

Pharmaceutical Care and Toxicology, a Synergy in High Risk Situation

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Received date: August 08, 2016; Accepted date: September 19, 2016; Published date: September 26, 2016

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Abstract

The rationale of this work is to analyse relationship in field of poisoning and toxicology between pharmaceutical care approach in order to improve the global management of the system and improving clinical outcomes in high risk situations. Observing the roles played by clinical pharmacy in toxicology medical team we can have relevant improving in the management of the systems. Starting from the analysis of some relevant literature we submit to international organization a rethinking about the toxicological medical team organization with a stable presence of clinical pharmacist. Poisoning therapy is a multidisciplinary bio- medical work and we have more benefit when clinical pharmacist is permanent member of toxicology team.

Keywords: Toxicology; Antidotes; Medicinal laboratory; Clinical pathology; Poison centre

Introduction

Before analysing the clinical ph. Role is crucial to evaluate the various poisoning situations that can arrive in emergency department. We can have poisoning in different situation: home, works, industry, agriculture as well as drug overdoses, terroristic attack and other situations. Poison substances can be in contact by gastro intestinal way, respiratory way, eyes and skin, parenteral.

Poisons

Poisons can be caustic, corrosive, solvents; drugs abuse substances, drugs, toxins, radioactive, heavy metals, gases, plants, fungus, smart drugs, other venom bites. Self-poisoning, drug abuse, other situation as bites (poisonous snakes, spiders, scorpions), botulinus, tetanus, amanita phalloides are example of a complex world. Some poisons are the same drugs (in example paracetamol used for children in high dosage can be very hepatic toxic). Poisoning can interest adults, children or baby, elderly or pregnant. We can have single case or multiple even: disaster situation with high number person involved and involving different kind of substances: biological substances, verbal, chemical, nuclear.

In order to give optimal response in this complex situation there is the need of an efficient emergency systems, diagnostic procedure and clinical therapy to be added to the adequate antidotes availability, supportive measure and also the really best knowledge in management of the clinical cases. Multidisciplinary team gives more efficacy results v/s monodisciplinary way Luisetto et al. 2015 ukjpb [1]. Right antidotes, right time, but also right knowledge and skills: all this mean also right decision making systems. In Emergency medicine departments we have every year several cases but only few cases with exits for this reason the medical equip must have the multiprofessional expertise.

Antidotes are not to be considered as simply drugs, and often the using condition (dosage, time, and posology) imply a deep knowledge in pharmacokinetics and dynamics applied to the single patient conditions. Toxicology, clinical pharmacy, and antidotes management are discipline strictly connected in toxicological medical team works.

This process needs multidisciplinary equipment (lab toxicologist, clinical toxicologist, and pharmacist, nurse, imaging team, ICU team and other as dialysis). Logistics of rare antidotes, communication activity with regional and national centre are often under hospital pharmacy control and the pharmacist expertise plays a relevant role.

The patients critical condition imply that the single cases must be treated under the poison centre guidance according biomedical literature, (EBM or other reference, as guideline, protocols and procedure, consolidated use). Even if the poisoning situation rare condition if not correctly treated since first time can give critical patient's condition (also death of patients) and the time factor is one of the most relevant factors to take in consideration. The medicinal chemistry, organic and inorganic chemistry, toxicology, biochemistry pathology knowledge of clinical pharmacist must be added to the other medical team competences to improve clinical outcomes.

We can see that in example in USA some Poison Centre is directed by pharmacist (with clinical toxicologist presence). In some cases pharmacist can suggest to physicians plans and strategies for handling exposures to toxins, chemicals, or life threatening drug interactions. The specific competence in pharmacokinetics, pharmacodynamics, metabolism, toxicology of iatrogenic substances is fundamental bases to apply correct antidotes therapy. (The pharmacist is the drug expert for excellence and this expertise is useful in event of poisoning by drugs). Pharmacists provide deep drug and poison information and are responsible for poison prevention initiatives (educational programs). They work closely with medical team in emergency room and ICU response personnel, and other health-care organizations to ensure early and up-to-date dissemination of life saving information regarding possibly fatal drug overdose events.

