Forensic analysis of adverse drug events and litigation claims in ob/gyn

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OBJECTIVES

- Review selected cases involving obstetric patients wherein a claim of injury was made related to the use of a drug
- Review the facts of the cases, relevant treatment details
- Liability and damage claims
- Explain the pharmacologic issues
  - Causation? No Causation?
  - Provide case resolution information (WHAT HAPPENED?)

PROBLEM

- Injury is a risk/complication of any drug therapy
- Injury does not = malpractice or negligence
- Drug injury 2nd most common reason for medical malpractice suits,
- OB patients (and fetus/newborn) are at greater risk of drugs given during pregnancy and the perinatal period.

Case 1 fatal electrolyte disturbance in hyperemesis gravidarum

- DIAGNOSES AS CONSTIPATED – NO BOWEL MOVEMENT IN 7 DAYS (NO EATING IN 7 DAYS EITHER)
- SEEN IN OB OFFICE; N/V X 3 WEEKS, 14 LB WT LOSS, CLINICAL DEHYDRATION
- SENT TO HOSPITAL; LABS 'STAT'; Soap Suds Enema (SSE)ordered and administered
- K 1.8; Na 121; 20 mEq KCl in D5NS at 50ml/hour ordered; patient admitted to L&D
- Second lab K 1.5
- Cardiac Arrest 60" after admission; unable to resuscitate

TOXICOLOGY ISSUES

- CRITICAL K & Na LEVELS REQUIRED IMMEDIATE ATTENTION WITH CAREFUL AND AGGRESSIVE REPLENISHMENT IN AN ICU
- SLOW ‘CLINICAL’ ELECTROLYTE REPLENSIHMENT INSUFFICIENT FOR TREATMENT OF ACUTE/CHRONIC SEVERE DEFICIENCY
- SEVERE HYPOKALEMIA - SIGNIFICANT RISK FOR FATAL ARRHYTHMIA
- SEVERE HYPONATREMIA - SIGNIFICANT RISK FOR SEIZURES
- TOO LITTLE, TO LATE, TO SLOW

LEGAL RESOLUTION

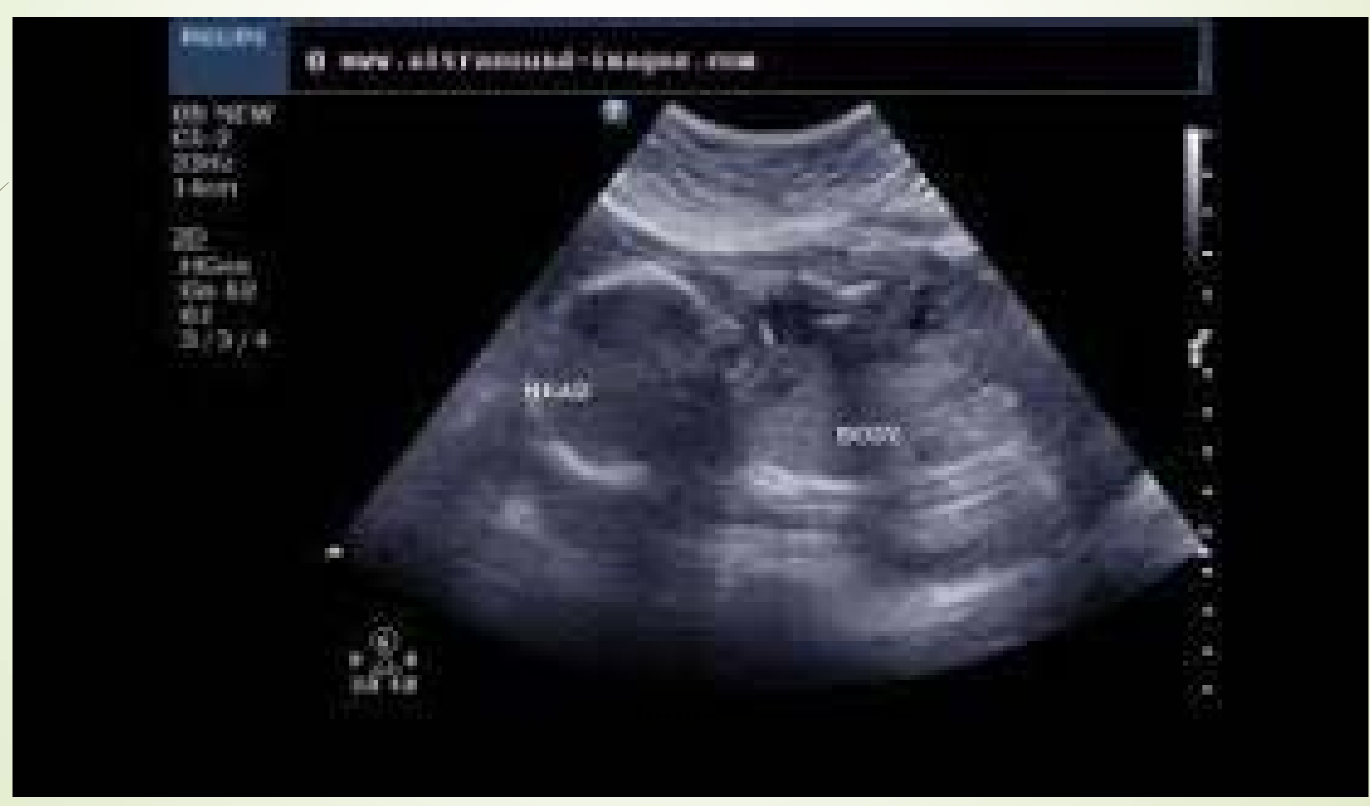
- OBGYN and HOSPITAL SUED FOR MALPRACTICE;
- INSUFFICIENT CLINICAL MONITORING AND CARE
- INADEQUATE URGENCY AND TREATMENT AT HOSPITAL
- CLAIMED ‘STANDARD OF CARE’
- OB EXPERT “VIOLATED STANDARD OF CARE”
- CASE SETTLED ON EVE OF TRIAL; CONTRIBUTION BY OBGYN AND HOSPITAL

