Oral Contraceptives

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Uses

- Prevention of pregnancy
- Treatment of the following:
  - Dysmenorrhea
  - Menorrhagia/iron-deficiency anemia
  - Acne
  - Endometriosis
  - Functional ovarian cyst
  - Hyperandrogenism and/or polycystic ovarian disease
  - Premenstrual syndrome and/or premenstrual dysphoric disorder
  - Perimenopausal vasomotor symptoms
  - Mittelschmerz

Perioperative Risks

- Hypercoagulability; increased risk of venous and arterial thrombosis when given without concomitant aspirin, especially in women with blood type A+.

Worry About

- Thromboembolic events; increased relative risk of 2.7 (without aspirin).
- Hyperkalemia (drospirenone and/or ethinyl estradiol).
- Treatment failure and/or pregnancy. "Typical user" failure rates reported as high as 9%. Preop beta-HCG assay may be indicated in sexually active pts.

Overview/Pharmacology

- Oral preparations of synthetic estrogen, progestin generally well absorbed
- Metabolized by the liver and excreted in urine and feces

Drug Class/Mechanism of Action/Usual Dose

- Estrogens:
  - Mestrol.
  - Ethinyl.
  - Estradiol.
- Progestins:
  - Norethindrone.
  - Norgestrel.
  - Norethindrone acetate.
  - Ethynodiol diacetate.
  - Levonorgestrel.
  - Norgestimate.
  - Desogestrel.
  - Drospirenone.
  - Prometrium.
- Combination estrogen and progestin drugs inhibit ovulation by negative feedback effect on the hypothalamus; altering normal pattern of gonadotropin secretion by the anterior pituitary; cervical mucus thickens and is unfavorable to sperm even if ovulation occurs. Classified as:
  - Monophasic: Same ratio of progestin and estrogen in each pill.
  - Biphasic: Two phases of altered progestin and estrogen ratio.
  - Triphasic: Progestin and estrogen ratio varied in three phases.
- Progestin-only agents act directly by inhibiting ovulation or creating thick cervical mucus impenetrable to sperm.
- First- and second-generation progestin-only drugs pose a lower risk of thromboembolism. Third-generation progestins carry a 6- to 9-fold increase of venous thromboembolism, similar to the risk during pregnancy if given without concomitant aspirin.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn Greatly increased risk of thromboembolic events Arrhythmia due to hyperkalemia Altered lipid/cholesterol profile	Hx of MI or CVA Hx of DVT/PE Palpitations	BP Deep venous exam	 Venous Doppler Serum K^+ Serum lipid cholesterol levels
GI	May exacerbate gallbladder disease	Hx of jaundice/cholestasis during pregnancy		Bilirubin level, US, ERCP
HEPAT	Increased incidence of hepatic adenoma and hepatocellular cancer			

Key References: Blanco-Molina A, Trujillo-Santos J, Tirado R, et al: Venous thromboembolism in women using hormonal contraceptives, *Thromb Haemost* 101(3):478–482, 2009; Chalhoub V, Edelman P, Staiti G, et al: Oral contraceptives and hormone replacement therapy: management of their thromboembolic risk in the perioperative period, *Ann Fr Anesth Reanim* 27(5):405–415, 2008.

Perioperative Implications

Preoperative Concerns

- Consider D/C of combination OCs and third-generation progestin-only OCs 1 mo prior to major surgery if administered without aspirin and adding barrier method or adding aspirin for surgery with anticipated prolonged period of immobilization.
- Must weigh OC cessation with the risk of unwanted pregnancy or termination. In addition, consider risk of anesthesia and surgery to pregnant woman and fetus, including possible teratogenicity and spontaneous abortion.

Induction/Maintenance

- Consider thromboprophylaxis on an individualized basis judged according to additional genetic and acquired risk factors.

Postoperative Period

- Surveillance for DVT and PE. Restart aspirin.
- Early mobilization; resume agents 2 wk after surgery or mobilization.

Oral Hypoglycemic Agents

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Uses

- Oral hypoglycemic agents are used to manage type 2 diabetes mellitus.
- The term oral hypoglycemic agents is becoming obsolete and is being replaced by the term noninsulin glucose-lowering drugs because the glucagon-like peptide 1 analogues are injected.

Perioperative Risks

- Hypoglycemia (sulfonylureas and meglitinides)
- Ketoacidosis (sodium/glucose cotransporter 2 [SGLT-2] inhibitors)
- Metformin-associated lactic acidosis
- Delayed gastric emptying and potential for aspiration (glucagon-like peptide 1 [GLP 1]analogues and dipeptidyl peptidase IV [DPP-IV] inhibitors)

Overview/Pharmacology

- There are currently eight different classes of noninsulin glucose-lowering drugs that can be used to treat diabetes:
  - Sulfonylureas
  - Meglitinides
  - Intestinal alpha-glucosidase inhibitors
  - SGLT-2 inhibitors
  - Biguanides
  - Thiazolidinediones
  - GLP-1 analogues
  - The gliptins/DPP IV inhibitors

Mechanism of Action

- These drugs work via four broad mechanisms:
  - By increasing the release of endogenous insulin and causing an actual drop in blood glucose (the sulfonylureas and meglitinides)
  - By inhibiting GI absorption and renal reabsorption of glucose (intestinal alpha-glucosidase inhibitors and the SGLT-2 inhibitors)
  - By altering effector-site sensitivity to endogenous insulin and reducing gluconeogenesis/glycogenolysis or endogenous metabolism (metformin and the thiazolidinediones)
  - By acting on the incretin pathway (GLP-1 analogues and the DPP-IV inhibitors)

