Adverse drugs reactions in intensive care unit

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ABC: Airway, Breathing and Circulation

ADRs: Adverse Drug Reactions

AIN: Acute Interstitial Nephritis

AKI: Acute kidney injury

ARB: Receptor Blocker

ASA: Acetylsalicylic Acid

ATN: Acute Tubular Necrosis

AV: Atrioventricular

CBZ: Carbamazepine

CPR: Cardiopulmonary Resuscitation

DIC: Disseminated Intravascular Coagulation

ECG: Electrocardiogram

FFP: Fresh Frozen Plasma

FVC: Forced Vital Capacity

HPA: Hypothalamic-Pituitary-Adrenal

ICU: Intensive Care Unit

IM: Intramuscularly

INR: International Normalized Ratio

IV: Intravenously

LFTs: Liver Function Tests

MHC: Major Histocompatibility Complex

MI: Myocardial Infarction

MRSE: Multi-Resistant Staphylococcus Epidermidis

NO: Nitric Oxide

NSAIDs: Non-Steroidal Anti-Inflammatory Drugs

NSTEMI: Non-ST Elevation Myocardial Infarction

PB: Phenobarbital

PCC: Prothrombin Complex Concentrate

PCN: Penicillin

rFVIIa: Recombinant activated Factor VII

rT_3: Reverse Tri-iodothyronine

STEMI: ST-Elevation Myocardial Infarction

SVT: Supraventricular Tachycardia

T_4: Thyroxine

TRH: Thyrotropin-Releasing Hormone

TSH: Thyroid-Stimulating Hormone

WHO: World Health Organization

Introduction

Adverse drug reactions have been creating headlines over the last forty years. Adverse Drug Reactions (ADRs) are a common problem which affect patients in the hospital and community setting. It has been suggested that ADRs were between the 4th and 6th leading cause of death in the USA in 1994 **(Lazarou et al., 1998)**.

Health Organization's definition from 1972 stated that an ADR is "a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease or for the modification of physiological function. The definition has been widely used and is intended to include all doses prescribed clinically, but to exclude overdose **(Vargas et al., 2003)**.

As regards epidemiology:

- Preventable ADE (adverse drug event):
  - About 0.6%-29%.
  - Most common is ″Penicillin″ (PCN) allergy.
- Non-preventable ADE:
  - Twice common as preventable ADE.
  - Bleeding from anti-thrombotics.
  - Renal failure from toxic medication.

(Kane-Gill et al., 2010)

Risk factors are:

- Old age.
- Gender (females > males).
- ICU environment.
- High risk patient population.(with systemic organ failure).
- High alert medications (e.g. heparin, insulin and sedatives).
- Intra venous infusion drugs (as vasopressor agents and opioids).

(Kane-Gill et al., 2010)

The World Health Organization recommend ***standardization of descriptions of frequency***. Although the WHO document is not currently available online, their recommendations have been summarized by others**:**

- Very common (> 1/10 patients).
- Common (> 1/100).
- Uncommon **(> 1/1000)**.
- Rare (> 1/10,000).
- Very rare (<1/100,000).

(Hoes et al., 2007)

The American Food and Drug Administration defines ***severe effects*** as:

- Requires Intervention to Prevent Permanent Impairment or Damage.
- Hospitalization (initial or prolonged).
- Disability; significant, persistent, or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities or quality of life.
- Congenital anomaly.
- Life-threatening.
- Death.

(Hoes et al, 2007)

Aim of the work

The aim of the work is to list and discuss adverse drug reactions and their manifestation in intensive care unit and how to deal with them.

Incidence of ADRs

Studies of ADRs in ICU patients tend to group patient into two categories: those experiencing ADRs in the community which result in admission to hospital ICU, and those who develop an ADRs during their stay as inpatients. Drug reactions in both groups have been extensively studied worldwide, although the bulk of the literature has originated from the USA. Studies are of varying size, quality and methodology, making comparisons difficult. Two recent UK prospective studies demonstrated that 6.5% of patients admitted to hospital ICU were experiencing an ADRs **(Howard et al., 2003)**.

Classification of ADRs:

Rawlins and Thompson first formally classified these in 1977 as type A and type B reactions:

- ***Type A (augmented) reactions*** are predictable through knowledge of the drug's pharmacology and are dose-dependent, for example (hypoglycaemia with anti-diabetic agents).

- ***Type B (bizarre) reactions*** are unpredictable from the known pharmacology of the drug, and do not show a clear dose-response relationship, for example (anaphylactic reactions to antibiotics). This classification remains the most accessible and is the most widely accepted and recognized in the literature. **(Aronson et al., 2002)**.

- ***Type C:*** Dose-related and time-related. This is related to duration and dosage of exposure. An example is hypothalamic-pituitary-adrenal suppression from glucocorticoid therapy.

- ***Type D:*** Time-related; delayed reaction. An example is tardive dyskinesia.

- ***Type E:*** Withdrawal; end of dose reaction. An example is narcotic or beta-blocker withdrawal.

- ***Type F:*** Unexpected failure of therapy. This may be caused by drug interactions. An example is failure of oral contraceptives due to induction of enzymes by a second drug.

(Aronson et al., 2003)

Types A and B were proposed in the 1977s and the other types were proposed subsequently when the first two proved insufficient to classify ADRs **(Aronson et al., 2002)**.

Etiology (causes):

As research better explains the biochemistry of drug use, less ADRs are type B ('idiosyncratic') and more are type A (pharmacologically predictable). Common mechanisms are:

- ***Abnormal pharmacokinetics due to:***

  - Genetic factors.

  - Comorbid disease states.

- ***Synergistic effects*** between either:

  - A drug and a disease.
  - Two drugs.

Immunity related classification:

Immunologic (unpredictable):

1- **Type I reaction (IgE-mediated):** Anaphylaxis from B-lactam antibiotic.

- **Mechanism:** Drug-IgE complex binding to mast cells, with release of histamine, inflammatory mediators.
- **Clinical manifestations:** Urticaria, angioedema, bronchospasm, pruritus, vomiting, diarrhea and anaphylaxis.
- **Timing of reactions:** Minutes to hours after drug exposure.

2- **Type II reaction (cytotoxic):** Hemolytic anemia from penicillin.

- **Mechanism:** Specific IgG or IgM antibodies directed, at drug-hapten coated cells.
- **Clinical manifestations:** Hemolytic anemia, neutropenia, thrombocytopenia.
- **Timing of reactions:** Variable.

(Igney et al., 2005)