

LONG TERM OUTCOMES OF CHILDREN BORN TO MOTHERS WITH SLE EXPOSED TO AZATHIOPRINE IN PREGNANCY

THU0013

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Introduction

• Certain immunosuppressive agents used in pregnancy in SLE to prevent flare, to ensure optimum outcome mother & child
• Little published literature regarding long term outcomes of children
• Previously published small studies have suggested a link between:

- Azathioprine and Increased use of Special Educational Services¹
- Anti-cardiolipin antibodies & developmental delay²
- Hydroxychloroquine +/- prednisolone and a reduction in congenital heart block

Aims

Does exposure to Azathioprine during pregnancy and/or lactation increase the risk of:

1. Congenital anomalies
2. Serious infections
3. Developmental delay

Methods

• Cross sectional, Retrospective study
• A standard questionnaire developed for multi-center study

• Inclusion criteria:
• Children under 17
• Born to women with a pregnancy AFTER fulfillment ≥ 4 ACR criteria for SLE

Results

200 women, 287 children

AZA during pregnancy &/or Breastfeeding

89 children
66 women

NO AZA during pregnancy &/or Breastfeeding

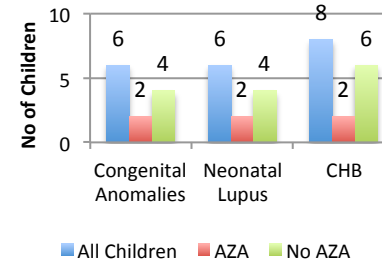
198 children
149 women

| Maternal Characteristics | All N=287 | AZA N=89 | No AZA N=198 | p value |
|---|-----------|----------|--------------|---------|
| Ro \pm La antibodies | 37% | 44% | 41% | 0.55 |
| Lupus anticoagulant and/or Anticardiolipin IgG and/or IgM | 43% | 60% | 49% | 0.03 |
| Lupus anticoagulant | 32% | 43% | 34% | 0.21 |
| Anticardiolipin IgG and/or IgM | 23% | 35% | 23% | 0.68 |
| Renal dx ever | 23% | 57% | 16% | <0.0001 |
| Hypertension prior to pregnancy | 17% | 16% | 18% | 0.85 |
| Pre-eclampsia | 10% | 11% | 8% | 0.16 |

| Maternal Demographics | All N=287 | AZA n=89 | No AZA N=198 | p value |
|------------------------------------|-----------------|-----------------|-----------------|---------|
| Maternal Age, yrs (sd) | 32 (± 6) | 32 (± 7) | 31 (± 9) | 0.36 |
| Maternal Disease Duration yrs (sd) | 7.5 (± 6) | 6.5 (± 5) | 8.6 (± 8) | 0.0078 |
| Maternal steroids | 59% | 87% | 47% | <0.0001 |
| Maternal Hydroxychloroquine | 53% | 49% | 46% | 0.69 |
| Maternal Aspirin | 70% | 83% | 66% | 0.0051 |
| Maternal Heparin | 24% | 32% | 22% | 0.84 |

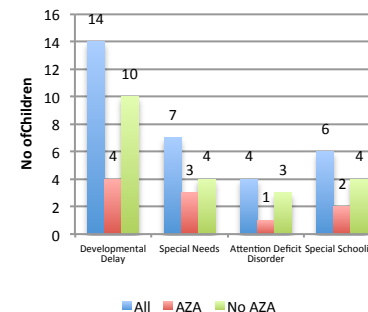
| Neonatal Outcomes | All Women N=287 | AZA N=89 | No AZA N=198 |
|-----------------------------|-----------------------------|----------------------------|----------------------------|
| Gestational age at delivery | median=38 range 27-42 | median=36 range 27-42 | median=38 range 25-42 |
| Birth weight | median=2.88kg range 0.6-4.7 | median=2.8kg range 0.6-4.4 | median=3.1kg range 0.7-4.7 |

Obstetric Outcomes



| Hospital Visits | All children N= 287 | AZA N=89 | No AZA N=198 | p Value |
|--|---------------------|----------|--------------|---------|
| Outpatient visit | 17% | 17% | 18% | 0.89 |
| Outpatient visit related to infection | 1.8% | 4% | 1% | 0.33 |
| Hospital admissions | 26% | 35% | 23% | 0.07 |
| Infection requiring hospital admission | 18% | 28% | 14% | 0.005 |

Developmental Problems



Statistical Analysis

Multifactor logistic regression used to investigate relationship between maternal AZA use and infection requiring hospital admission

NO longer significantly associated (OR 1.73(0.85-3.5), $p=0.13$, when adjusted for: Maternal renal disease, Maternal prednisolone)

However, due to the lower sample size its power was <80%.

Conclusions

Does exposure to AZATHIOPRINE in pregnancy and/or lactation increase congenital anomalies?

• No

Does exposure to AZATHIOPRINE in pregnancy and/or lactation increase the risk of serious infections?

• No
• Using multivariate analysis

Does exposure to AZATHIOPRINE in pregnancy and/or lactation increase the risk of developmental delays?

• No

Summary

This UK cross sectional survey highlights that azathioprine is compatible with pregnancy and should be continued during pregnancy & breast feeding

References

1. Akhtar S et al. Maternal Anticardiolipin Affects Childhood development. Arthritis & Rheumatism. 2008;5:759,443
2. Marder Wiet al. In utero azathioprine exposure and increased utilization of special educational services in children born to mothers with SLE. Arthritis & Rheumatism. 2012;8:288