Meta-analysis of Early-Term Induction Studies involving AMOR-IPAT: evidence of the relative safety of risk-based early term labor induction.

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ABSTRACT

Objective: To combine the results of studies involving risk-based early term preventive labor induction (AMOR-IPAT) so as to assess the relative safety of this intervention. **Findings:** Over the past six years the AMOR-IPAT Research Program has produced seven publications. Each publication reported significant improvements in overall birth health following the regular use of risk-based preventive labor induction during the term period of pregnancy. This poster focuses on the parturients of these studies who were preventively induced in the 38th week of pregnancy and compares their birth outcomes to parturients who were expectantly managed beyond 38w 6d. Women with significant risk profiles who were preventively induced in the 38th week of pregnancy were less likely to deliver by cesarean section (cesarean section: 3.9% vs. 14.7%, p=0.002), trended towards lower rates of NICU admission (3.9% vs. 8.3%, p = 0.10), and trended towards lower rates of prolonged NICU admission (0% vs. 1.7%, p=0.09). **Conclusions:** The regular use of risk-based preventive labor induction in the 38th week of pregnancy may have a positive impact on the birth health. The risk of maternal and neonatal morbidity associated with 38-week preventive labor induction in parturients with increased risk profiles has probably been over-estimated in the literature. This area of investigation deserves further study in prospective randomized format.

BACKGROUND

Previous studies have found associations between labor induction prior to 39 week 0 days of gestation and at least four adverse birth outcomes: 1) Cesarean delivery, 2) NICU admission, 3) Prolonged NICU admission, and Neonatal injury.

However, previous studies – including the recent study by Glantz - of labor induction in general, and early term labor induction in particular, may have contained significant methodological flaws including: 1) The comparison of the outcomes of deliveries occurring after indicated labor induction to the outcomes of deliveries that occur following the spontaneous onset of labor *(confounding by indication); 2)* The failure to differentiate between indicated, elective, and preventive labor induction (*selection bias);* and 3) The failure to differentiate between 36, 37 and 38 week labor induction (misclassification bias). Finally, previous studies of early-term labor induction have not addressed the issue of clinical choice: induction now vs delivery later.

In Contrast, several recent papers have suggested that, in low risk women, the quality of birth outcomes worsen as a function of increasing gestational age during the term period (38.0 - 42.0 weeks). Caughey recently reported that the rate of serious neonatal pulmonary morbidity, in low-risk pregnancy, was lowest when delivery occurred in the 38th week of gestation. Studies focusing on the potential benefit of early term *preventive* induction are lacking.

METHODS

Sub-analysis, and meta-analysis, of data from five AMOR-IPAT databases (four published and one unpublished).

Women in each database who were exposed to AMOR-IPAT and who delivered following preventive labor induction initiated before 39w 0d were identified as "exposed" subjects. "Exposed" women did not have a standard indication for induction, but rather had sufficient obstetric risk to qualify for preventive labor induction in the 38th week under the AMOR-IPAT protocol.

Women in each database who were not exposed to AMOR-IPAT and who delivered at a gestational age of 39 weeks 0 days or greater were identified as "non-exposed" subjects. "Non-exposed" women delivered following spontaneous labor, augmented labor, or indicated labor induction.

Statistical Analysis: Comparison within each study of group levels of covariates and birth outcomes using univariate techniques.

RESULTS

Data from the Annals of Family Med "Rural" Study - 2007

	IOL* (%)	Cesarean (%)	NICU (%)	L-NICU (%)	Neo Injury**
AMOR-IPAT (<39w: n=26)	100%	0%	0%	0%	3.8%
Standard Care (n=916)	21.9% *****	12.5% ***	7.3%	0.3%	4.4%

Data from the AJOG "Urban NULLIP" Study - 2009

	IOL* (%)	Cesarean (%)	NICU (%)	L-NICU (%)	Neo Injury**
AMOR-IPAT (<39w: n=23)	100%	17.4%	4.4%	0%	4.4%
Standard Care (n=293)	25.3% *****	24.9%	12.6%	6.1% ***	8.5%

Data from the AJOG "Urban MULTIP" Study - 2009

	IOL* (%)	Cesarean (%)	NICU (%)	L-NICU (%)	Neo Injury**
AMOR-IPAT (<39w: n=39)	100%	0%	7.7%	0%	7.7%
Standard Care (n=246)	17.5% *****	10.6% ***	8.1%	2.4%	5.2%

Data from the AJOG "HUP-POP" RCT Study - 2008

	IOL* (%)	Cesarean (%)	NICU (%)	L-NICU (%)	Neo Injury**
AMOR-IPAT (<39w: n=15)	100%	0%	0%	0%	0%
Standard Care (n=105)	22.9% *****	15.2%	5.7%	2.9%	2.9%

SUMMARY DATA

	IOL* (%)	Cesarean (%)	NICU (%)	L-NICU (%)	Neo Injury**
AMOR-IPAT (<39w: n=103)	100%	3.9%	3.9%	0%	4.9%
Standard Care (n=1560)	21.9% *****	14.7% *****	8.3% ***	1.7%	5.2%

* IOL: Induction of labor; ** Neo Injury: clav fx, Erb's palsy, cephalo-hematoma;
***p <0.05, ****p <0.001, *****p<0.0001

RESULTS

The association between AMOR-IPAT-based preventive labor induction prior to 39 weeks 0 days of gestation and and NICU admission reveals a R 0.47 (95% CI 0.18-1.24), p=0.11, suggesting no increased risk and the potential for decreased risk in the setting of a study with additional power. Cesarean delivery rates and complicated NICU admissions appeared to occur with decreased frequency when preventive induction was used prior to 39 week gestation.

Additional Preliminary Urban Data (2003 – 2010)

	IOL (%)	C/S (%)	NICU (%)	L-NICU (%)	Neo Injury
AMOR-IPAT (<39w: n=257)	100%	7.0%	6.0%	0%	-
Standard Care (n=470)	20.4% *****	14.3% ****	6.1%	1.7%	-

CONCLUSIONS

This preliminary study suggests that early term preventive labor induction, i.e. in women with increased risk profiles in the 38th week of pregnancy, may be beneficial. Improved outcomes include trends towards lower rates of cesarean delivery, NICU admission, long NICU admission and neonatal injury.

IMPLICATIONS / FUTURE DIRECTIONS

1. Preventive labor induction in the 38th week of gestation has not been previously studied, and existing research on early term labor induction contains significant methodological flaws.
2. Preventive labor induction in the 38th week of gestation needs to be tested in the context of an adequately powered prospective randomized trial (RCT), and such research in not only ethical but necessary.
3. If additional evidence can be found to support the possible benefit of risk-based early term labor induction, then the current restrictions on early term preventive induction should be reconsidered.