Literature Surveillance for Pharmacovigilance; Tools and Systems for Driving Efficiency

Panel Discussion led by:

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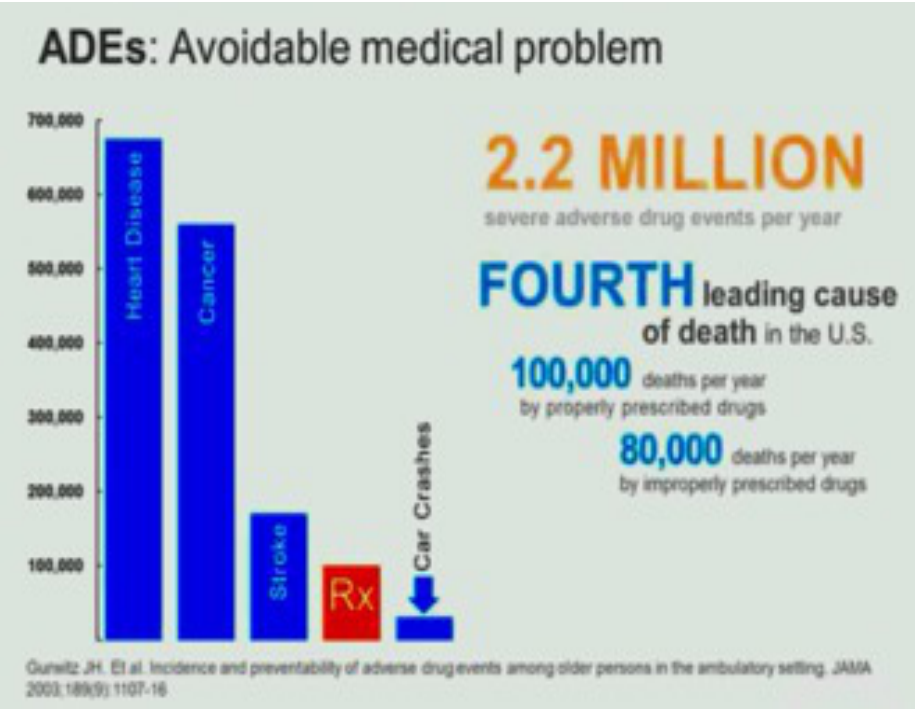
Adverse drug reactions have a major impact on public health

- 5% of all hospital admissions in EU are related to adverse drug reactions
- 28% of patients visit emergency department of hospital due to adverse events
- Nearly 197,000 death per year due to adverse drug reactions
- ADR's are 4th Leading Cause of death in US hospitals
- High societal costs: $75 Billion per year



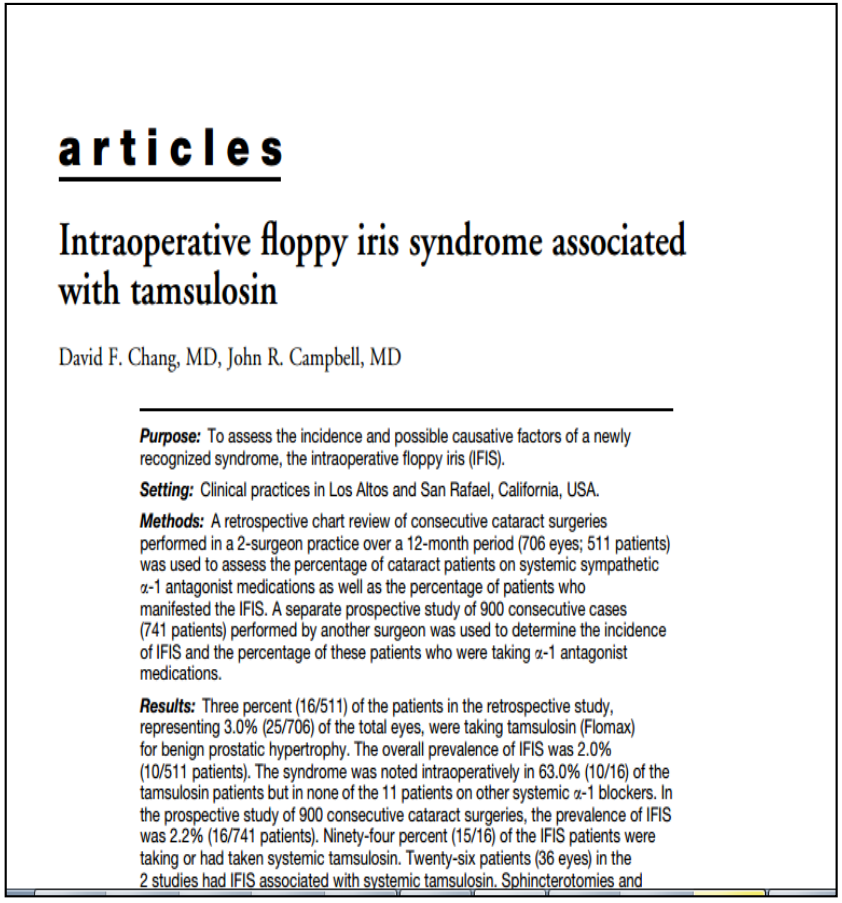
Why searching scientific and medical literature?

