10.7861/clinmed.20-2-s98

A systematic review of the safety of non-tumour necrosis factor inhibitor and targeted synthetic drugs in rheumatic disease in pregnancy

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Table 1. Summary of maternal exposure to non-tumour necrosis factor inhibitor and targeted synthetic disease-modifying anti-rheumatic drugs

Drug	Studies	Pregnancy exposures	Live births	Spontaneous miscarriages	Congenital malformations	Breastfeeding exposures	Adverse effect of drug
Abatacept	3ct, 1cs	151	87	40	4	ns	No
Anakinra	4cs, 2cr, 2ct	46	43	ns	1	13	No
Belimumab	4cr, 2rv	250	104	58	12	ns	No
Canakinumab	1cr, 1ct	9	8	1	ns	4	No
Ixekizumab	1ct	3	ns	ns	ns	ns	ns
Rituximab	22cr, 9cs, 4ct	198	131	36	3	2	No
Secukinumab	1cr	1	0	1	ns	ns	ns
Tocilizumab	2cs, 4ct	361	220	82	59	4	No
Tofacitinib	1cs	41	26	7	1	0	No
Ustekinumab	7cr, 7cs, 2ct	29	26	4	0	ns	No

cc = case–control; cr = case report; cs = case series; ct = cohort; ns = not stated; rv = review.

Background

Despite increasing evidence to support safe use of tumour necrosis factor inhibitor (TNFi) drugs in pregnancy, there remains a paucity of evidence regarding non-TNFi and targeted synthetic disease-modifying anti-rheumatic drugs (tsDMARDs) in pregnancy. Therefore, we conducted a systematic review to summarise use of these drugs in pregnancy and breastfeeding.

Method

We performed a systematic search of databases including EMBASE, PubMed (MEDLINE) and Cochrane up to December 2018, using keywords including commonly prescribed non-TNFi and tsDMARDs, pregnancy, conception/pre-conception, lactation/breastfeeding, childhood and vaccination/infection.

Results

From an initial screen of 700 papers, 92 full-text papers were included in the final analysis. A summary of findings from known outcomes of pregnancy and breastfeeding exposures, as well as long-term follow-up of infants where available, is shown in Table 1. Overall, these data do not identify an increased risk of adverse pregnancy outcomes with these drugs in this population of patients.

Conclusion

These findings do not suggest an increased risk of non-TNFi and tsDMARDs in pregnancy. However, given that the total number of exposures remains limited, these drugs should only be considered in pregnancy if the benefit of maintaining disease control in the mother justifies any potential risk to the fetus. This body of evidence will be useful when counselling women about the potential risks of using these types of drugs during pregnancy and the breastfeeding period, as well as following accidental exposure to drugs at conception. ■

Conflicts of interest

None declared.

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