2. Renal fetotoxicity – ARB in pregnant woman

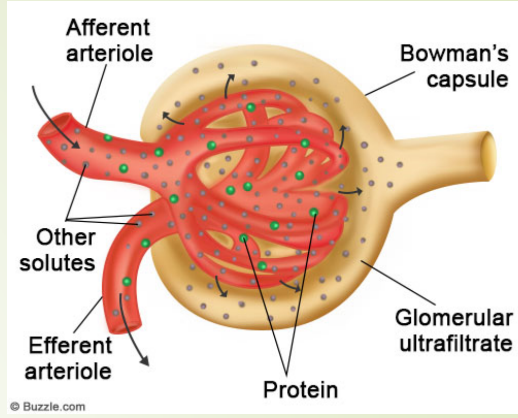
- Valsartan prescribed for HTN in 30 y/o woman
- Pharmacist filled prescription
- Pre-natal vitamins prescription on profile
- Pharmacist did not inquire or warn about pregnancy
- Prescription discovered late pregnancy; discontinued
- Oligoamnios viewed on US

Oligohydraminos ultrasound

www.ultrasound-images.com/amniotic-fluid/



TOXICOLOGY ISSUE



- Fetal urine production is the major source of amniotic fluid (AF) production in 2nd and 3rd trimesters.
- If blood pressure drops, angiotensin II maintains kidney perfusion and thus GFR due to autoregulation.
- Late pregnancy usage of angiotensin converting enzyme inhibitors (ACE-I) and angiotensin II receptor blockers (ARB) may cause severe oligohydramnios due to fetal renal impairment (second and third trimester)

O **BLACK BOX** Warning(s)

May cause fetal and neonatal morbidity and mortality if used during pregnancy.

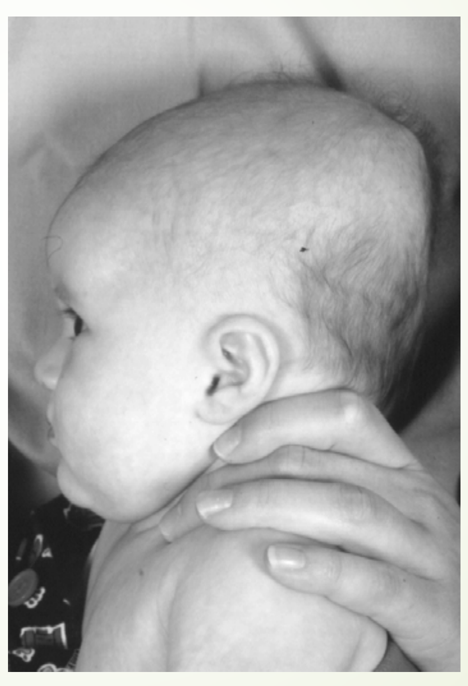
ACE inhibitors also may increase the risk of major **congenital malformations** when administered during the first trimester of pregnancy.