'…*Scientific and medical literature is a significant source of information for the monitoring of the safety profile and of the risk benefit balance of medicinal products, particularly in relation to the detection of new safety signals or emerging safety issues…*

Reference: *Guideline on good pharmacovigilance practices (GVP): Module VI-Management and reporting of adverse events to medicinal products*

Signal from literature: Tamsulosin and 'Floppy Iris Syndrome' (2005)

- Intraoperative floppy iris syndrome occurred in approximately 2% of a cataract surgery population
- Appeared to be caused by tamsulosin, a systemic sympathetic alpha-1A antagonist
- Chang et al. mention 15 patients with IFIS
- At the time of publication, none had been reported to the Regulatory Authorities!



articles

Intraoperative floppy iris syndrome associated with tamsulosin

David F. Chang, MD, John R. Campbell, MD

Purpose: To assess the incidence and possible causative factors of a newly recognized syndrome, the intraoperative floppy iris (IFIS).

Setting: Clinical practices in Los Altos and San Rafael, California, USA.

Methods: A retrospective chart review of consecutive cataract surgeries performed in a 2-surgeon practice over a 12-month period (706 eyes; 511 patients) was used to assess the percentage of cataract patients on systemic sympathetic α-1 antagonist medications as well as the percentage of patients who manifested the IFIS. A separate prospective study of 900 consecutive cases (741 patients) performed by another surgeon was used to determine the incidence of IFIS and the percentage of these patients who were taking α-1 antagonist medications.

Results: Three percent (16/511) of the patients in the retrospective study, representing 3.0% (25/706) of the total eyes, were taking tamsulosin (Flomax) for benign prostatic hypertrophy. The overall prevalence of IFIS was 2.0% (10/511 patients). The syndrome was noted intraoperatively in 63.0% (10/16) of the tamsulosin patients but in none of the 11 patients on other systemic α-1 blockers. In the prospective study of 900 consecutive cataract surgeries, the prevalence of IFIS was 2.2% (16/741 patients). Ninety-four percent (15/16) of the IFIS patients were taking or had taken systemic tamsulosin. Twenty-six patients (36 eyes) in the 2 studies had IFIS associated with systemic tamsulosin. Sphincterotomies and

Intraoperative floppy iris syndrome associated with tamsulosin
Chang D.F., Campbell J.R.
Journal of Cataract and Refractive Surgery 2005 31:4 (664-673) Cited by: 285

Safety information from spontaneous and literature adverse reactions reports differ

Reporting rates may differ depending on the type of adverse reaction reported

Drug Substance	System Organ Class	Literature Cases (%)	Spontaneous Cases (%)	% Difference
Acetylsalicylic Acid	Nervous System Disorders	25.6	8	17.6
	Gastrointestinal Disorders	8.4	25.4	17.0
Fentanyl	Injury, poisoning, complications	35.9	7.5	28.3
Alendronic acid	Gastrointestinal disorders	4.6	21.0	16.5
	Injury, poisoning, complications	28.3	5.4	22.9
Tamsulosin	Injury, poisoning, complications	50	4.1	45.9
Etoposide	Congenital, familial, genetic	0	24.3	24.3

Extracted from Table 4

Klose J, Fröhling S, Kroth E, Dobmeyer T, Nolting A. Safety information from spontaneous and literature adverse reactions reports: a comparison. *Ther Innov Regul Sci.* 2013;47:248–55.

