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Editorial

Sex differences in kinetic handling of various therapeutic molecules

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1. Prologue

Women have less body weight, can have higher concentrations of drug, because drugs have lower clearance and/or lesser volume of distribution. The gastric transit time are also shorter in men about 45 hours compared to women 92 hours. Cmax was more in women 87% of the time and AUC was more in women 71% of the time. Bile acid composition is also variable, women have higher concentrations of Chenodeoxycholic acid as compared to Cholic acid in men.[1–5] The Activities of microsomal enzymes of CYPs 1A2 and 2E1 were decreased in women, thus metabolic handling is highly variable. The fatty oxidation is also higher in women as compared to men. Likely Women have better insulin sensitivity as compared to men.

2. Critical Analysis

Different response of drugs in women is shown by fact that females have a nearly 2-fold greater risk than males for exhibiting Adverse drug reactions (ADR). Women over the age of 19 were 43 - 69% more likely to have an ADR recorded by their general practitioner. Fat composition higher and water content is lower in women. Hence women have different responses to various drugs.[6–12]

Gastric emptying and small intestine motility are reduced in pregnancy. Drug absorption is also reduced by nausea and vomiting. Selective serotonin reuptake inhibitors (SSRIs) including fluoxetine, sertraline, and paroxetine. The relative concentrations of these drugs is decreased, though caution is required in pregnancy. The dose requirements for volatile anaesthetic agent, such as halothane, is reduced in pregnancy. Acute liver failure is serious adverse event that occurs more frequently in women. Certain of ADR were also more common in women, such as nausea, alopecia, headache and dizziness, while men were more likely to experience ADRs such as aggression, sexual dysfunction and tendon rupture. Women undergoing treatment with Clozapine or olanzapine have a remarkably higher risk for metabolic dysfunction but also are more prone for adverse cardiovascular outcomes. Women taking antipsychotics are nearly 4 times more likely to have a prolonged QTc interval than men. 5-fluorouracil (5-FU) difference in its clearance, increases ADR risk in women. Causes for more ADRs in women include: smaller volume of distribution, alteration

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Table 1: Women have different responses than men

Drug	Results in females
Alfentanil	Decreased Plasma Concentration. Males required 25% higher doses.
Oxazepam / Paracetamol	Increased Plasma Concentration
Metoprolol	Lower hepatic clearance
Methylprednisolone	Higher hepatic clearance
Morphine	Increased effect
Rocuronium / Vecuronium	Increased effect
Propofol	Decreased effect
Desflurane	Females requires 20 % higher dose than men.
Pentazocine	Produces more analgesia in women
Lignocaine	50% larger elimination half life and 62 % larger volume of distribution
Beta Blockers – Propranolol	Clearance was 50 % as compared to males and there is greater reduction in blood pressure in women
Cimetidine	Intrasubject Bioavailability variation is 16% in males and 10% in females
Erythromycin	C max with erythromycin was 42% higher in men than in women
NSAIDs – Piroxicam	Plasma concentrations of piroxicam increase with aging and women exhibited higher concentrations than men .
Cardiac glycosides – Digoxin	Clearance is 12 % less in women as have lesser Glomerular filtration rate
Antipsychotic Therapy	Clinically superior response in females
Quinolones – Ciprofloxacin	Clearance is lower in women
Aspirin	omen might be less responsive (2.3 times) to aspirin than men.
Cefotaxime	Clearance is decreased in women.
Cortisol Suppression	Women are more Susceptible
Apixaban	Exposure is 15 % greater in female subjects than in male subjects.
Zolpidem	35% lower apparent clearance of drug.

in receptor binding, lesser BMI in women.

3. Epilogue

Sex differences are critical for many drugs used in therapeutics. Physicians should be aware of critical dose calculation in females, as significant variability is observed with most therapeutic drugs. For diabetics, glitazones (Pioglitazone) act better in women, whereas sulfonylureas act better in men. Its well known fact that towards vaccination females develop higher antibody response and are prone to more adverse effects, true for the novel SARS-CoV-2 vaccines. Most of the clinical trials for drug evaluation are done in men as female subset is generally excluded. Therefore there is dose disparity in most of the therapeutic groups. It was in only in 1993, the National Institute of Health has approved trials in both sexes with due precautions.

4. Source of Funding

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5. Conflict of Interest

None.

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