=1) 26 weeks (n=1) Post-partum (n=1)	* 10 weeks (n=1)	*	*
Elective abortion (n,%)	39 (28%)	26 (25%)	7 (54%)	3 (25%)	3 (30%)
Ongoing pregnancies (n, %)	101 (72%)	79 (75%)	6 (46%)	9 (75%)	7 (70%)
Missing offspring outcome (n,%) **	1 (1%)	0	1 (17%)	0	0
Live birth (n,%) **	69 (68%)	55 (69%)	3 (50%)	5 (56%)	6 (86%)
Miscarriage (n,%) **	31 (31%)	24 (30%)	2 (33%)	4 (44%)	1 (14%)
Perinatal death (n,%) **	0	0	0	0	0

the

Results

Study	Trimester of Rivaroxaban use	Pregnancy outcome	Abnormality	WHO-UMC causality category
Beyer-Westendorf et al.	1st	Live birth	Renal pelvis dilatation Facial dimorphism	Unlikely Possible
	1st	Live birth	Mild hip dysplasia	Possible
	1st	Live birth	Septum pellucid cyst	Unlikely
	1st	Miscarriage	Anhydramnios	Unlikely
	1st	Miscarriage	Intra-uterine growth retardation	Possible
Hoeltzenbein et al. Beyer-Westendorf et al.	1st	Elective termination	Complex foetal heart defect	Unlikely
	1st	Miscarriage	Abnormal limbs ('crumpled')	Possible

the

Discussion

Outcomes of pregnancies were only available in 59%

The data suggest an increased miscarriage rate and raise concern about a possible association with foetal anomalies

Thrombotic and bleeding complications were highly underreported, no firm conclusions about their incidence can be made

the

Discussion

DOAC*	FDA pregnancy category	FDA and EMA information on embryo-foetal toxicity in animal studies
Rivaroxaban	C	At clinically relevant plasma concentrations. – *post-implantation loss* – *retarded/progressed ossification* – hepatic multiple light coloured spots – increased incidence of common malformations – placental changes At 4x human exposure dose: – *increased resorptions* – decreased number of live foetuses – *decreased foetal body weight*

the Conclusion

Safety and efficacy of the use of DOACs during pregnancy is not supported by current literature.

The limited available evidence raises concern regarding embryo-foetal safety

This justifies avoidance of DOACs in pregnant women

Switch to LMWH or, depending on indication, dosage, and stage of pregnancy, VKA

Thank You

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