Literature surveillance as a component of the PV workflow

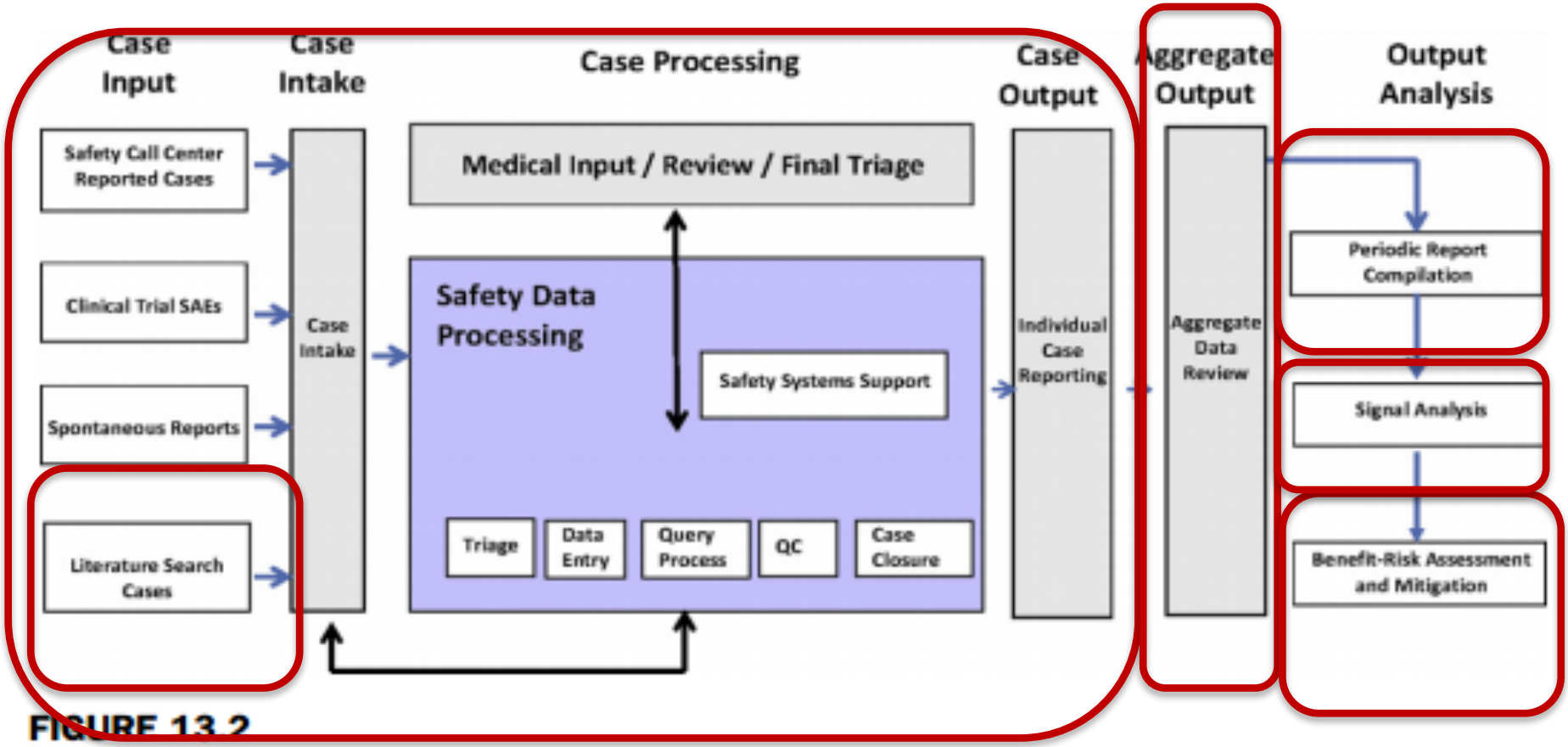


FIGURE 13.2

Summary of the major activities associated with pharmacovigilance. SAE: serious adverse event; QC: quality control. (Please refer to color plate section)

https://www.elsevier.com/__data/assets/pdf_file/0010/96967/Pharmacovigilance-and-risk_link.pdf

Many of the challenges we hear about fall in these categories:

- Complying with different regulations
- Monitoring the increasing volume of literature
- Building ideal search strategies
- Preparing for inspections and audits
- Monitoring local language journals
- Integrating EMA MLM results

Guidelines for literature screening may differ between authorities

FDA

Guidance for Industry

Postmarketing Safety Reporting for Human Drug and Biological Products Including Vaccines

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 December 2012
EMA/228028/2012 (superseded version)

Guideline on good pharmacovigilance practices (GVP)
Module IV – Pharmacovigilance audits

ICH
harmonisation for better health

POST-APPROVAL SAFETY DATA MANAGEMENT: DEFINITIONS AND STANDARDS FOR EXPEDITED REPORTING
E2D

Current *Step 4* version
dated 12 November 2003

Increased regulatory focus on role of literature in PV

VI.B.1.1.2. Literature reports
The scientific and medical literature is a significant source of information for the monitoring of the safety profile and of the risk benefit balance of medicinal products, particularly in relation to the detection of new safety signals or emerging safety issues. Marketing authorization holders are therefore expected to maintain awareness of possible publications through a systematic literature review of widely used reference databases (e.g. Medline, Excerpta Medica or Embase) no less frequently than once a week. The marketing authorization holder should ensure that the literature review includes the use of reference databases that contain the largest reference of articles in relation to the medicinal product properties

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A. Good reporting Practice
Spontaneous case reports of adverse events submitted to the sponsor and FDA, and reports from other sources, such as the medical literature or clinical studies, may generate signals of adverse effects of drugs. The quality of the reports is critical for appropriate evaluation of the relationship between the product and adverse events. FDA recommends that sponsors make a reasonable attempt to obtain complete information for case assessment during initial contacts and subsequent follow-up, especially for serious events, and encourages sponsors to used train...

The **quality of the reports is critical** for appropriate evaluation of the relationship between the product and adverse events.

Our Panelists

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