Renal fetotoxicity – ARB in pregnant woman –resolution/legal outcome

- Neonate recovered without long term renal toxicity
- Pharmacist claimed – "doesn't inquire about pregnancy – embarrass patient"
- Pre-natal vitamins "used for other things"
- Pharmacist sued for violation of SOC
- Should have inquired; advised both physicians of the prescription for the ARB
- Case settled by pharmacy

3. Flattened Occiput

(Oschsner J. 2001 Oct; 3(4): 191-199)



3. Deformed skull/ pregnant mom on opiates

- Claim opiates caused fetus to decrease movement
- Claim Cause of skull deformity

- Severe chronic pain – Mom and Drs knew of opiate use
- Lawsuit against OB

3. TOXICOLOGIC CAUSATION: NONE

- Multiple causes of deformed cranium identified in literature and in antiquity, and even some post-partum causes in floppy babies due to inactivity in crib
- No literature support for opiate induced in-utero flaccidity or decrease movement to cause cranial deformity
- Resolution Plaintiff dismissed case after defense pharmacologist opinion/report disclosed.

4. “off-label” tocolytics and CC Blockers in Hypertensive Labor >>> fetal loss

- 33 Wk gestation woman with uterine contractions and 149/92 BP admitted for tocolysis; antihypertensives (CCB-nifedipine) and tocolytic (terbutaline) prescribed; BP controlled, contractions stopped; patient discharged
- Patient found unresponsive 8 days later at home; eclamptic seizure suspected
- Ultrasound showed fetal demise (both twins) along with placental blood clot – abruption. Mother continued hemorrhaging and required hysterectomy

OB EXPERT FOR PLAINTIFF OPINION

- TWINS SHOULD HAVE BEEN DELIVERED EARLIER – NO BAD OUTCOME EXPECTED
- MFM MD "SHOULD HAVE DISCONTINUED THE ANTIPHYPERTENSIVES TO GET TRUE PRESSURE READINGS"
- "PROCARDIA IS KNOWN TO MASK HYPERTENTSION THEREFORE THE SOC REQUIRED DC TO GET TRUE BP READINGS"

TOXICOLOGY: SOC/Literature

- Pregnancy Hypertens. 2012 Jul;2(3): Which first-line drug to control severe hypertension in pregnancy?A pilot study. (nifedipine)
- COCHRANE: Oral antihypertensive therapy for severe hypertension in pregnancy and postpartrauma systematic review (NIFEDIPINE) BJOG
- J Obstet Gynaecol Res. 2015 Jan;41(1):1722. 2014 Aug 27.Hemodynamic effects of nifedipine tocolysis.Yamasato K , Burlingame J, Kaneshiro B. (NIFEDIPINE SAFE)

DEF PHARM OPINIONS / LEGAL RESOLUTION

- Procardia / CCB antihypertensive << systemic blood pressure. When a preg pt is treated, it does not mask hypertension – it treats hypertension by lowering blood pressure and thus eliminates / controls hypertension.
- "Under the circumstances, as a pharmacologist, the use of nifedipine in this case is completely appropriate – the best drug choice for treatment" JTOD
- MFM AND HOSPITAL REFUSED TO SETTLE. Nuisance settlement immediately pre-trial/ cost to defend.

5. Meconium – common matrix for post-partum drugs of abuse testing

5. Meconium positive morphine – DCFS files action against Mom

- Admitted Heroin user
- Last used in first trimester "when I learned I was pregnant"
- OB continued use of Xanax (alprazolam) to lessen risk for heroin use
- Xanax use continued through labor and after delivery
- Baby's meconium test positive for Morphine (screening), confirmed with GCMS
- DCFS Action
- Pro-bono Law Firm Defense for Indigent Client

5. TOXICOLOGY ISSUE

- KINETICS OF MECONIUM DRUG DISPOSITION, DETECTABILITY
- ESTIMATION OF TIME OF USE
- AMNIOTIC FLUID – 8 WEEKS
- TIMING OF MECONIUM FORMATION (12 WEEKS)
- RESIDENCE OF DRUGS (MORPHINE) IN MECONIUM
- DETECTABILITY – 20 WEEKS (RANGE)
- EXPECTED RESULTS OF TOXICOLOGY TESTS
  - MORPHINE
  - XANAX/ALPRAZOLAM
  - NO BENZODIAEPINES PRESENT – FALSE NEGATIVE