Drug Effects

Drug Class	Examples	Mechanism of Action	Adverse Effects	Contraindications	Perioperative Concerns	Perioperative Implications
Sulfonylureas	Glibenclamide Gliclazide Glipizide Tolbutamide Glimepiride	Binds to an ATP-sensitive channel on the cell membrane of pancreatic beta cells Resultant depolarization leads increased secretion of (pro)insulin	Hypoglycemia GI disturbances Blood disorders	Type 1 diabetes Hepatic impairment Severe renal impairment Ketoacidosis	Hypoglycemia Blood disorders	Omit during period of starvation
Meglitinides	Repaglinide Nateglinide	Binds to the ATP-dependent K+ channel on the cell membrane of pancreatic beta cells in a similar manner to sulfonylureas but have a weaker binding affinity Resultant depolarization leads to increased secretion of (pro)insulin	Hypoglycemia GI disturbances	Type 1 diabetes Hepatic impairment Severe renal impairment Pregnancy	Hypoglycemia	Omit during period of starvation
Alpha-glucosidase inhibitors	Acarbose Voglibose	Inhibits digestive enzymes needed to digest complex carbohydrates in the gut Less glucose is absorbed because carbohydrates are not broken down into absorbable glucose molecules	GI disturbances	IBS Predisposition to intestinal obstruction	GI disturbances	Omit during period of starvation
SGLT-2 inhibitors	Dapagliflozin Canagliflozin Empagliflozin	Prevents the kidneys from reabsorbing filtered glucose and thus promotes glucose loss	Increased risk of UTI Dysuria Dehydration and renal impairment Ketoacidosis	Ketoacidosis Renal impairment Pregnancy and breast feeding	Ketoacidosis Dehydration	Omit during period of starvation
Biguanides	Metformin	Decreases hyperglycemia primarily by suppressing hepatic gluconeogenesis Enhances peripheral glucose uptake Decreases absorption of glucose from the GI tract	GI disturbances Taste disturbance Lactic acidosis	Ketoacidosis Surgery	Metformin associated lactic acidosis	Generally omit However, may be continued if starvation is short and there is no risk of AKI
Thiazolidinediones	Pioglitazone	Increases the expression of insulin cell-surface receptors in the tissues Increases insulin sensitivity Is glucose-dependent; therefore the risk of hypoglycemia is low	Heart failure Bladder cancer (small risk) Bone fractures GI disturbance Anemia Macular edema	Heart failure Bladder cancer Hematuria	Heart failure Fluid retention	May be continued if periop period of starvation is short
Incretin mimetics/ GLP-1 analogues	Exenatide Liraglutide Lixisenatide Dulaglutide	Stimulates insulin release in response to food Reduces gluconeogenesis Reduces gastric emptying Promotes satiety (therefore reduces calorific intake)	Delayed gastric emptying	Ketoacidosis Severe GI disease	Delayed gastric emptying	May be continued Supraglottic airways may be contraindicated
The gliptins/DPP IV inhibitors	Sitagliptin Vildagliptin Saxagliptin Alogliptin Linagliptin	Inhibit breakdown of the naturally occurring incretins Prolongs action of naturally occurring incretins	GI disturbances Delayed gastric emptying Pancreatitis	Ketoacidosis	Delayed gastric emptying	May be continued Supraglottic airway may be contraindicated

Key References: Dhatariya K, Levy N, Flanagan D, et al.: Management of adults with diabetes undergoing surgery and elective procedures: improving standards. Joint British Diabetes Societies. Revised March 2016. http://www.diabetologists-abcd.org.uk/JBDS/Surgical_guidelines_2015_full_FINAL_amended_Mar_2016.pdf (Accessed February, 21 2017); Inzucchi SE, Bergenstal RM, Buse JB, et al.: Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach: update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care* 38(1):140–149, 2015.

Perioperative Implications

- Pts on glucose-lowering drugs must be assessed preop to determine suitability for continuation of drugs.
- Continued use is associated with severe metabolic disturbance and is class-specific.
- Continued use is associated with risk of PONV.
- Most of these drugs must be discontinued during the periop period.
- If these drugs are omitted during the periop period, alternative strategies must be implemented to maintain and ensure periop glycemic control.
- Renal function must be monitored and ensured.
- If omitted, these agents should be reintroduced only once normal diet has been resumed and adequate renal function is ensured.

$P2Y_{12}$ Receptor Blockers

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Uses

- $P2Y_{12}$ RBs used alone or in combination with ASA (DAPT).
- ACS, those undergoing PCI with stent placement, and pts with NSTEMI or STEMI.
- Continue for 6–12 mo after insertion of drug-eluting stent (DES), and 4–6 wk after insertion of bare metal stent (BMS).
- Peripheral arterial disease
- AF when warfarin/coumadin is contraindicated
- Ischemic cerebrovascular disease, carotid or vertebral artery dissection (3–6 mo), postcarotid endarterectomy (long term), and carotid artery stenting (DAPT for 30 d).

Perioperative Risks

- Plt dysfunction
- Bleeding if $P2Y_{12}$ RB not stopped 5 d before surgery; ASA to be continued if possible
- Coronary event due to stent thrombosis after DES implantation if $P2Y_{12}$ RB stoppedl risk of ST to be balanced against risk of delay to surgery

Worry About

- Increased bleeding intra- and postop
- Surgery undertaken <30 d after BMS insertion or <6 mo after DES insertion due to increased stent thrombosis risk