Drug abuse is not a rare condition and toxicological lab data and clinical assessment are crucial phases in therapy. During the treatment of poisoned overdosed patient clinical pharmacist works with physicians to give more chances to patients to save their life. Hospital pharmacist takes care about antidotes hospital stocks and are applied in logistics of this kind of drugs (antidotes, vaccines, mabs, serum, immunoglobulin). The stocks of antidotes are chosen by clinicians, toxicology physicians of emergency medicine and ICU but also evaluated also by hospital pharmacist.

The management of the systems imply evaluation of costs

Direct Costs in hospitalization due to poisoning involved in diagnostic procedure. For the treatments of the cases (in example for oxygen therapy, blood therapy, antidotes others) and indirect costs as working days lost, by patients, an incorrect diagnosis and therapy increase these costs in high way. The hospital pharmacist rationalizes the use and antidotes stoke preventing that some arrives in expiration data by giving disponibility to other hospital before. In the first time in poisoning event is crucial a description of the place to emergency professional (scenario) of poisoning, collecting blister of medicine, syringe and other can help in diagnostic activity. This gives great help (in example odours, gases, chemicals). The clinical observe than the way of poisoning (GI; Parenteral, cutaneous, respiratory, eyes and other) and other relevant signs and symptoms then med lab toxicology test, imaging, toxicological screening tests, biochemistry and ematological or coagulate tests. Clinical Instrumental test (ECG, Spiro metric, and blood pressure) and then using differential diagnosis choose the right treatment. Second level toxicological tests to prove the poison presence (in example blood).

In Logistics of antidotes v/s normal drugs we have some peculiarity

Rare use of antidotes, difficult in ordering, high costs, expiration data, reduce number of cases, long treatment in some cases, multiple cases, rapid necessity near to treat poisoning event, disaster situations. This need a special logistics system in order to assure the right treatment to patient in very critically situations (is a pharmacist role). Antidotes are classified classify IPCS by time to have the drugs in emergency medicine (in 30 minutes, 2 hours, 6 hours). The antidote that must be viable in 30 minutes is recommended that are stoked in emergency medicine or Intensive care unit.

These conditions need rigorous systems of logistic

Managed currently by hospital pharmacist and emergency request are evaluated by them. In rare cases are involved in emergency logistics also public authorities (in example for terroristic attack) or in cases involved with national stokes of some antidotes (botulism).

In hospital settings we can have

Medical responsible antidotes stoke and Pharmacist responsible antidotes stoke that works in strictly way (In collaboration with anti-poisoning centre and institution involved in emergency).

Logistics of antidotes

Emergency situation or not emergency in some cases the need of quantity antidotes can not to be obtained from only one hospital stokes and there is the need for regional or national support (rare antiserum antitoxin). Antidotes stoke in ex emergency, ICU, blood bank, hospital pharmacy, regional or national stokes. Tdm is often used in situation involved in toxicology so the medicine laboratory or imaging and also clinical pharmacist must have this new competence [2]. Other pharmacist activity is involved in toxicological treatment as galenic activity of hospital pharmacies that play a crucial role for example in magisterial formula as paediatric dosage. Antidotes as active charcoal, starch, sodium thiosulfate and many other. Analysing the clinical pharmacist works in last centuries we have find positive effect in clinical activities when part of medical team in stabile way (Luisetto et al.) 2016 Steps and Impacts of Pharmaceutical Care and Clinical Pharmacy Development on Clinical Outcomes 2016: A Historical Analysis Compared with Results [3].