MECONIUM DRUG TESTING – LEGAL RESOLUTION

- EXPERT OPINION SAMPLE MUST BE FROM ANOTHER PATIENT. (COD)
- CONTINUOUS USE OF BENZODIAZEPINES, MECONIUM TEST SHOULD HAVE BEEN POSITIVE FOR BENZO (XANAX)
- SINCE THE TEST WAS NEGATIVE, IT CREATES GREAT DOUBT AS TO THE CHAIN OF CUSTODY OF THE MECONIUM TESTED AT THE CONFIRMATION LEVEL. "TEST CANNOT BE ACCURATE"
- BROCHURE FROM ARUP LABS STATES: "NOT FOR FORENSIC PURPOSES"
- DCFS DROPPED ACTION AGAINST MOTHER DUE TO QUESTIONABLE IDENTITY OF THE MECONIUM POSITIVE MORPHINE TEST

6. EPIDURAL MAGNESIUM SULFATE

- Magnesium sulfate (MgSO4) is the agent most commonly used for treatment of eclampsia and prophylaxis of eclampsia in patients with severe pre-eclampsia. It is usually given by either the intramuscular or intravenous routes. ... A concentration of 1.8 to 3.0 mmol/L has been suggested for treatment of eclamptic convulsions.
- WHAT HAPPENS WITH EPIDURAL ADMINISTRATION?

Epidural Magnesium Sulfate Epidural Infusion in Laboring woman

- Pyxis (drug storage cabinet) acquisition of $MgSO_4$ instead of LIDOCAINE, obtained by Nursing Student
- Connected to Epidural catheter in laboring patient
- Complaints of increased pain, burning, paralysis by patient
- Discovery of medication error
- Monitoring for several days – patient made full recovery – no residual

6. EPIDURAL MAGNESIUM SULFATE toxicology issues

- ANESTH ANALG 1987:hb: 1020-1,Accidental Epidural Magnesium Sulfate Injection Alan Dror, MD, and Eva Henriksen, MD (reported case)
- Survival best evidence
- No residual toxicity
- Murphy's Law – What ever can go wrong WILL!

RESOLUTION ; EPIDURAL MAGNESIUM MEDICATION ERROR

- LIABILTY – HOSPITAL BLAMED NURSING SCHOOL
- JTOD EXPERT CRITICIZED HOSPITAL ACCESS AND LACK OF SUPERVISION OF NURSING STUDENT/VERIFICATION OF IV CONNECTION
- HOSPITAL PAID SETTLEMENT (PAIN AND SUFFERING)

7. OPIATE TOXICITY / RESPIRATORY ARREST IN UNMONITORED WOMAN POST C-SECTION

- POST C-SECTION
- FENTANYL EPIDURAL
- ANTIPSYCHOTICS, ANXIOLYTICS, ANTIHISTAMINES
- LUNG FINDINGS – WHEEZING BL MORBID OBESITY
- NO PULSE OX USED
- PATIENT ARRESTED 16 HOURS POST OP/ BRAIN DAMAGE

OPIATE TOXICITY / MATERNAL ARREST IN UNMONITORED WOMAN IN LABOR

- OPIATES CAUSE RESPIRATORY DEPRESSION AT THERAPEUTIC DOSES
- CNS DEPRESSANTS ADD TO THE RESP DEPRESSANT EFFECT OF OPIATES
- SLEEP APNEA/ MORBID OBESITY / ADD SURGERY INCREASES THE RISK OF OPIATE RESPIRATORY DEPRESSION
- ONLY EFFECTIVE MEANS OF MONITORING IS FREQUENT VITAL SIGNS, PULSE OX (and CAPNOGRAPHY)

OPIATE TOXICITY / MATERNAL DEATH RESOLUTION

- HOSPITAL HAD PULSE OX POLICY
- ANESTHESIA POST OP ORDERS HAD PULSE OX ORDERS
- L&D NURSES : "WE DON'T USE PULSE OX IN L&D"

- CASE WENT TO TRIAL
- $16,000,000 VERDICT AGAINST HOSPITAL
- $8,000,000 CASH SETTLEMENT TO AVOID APPEAL.

O'Donnell's

Drug Injury

FOURTH EDITION

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