The Effect Of Maternal Antimalarial Intake During Pregnancy On The Risk Of Neonatal Lupus

Abstract: #2832

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Description:

Background/Purpose: Neonatal Lupus (NLE) results from passive transfer of anti-Ro and/or anti-La antibodies to the fetus during gestation. It has been suggested that prenatal exposure to hydroxychloroquine (HCQ) reduces the risk of cardiac NLE through disruption of toll-like receptors signalling. The effect of HCQ on the risk of extra-cardiac NLE has not been specifically studied. The aim of this study was to assess if maternal intake of HCQ or chloroquine throughout pregnancy reduces the risk of NLE in the offspring. We hypothesized that these drugs would confer protection against NLE.

Methods: A case-control study was performed on a large single-center cohort of NLE and unaffected children, on whom prospective data has been collected since 1984. Inclusion criteria were: (1) first child born from a mother positive for anti-Ro and/or anti-La antibodies with a diagnosis of either cutaneous lupus, systemic lupus erythematosus, Sjogren's syndrome, dermatomyositis or rheumatoid arthritis and, (2) assessment of the child in the NLE clinic at least once in his first 6 months of life. Descriptive statistics and logistic regressions were performed.

Results: The study population consisted of 220 children, of whom 62 were exposed to HCQ or chloroquine throughout gestation (Table). NLE was diagnosed in 98 patients; 12 had cardiac NLE (11 congenital heart block and 1 cardiomyopathy). Neutropenia (n=41) was the most frequent extra-cardiac NLE feature followed by hepatitis (n=36), skin involvement (n=32), thrombocytopenia (n=4) and extraventricular obstructive hydrocephalus (n=4). One hundred and twelve children did not develop NLE. Ten children were classified as having no cardiac NLE involvement but could not be diagnosed as true unaffected children as one or more blood test components were missing. No statistically significant protective effect of HCQ or chloroquine exposure was found on the risk of NLE (OR 0.79; p=0.45). Similar results were found when extra-cardiac NLE cases were analyzed separately (OR 0.85; p=0.60). Only 1 of 62 children exposed to HCQ or chloroquine developed cardiac-NLE compared to 11 of 158 unexposed children (OR 0.22; p=0.19). On multivariable logistic regression, anti-La titer ≥100 U/mL was the only significant predictor of NLE (OR 2.23; p=0.03). The mother's age, diagnosis, intake of azathioprine, anti-Ro titers ≥50 U/mL and the child's gender did not significantly impact on the risk of NLE.

Conclusion: In the largest single-center case-control study of children born to anti-Ro and/or anti-La antibody positive women diagnosed with a connective tissue disease, HCQ or chloroquine exposure throughout gestation did not result in a significantly lower risk of NLE. High titers of anti-La antibodies in the mother were associated with an increased risk of NLE.

Table. Characteristics of mothers of NLE cases and unaffected children

	NLE (n=98)	Unaffected children (n=112)	p value
Mothers			
Age at birth of child	31.7 ± 4.8	32.2 ± 4.6	0.44
Diagnosis			0.13
SLE or cutaneous lupus	71 (72)	93 (83)	
Sjogren's syndrome	20 (21)	12 (11)	
Others	7 (7)	7 (6)	
Anti-Ro ≥50 U/mL*	62 (67)	63 (66)	0.96
Anti-La ≥100 U/mL§	26 (28)	14 (14)	0.01
On HCQ or chloroquine	26 (27)	35 (31)	0.45
On azathioprine	5 (5)	13 (12)	0.09
On prednisone	28 (29)	40 (36)	0.32
Older child with CHB	1 (1)	2 (2)	1.00

Mean±SD; n (%)

*n=93 NLE and 95 unaffected children; §n=94 NLE and 103 unaffected children