Treatment of poisoning Faces

After emergency call, anamnestic data are collected next toxicological data from laboratory are frequently asked. (med lab and imaging data, clinical data, treatment, monitoring Epidemiologic register, Anamnestic, clinical data sign and symptoms, other diagnostic data TDM, differential diagnosis, therapy, monitoring). Syndromes can help in differential diagnosis (cholinergic, excitatory, and depressive). The Toxic characteristics as molecular weight, $t_{1/2}$, clearance, VD and other kinetics and dynamics properties help in the choosing of appropriate treatment (dialysis properties of the poison or not) and in this faces deep Knowledge in molecular chemistry ant toxicology give great help. Clinical patient's characteristics; comorbidity, age, organ and apparatus state sign and symptoms (neurological status, cardio logical, metabolic) drive the treatment (Med lab: emogas, lattice acid, anionic balance and other as carbossiHB, metahemoglin, haematuria, acid bases balances, respiratory profile).

Other measure and procedure currently used

Often are applied decontaminant procedures and supportive measures: In example oxygen therapy, diuretics, plasma expanders, decontaminant measures, gastric washing, forced diuresis, colon washing, emodialisis, peritoneal dialysis, Iperbaric oxygen, plasmapheresis, plasma exchange, washing procedures, and saline solutions.

Antidotes pharmacist management

Definition: From Latin antidotum, from Greek antidote medicine taken or given to counteract a particular poison. We can have specific antidotes (acting v/s one poison) or a specific (used towards different substantives), active towards one or plus substantives. They are classified as first clinical choice, second choice or consolidate use.

Antidotes efficacy: Good evidence presence on efficacy commonly used but other research is necessary efficacy not yet demonstrate, doubt efficacy.

Classification systems: IPCS WHO 1997 Time To Have Antidotes (30,2h,6h) and Efficacy Demonstrated International Programme On Chemical Safety Join Venture With WHO, Intern. Labour Organisation and United Nations Environment Programme Clinical Toxicol [4].

Evaluation of Antidotes: Activities of the International Programme on Chemical Safety OMS.

Groups:

Antidotes.

Agents used to prevent absorption of poison, to enhance elimination, or to treat symptomatologically the effects on body functions.

Other agent's useful for the treatment of poisoning.

Antidothes and related agents considered obsolete.

The first classification was made by mechanism of actions.

JACHO 1997 GUIDELINE

Expert consensus guideline for stoking of antidotes in hospital that provides emergency care Dart RC et al ann. em med, 2009. Rare's antidote's (in examples anti botulinum) regional, national stokes Symptomatic drugs.

Antidotes

Indication use: According registered drugs use and by official poisoning centre, procedure, protocols, consolidated use. Contraindications, side effects, risk - benefit balances.

Contraindications: As the drugs they have this Side effects, allergy, modality of conservation efficacy, safety, time to use, total during of therapy, mono therapy or association the clinical situation, patients clinical data information anamnesis, toxicological data, kind of poisoning are other factors that drive the therapy.

Antidotes hospital stokes: In order to provide the necessary antidote's there are national, regional and local stokes related to local situation (In ex industry presence). The stokes recommended (in order to rationalize stokes reducing costs) nationally registered or produced or internationally drugs registered, officinal drugs, galenic, orphan drugs.

Hospital wards involved in stokes management

Many professionals and wards are involved in this field, in example emergency medicine, Intensive care unit, Blood bank, pharmacy, pediatric (24 h or on call pharmacy service help the emergency medical team in logistics and other cognitive service). Toxicologist, medicinal laboratories, chemists, nurse, clinical pharmacist, nephrologist, neurologist and other service as dialysis, imaging, and surgery works together. Some type of poisoning is real emergences and the efficacy of treatments depends on the rapid and correct response by the professional involved. The pharmaceutical competencies of clinical pharmacists must be added to the physician's clinical toxicology knowledge.

Other specific pharmacists competences in toxicology medical team are

Poison centre pharmacists and toxicology lab, Pharmacokinetics, molecular and clinical toxicology. Clinical chemistry lab analysis, analytical chemistry. Target organ specific toxicity antidote's stokes evaluation (quality-quantitative, local situation, clinician's request) Starter dosage (and to continue the treatment). Drug text assay; ex THC, cocaine, amphetamine, barbiturate, ethanol formative program to medical equipe (pharmaceutical aspects) Adr report (specialist support to the physicians). Antidotes consultant and informative activities (pharmacology, toxicology) Side effects.

