

DRUG INFORMATION

Jonathan Banks
Bob Buckham
Sharon Gardiner



CLINICAL PHARMACOLOGY

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

SAFETY OF CODEINE IN PREGNANCY

Question:

What is the safety of codeine in pregnancy?

Answer:

First trimester

The use of standard therapeutic doses of codeine in the first trimester of pregnancy does not appear to be considered overtly teratogenic^[1,2] although codeine has been associated with foetal malformations in some studies:

The Collaborative Perinatal Project monitored 50,282 mother-child pairs and described 563 first trimester exposures to codeine. They did not identify any relationship between maternal codeine ingestion and large categories of major or minor malformations. However, associations were found with six individual defects (respiratory, genitourinary (other than hypospadias), Down's syndrome, tumours, umbilical hernia, and inguinal hernia). Only the association with respiratory malformations (not otherwise specified) was statistically significant^[3].

In a study comparing 1427 malformed newborns with 3001 controls, first trimester use of narcotic analgesics (codeine most frequently used) was associated with inguinal hernias, cardiovascular defects, cleft lip and palate, dislocated hips and other musculoskeletal defects. Second trimester use was associated with alimentary tract defects. In another retrospective study, an increased incidence of cleft lip and palate was associated with first trimester use of opioids (primarily codeine). A survey identified an increase in codeine exposure amongst 390 infants with congenital heart disease compared with 1254 controls^[3].

In a surveillance study of Michigan Medicaid recipients, 7640 newborns had been exposed to codeine during the first trimester. A total of 375 (4.9%) major birth defects were observed (325 expected). There was no pattern in the type of defects although the overall number of defects suggested that there was a relationship between codeine and malformations^[3].

Perinatal complications

The use of codeine (as with other narcotics) near or during labour may produce neonatal respiratory depression^[2,3].

Symptoms of codeine withdrawal have been reported in neonates following maternal ingestion of medications containing codeine^[2]. Maternal use of codeine-containing analgesics and cough preparations in the week prior to birth has been associated with codeine addiction in two neonates. Both babies developed irritability, tremors, and jitteriness. The use of subcutaneous codeine in one of the infants resulted in a decrease of the symptoms and increased suckling^[4].

Conclusions:

There is limited evidence suggesting that maternal use of codeine in the first trimester of pregnancy may be associated with an increased incidence of malformations. However, the data is conflicting and the influence of confounders such as maternal disease state and other drug therapy cannot be excluded. It is prudent to avoid all drug exposure in the first trimester where possible.

The use of codeine in the third trimester of pregnancy may result in foetal addiction to codeine, neonatal withdrawal, and respiratory depression. If codeine is deemed necessary in the latter stages of pregnancy, then the attending paediatrician should be aware of the situation. If, after assessment of the risks and benefits, treatment with codeine is clearly indicated in pregnancy, then the lowest effective dose should be used for the shortest possible time.

References:

1. Rubin P (ed). Prescribing in pregnancy (2nd ed), 1995
2. Drugdex, Micromedex database
3. Briggs GG *et al.* Drugs in Pregnancy and Lactation (5th ed), 1998
4. Mangurten *et al.* Pediatrics 1980; 65: 159-60

Date prepared: December 2000

The information contained within this document is provided on the understanding that although it may be used to assist in your final clinical decision, the Drug Information Service at Christchurch Hospital does not accept any responsibility for such decisions.