DRUG INFORMATION
Jonathan Banks
Bob Buckham
Sharon Gardiner

Canterbury DHB
District Health Board
Te Poari Hauora o Waitaha

CLINICAL PHARMACOLOGY
Murray Barclay
Evan Begg
Chris Hutchinson
Petra Lowe
Jane Vella-Brincat
Mei Zhang

SAFETY OF PROPOFOL IN PREGNANCY

Question:
What is the safety of propofol in pregnancy?

Answer:
Propofol has been allocated an FDA risk category B meaning that *"animal studies do not indicate a risk to the fetus and there are no controlled human studies, OR animal studies do show an adverse effect on the fetus but well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus"* [1,2] .

The manufacturer's stance is that propofol *"should not be used in pregnancy"* and that it *"may be associated with neonatal depression"* and *"should not be used for obstetric anaesthesia"* [3].

First and second trimesters
We are not aware of any data describing the use of propofol in the first or second trimester of pregnancy[1,2,4,5].

Third trimester
Propofol has been used in women undergoing caesarean section[1,2]. Reviews on propofol use in pregnancy[2,6] reported that several researchers have investigated the effects of propofol on Apgar scores, time to sustained spontaneous respiration and neurobehavioural scores (Neurologic and Adaptative Capacity Score, Early Neonatal Neurobehavioural Scale). The majority of studies failed to observe a difference in Apgar scores in infants exposed to propofol alone, or compared to other forms of general anaesthesia e.g. thiopentone + enflurane or isoflurane[2].
Most studies did not identify a difference in Neurologic and Adaptative Capacity Scores or time to spontaneous respiration with intravenous bolus doses of up to 2-2.5mg/kg or continuous infusions up to 6mg/kg/h. Higher doses (e.g. 9mg/kg/h or boluses above 2mg/kg) have been associated with depressed scores (e.g. decreased pinprick responses) although these were reported to resolve rapidly with no difference between propofol or thiopentone[2,6].
One study reported that infants exposed to propofol 2.8mg/kg had reduced Apgar scores at 1 and 5 minutes compared with those exposed to thiopentone 5mg/kg. The scores in both groups were lower than for infants born by spontaneous vaginal delivery. Five of the 20 infants exposed to propofol had profound muscular hypotonus during the first five minutes of delivery and one was described as somnolent. Propofol-exposed infants were also reported to have depressed neurobehavioural scales within the first hour of delivery. Generalised irritability and crying was also observed in 5 of the 25 propofol-exposed infants[2].
D'Alessio and Ramanathan[6] advised that the studies investigating obstetric use of propofol have been in healthy women with no obstetric complications. They indicated that there is little information on the use of propofol on a stressed foetus.

Conclusions:
We are not aware of any data describing foetal outcomes following first trimester exposure to propofol. In the third trimester, propofol appears to be relatively 'safe' for bolus administration as an

induction agent provided that the dose is appropriately controlled (e.g. < 2mg/kg). Low dose infusions with a short induction-to-delivery time should have minimal impact on neonatal outcomes.

References:

1. Drugdex, Micromedex database
2. Briggs GG *et al*. Drugs in Pregnancy and Lactation (5th ed), 1998
3. Diprivan datasheet, AstraZeneca Limited
4. Medline database 1966-2001
5. Embase database 1988-2001
6. D'Alessio JG, Ramanathan J. Seminars in Perinatology 1998; 22(5): 350-62.

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