Diabetic pregnancy: An overview of current guidelines and clinical practice

The authors review the recent changes in diagnostic criteria of gestational diabetes mellitus (GDM), describe problems with maintaining and monitoring adequate blood glucose, especially in type 1 diabetes, and provide a brief overview of the currently approved glucose–lowering therapies in pregnancy.

After the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study, the definition of GDM was revised under the auspices of the International Association of Diabetes and Pregnancy Study Groups. Despite a very good glycaemic control, the prevalence of macrosomia remains high. So far, the only glucose–lowering medications approved for use during pregnancy are insulins.


Oral nifedipine versus intravenous labetalol for severe hypertension during pregnancy: A systematic review and meta-analysis

In this study, authors want to determine the efficacy and safety of oral nifedipine for treatment of severe hypertension of pregnancy compared with intravenous labetalol. Oral nifedipine is as efficacious and safe as intravenous labetalol and may have an edge in low resource settings.

They systematically searched for articles comparing oral nifedipine with intravenous labetalol for the treatment of severe hypertension during pregnancy over Medline, Cochrane Central Register of Clinical Trials and Google Scholar from inception till February 2014.

They included all RCTs that compared intravenous labetalol with oral nifedipine for treatment of severe hypertension during pregnancy, addressing relevant efficacy and safety outcomes. Eligible studies were reviewed, and data were extracted onto a standard form. They used Cochrane review manager software for quantitative analysis. Data were analyzed using a fixed effect model.

The pooled analysis of seven trials (four from developing countries) consisting of 363 woman–infant pairs showed that oral nifedipine was associated with less risk of persistent hypertension (RR 0.42, 95% CI 0.18–0.96) and reported maternal side effects (RR 0.57, 95% CI 0.35–0.94). However, on sensitivity analysis the outcome ‘persistent hypertension’ was no longer significant. Other outcomes did not reach statistical significance.


Aspirin and acetaminophen use and the risk of cervical cancer

Authors investigated whether regular use of aspirin or acetaminophen was associated with risk of cervical cancer in women treated at an American cancer hospital. This findings suggest that frequent and frequent, long–term use of aspirin is associated with decreased odds of cervical cancer. This is the first US–based study examining these associations. Given the widespread use of nonsteroidal anti–inflammatory drugs and acetaminophen worldwide, further investigations of the possible role of analgesics in cervical cancer, using a larger sample size with better–defined dosing regimens, are warranted.

This case–control study included 328 patients with cervical cancer and 1,312 controls matched on age and decade enrolled. Controls were women suspected of having but not ultimately diagnosed with a neoplasm. Analgesic use was defined as regular (at least once per week for ≥ 6 months), frequent (≥7 tablets/week), very long term (≥ 11 years), or frequent, long term (≥ 7 tablets per week for ≥ 5 years).

Compared to nonusers, frequent aspirin use was associated with decreased odds of cervical cancer (odds ratio, 0.53; 95% confidence interval, 0.29–0.97).
A slightly larger association was observed with frequent, long–term use of aspirin (odds ratio, 0.46; 95% confidence interval, 0.22–0.95). Acetaminophen use was not associated with the risk of cervical cancer.


Increased 3 gram cefazolin dosing for cesarean delivery prophylaxis in obese women

The authors conducted a two–phase investigation. The current is a prospective cohort study of the effects of obesity on tissue concentrations following prophylactic 3g cefazolin doses at the time of cesarean delivery.

Concentration data following 3g were compared to historical controls who had received 2g.

3g of parenteral cefazolin was given 30–60 minutes prior to skin incision. Adipose samples were collected at both skin incision and closure. Cefazolin concentrations were determined using a validated high–performance liquid chromatography assay.

28 obese subjects were enrolled in the current study; 29 subjects were enrolled in the historic cohort. BMI had a proportionally inverse relationship on antibiotic concentrations.

