# SMFM Statement

**Society for Maternal-Fetal Medicine, with the assistance of Robert W. Silver, MD and George Saade, MD**

## Labor Induction or Augmentation and Autism Spectrum Disorders

Autism spectrum disorders (ASDs) include a range of cognitive and behavioral disturbances in childhood development. The condition has increased in frequency over the past several decades (1,2) and is now estimated to affect 1 in 88 children in the United States (3). It is a source of considerable loss of quality of life, costs to society and emotional duress for families (4).

Given the apparent increasing prevalence of the condition (in part due to increased awareness and diagnosis), considerable efforts have been undertaken to identify potential risk factors and causal pathways. Genetic factors have clearly been implicated (5). However, environmental factors have been hard to establish. Although reviews concluded that there is an excess of perinatal complications associated with ASD, it is premature to implicate any specific pregnancy complication (6,7).

A recent paper links ASDs to induced or augmented labor (8). The authors were very careful to point out the limitations of their study and to advise against changing clinical practice based on their results. Nonetheless, the study has received considerable media coverage. Consequently, some patients and physicians are concerned about the

implications of this report on labor induction and augmentation, particularly with oxytocin.

Concerns about labor induction and augmentation have the potential to translate into adverse outcomes for mothers and babies. The most obvious is a further increase in the already inflated rate of cesarean delivery. Patients may be more reluctant to receive oxytocin in cases of inadequate labor or medically indicated induction. The downsides of cesarean delivery, especially multiple cesareans, are well documented (9). Also worrisome is the possibility that patients and physicians will avoid or delay medically indicated inductions. This may lead to an increase in adverse outcomes such as stillbirth, neonatal death and hypoxic ischemic encephalopathy.

The study by Gregory et al, has to be viewed within the context of its many limitations, given its study design. This is primarily an observational study relying on birth and administrative records. Consequently, it was impossible to adequately assess and control for confounding variables, and such a study design cannot prove causality. Most women receiving oxytocin have medical or obstetric complications or abnormal labor, many of which have been associated with ASDs. These are difficult to account for under optimal circumstances, and are extremely hard to assess given the limitations of an administrative database that was not designed to address this question. Ascertainment of the exposure (induction/augmentation) and outcome (ASD) variables is also limited when using such a database. Also, an argument could be made that the optimal control group should have been ongoing pregnancies rather than pregnancies that did not require induction or augmentation (i.e. spontaneous labor). Providers and patients are faced with a choice to use oxytocin or not when confronted with a need for induction or

augmentation. If they choose to not undergo induction, they instead choose expectant management. In many of these cases they will end up with an induction anyway, often under worse circumstances. The data also are limited by a lack of depth and obstetric detail, such as the use of the term "fetal distress." Finally, there are well known inaccuracies in administrative databases (10).

Of equal importance, other studies have found no association between oxytocin use, labor induction and/or augmentation, and ASDs (6,11,12). The inconsistent results among studies make a true and clinically important effect less likely. Given that it is the most recent publication, the Gregory et al study carries a disproportionate amount of weight in the public consciousness. However, it should be viewed within the overall available evidence.

The relatively small odds ratios for ASDs in association with induction or augmentation also are noteworthy. These were typically in the range of 1.25, with barely significant confidence intervals. Statistical significance was achieved in large part due to large numbers of patients in the database. Such results may be statistically significant but clinically unimportant.

ASDs constitute a devastating group of conditions that undeniably warrant better research into causes, prevention and treatment. Potential risk factors and causes should be investigated, including exposure to oxytocin with labor augmentation and induction. However, at present the link between oxytocin, induction or augmentation of labor and ASDs remains unclear. As stated by Gregory et al, clinical care and the use of oxytocin in labor management should not be changed in light of their findings. While this study certainly adds to the academic debate, it should not change care or lead to avoidance of

labor augmentation and induction; these important obstetric interventions should continue to be used for the usual clinical indications.

SMFM has reviewed the evidence and feels that the recent publication is far from definitive, uses methodology that cannot prove causality and does not indicate a causal relationship between labor induction/augmentation and ASD. Therefore, this single study should not be viewed as an incentive or provide justification for any change in practice regarding labor induction and management.

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