Increasing the cefazolin dose dampened this effect and improved the probability of reaching the recommended MIC of ≥ 8 µg/ml. Subjects with BMI 30–40kg/m² had a median concentration of 6.5 µg/g after receiving 2g vs 22.4 µg/g after receiving 3g. Women with BMI >40kg/m² had a median concentration of 4.7 µg/ and 9.6 µg/g after receiving 2 and 3g respectively. With 2g of cefazolin only 20% of the BMI 30–40kg/m² cohort and none of the BMI >40kg/m² reached an MIC of ≥8 µg/ml. With 3g, all women with BMI 30–40kg/m² reached target MIC values while 71% of BMI >40kg/m² attained this cutoff.

Higher adipose concentrations of cefazolin were observed following administration of an increased prophylactic dose in obese women.


Intravenous iron sucrose versus oral iron in the treatment of pregnancy with iron deficiency anaemia: A systematic review

For pregnant women who could not tolerate the side effects of oral treatment or required a rapid replacement of iron stores, intravenous iron sucrose was associated with fewer adverse events and was more effective than regular oral iron therapy.

A systematic review was done to investigates the intravenous iron sucrose versus oral iron in the treatment of pregnancy with iron deficiency anaemia.

A meta–analysis of Six randomised controlled trials involving a total of 576 women were performed. patients treated with intravenous iron sucrose (intravenous group) were compared with those treated with oral iron (oral group) for IDA during pregnancy.

Significant increases in haemoglobin [mean difference (MD), 0.85; 95% confidence interval (CI), p = 0.002] and ferritin levels (MD, 63.32; 95% CI, p < 0.00001) were observed in the intravenous group.

Compared with the oral group, there were fewer adverse events in the intravenous group (risk ratio, 0.50; 95% CI, p = 0.0003). There was no significant difference in birth weight between the two groups.

The primary outcomes of interest were mean maternal haemoglobin and serum ferritin levels at the end of treatment. Secondary outcomes were treatment–related adverse events and foetal birth weight.


Standard first-line chemotherapy with or without nintedanib for advanced ovarian cancer (AGO-OVAR 12): a randomised, double-blind, placebo-controlled phase 3 trial

Angiogenesis is a target in the treatment of ovarian cancer. Nintedanib, an oral triple angiokinase inhibitor , has shown activity in phase 2 trials in this setting. Investigation was done comparing the combination of nintedanib with standard carboplatin and paclitaxel chemotherapy in patients with newly diagnosed advanced ovarian cancer.
In this double-blind phase 3 trial, chemotherapy-naive patients (aged 18 years or older) with advanced ovarian cancer and upfront debulking surgery were stratified by postoperative resection status, FIGO stage, and planned carboplatin dose. Patients were randomly assigned to receive six cycles of carboplatin and paclitaxel in addition to either 200 mg of nintedanib (nintedanib group) or placebo (placebo group) twice daily on days 2–21 of every 3-week cycle for up to 120 weeks. The primary endpoint was investigator-assessed progression-free survival analyzed in the intention-to-treat population.

Between 9.12.2009, and 27.7.2011, 1503 patients were screened and 1366 randomly assigned by nine study groups in 22 countries: 911 to the nintedanib group and 455 to the placebo group. 53% of the nintedanib group experienced disease progression or death compared with 58% of the placebo group. Median progression-free survival was significantly longer in the nintedanib group than in the placebo group (17·2 months vs 16·6 months; hazard ratio 0·84 [95% CI 0·72–0·98]; p=0·024).

The most common adverse events were gastrointestinal (diarrhoea: nintedanib group 21% vs placebo group 2% . Haematological (neutropenia: nintedanib group 20% vs placebo group 20%; thrombocytopenia: 12% vs 5%. anaemia: 12% vs 6%. Serious adverse events were reported in 42% of the nintedanib group and 34% of the placebo group. 3% of the nintedanib group experienced serious adverse events associated with death compared with 4% of the placebo group, including 1% in the nintedanib group and 1% in the placebo group with a malignant neoplasm progression. Drug-related adverse events leading to death occurred in three patients in the nintedanib group and in one patient in the placebo group (cause unknown).

**Conclusion:** Nintedanib in combination with carboplatin and paclitaxel is an active first-line treatment that significantly increases progression-free survival for women with advanced ovarian cancer, but is associated with more gastrointestinal adverse events. Future studies should focus on improving patient selection and optimisation of tolerability.