Emergency med. Pharmacist role and ICU:

Monitoring antidote's use, biomedical-toxicology documentation web scientific database resource evaluation, poisoning biomedical database posology, registered and unregistered drug and antidote's use, Diagnostic methods, Toxicology labH24 service (poison centre, med lab toxicology). Therapeutic index SAR Acute-retarded toxicity.

University and postgraduate pharmacy Courses: Core curriculum can be clinical toxicology, Molecular toxicology, Environmental and occupational toxicology, Medicinal chemistry, General and Clinical pharmacology, General chemistry, Pharmacokinetics (VD, CLEARANCE, KINETICS, AUC, T/2, molecular weight is fundamental parameter to take in consideration). Pharmaco dynamics (action mechanism, receptor, at other). Availability of specific antidote's TDM Nephrology and dialysis, renal failure Liver, cardiac, neurology, metabolic diseases Anaphylaxis and allergy ,Immunotherapy IG, and Vaccines status.

We observed also some curriculum studio rum of hospital pharmacy school

Pharmacy Practice Residency the toxicology in example we can see this program: University of Arizona Poison Information-Toxicology Rotation Oregon health and science university toxicology fellowship, University of Sothern California master in MS in Molecular Pharmacology & Toxicology, University of Virginia toxicology rotation.

The Carolinas Poison Centre offers a one-year specialty residency in toxicology for a pharmacist. The residency experience includes all facets of clinical toxicology and prepares the resident for successful credentialing by the American Board of Applied Toxicology (ABAT). Activities include care of the poisoned or overdosed patient, formal teaching from Medical and Pharm D toxicologists, poison center management, clinical research, and manuscript preparation. The primary focus is recognizing, assessing, and managing toxic patients. The resident functions as an essential member of the toxicology service at Carolinas Medical Center. Minimum requirements include a Pharm D from an accredited school of Pharmacy. Completion of a general pharmacy practice residency is preferred but not required and many others.

We observed some relevant bibliography (in our opinion) and we have found that:

Pharmacotherapy 2002 November. The critical care pharmacist: an essential intensive care practitioner: Papadopulos et al., measurable clinical effects of clinical PH. services decreased morbidity and mortality rates.

Intensive care med 2003 may the impact of critical care pharmacist on enhancing patient outcomes. Kane et al and about Pharmaceutical care and therapy error hospital management.

Res AP (2001) 2 COUNCIL OF EUROPE, concerning the pharmacist's role in the framework of health security "one of the pharmacist's basic functions, as expert in medicinal products, is to help prevent avoidable iatrogenic risks".

ASHP Guidelines: "pharmacist for processing drug orders should have routine access to appropriate clinical info about patient (medications allergy, diagnosis, lab values, and pregnancy status)".

The clinical pharmacist presence in medical team gives improving in some clinical outcomes (Luisetto et al., 2015 ukjpb).

Eur J Intern Med. [5]. Epub 2015 Jun 9. Drug-related problems identification in general internal medicine: The impact and role of the clinical pharmacist and pharmacologist Guignard et al [6].

"Patients admitted to general internal medicine wards might receive a large number of drugs and be at risk for drug-related problems (DRPs) associated with increased morbidity and mortality. This was a 6-month prospective study conducted in two internal medicine wards. Physician rounds were attended by a pharmacist and a pharmacologist. An assessment grid was used to detect the DRPs in electronic prescriptions 24hr in advance. One of the following interventions was selected, depending on the relevance and complexity of the DRPs: no intervention, verbal advice of treatment optimization, or written consultation. The acceptance rate and satisfaction of prescribers were measured."

"In total, 145 patients were included, and 383 DRPs were identified (mean: 2.6 DRPs per patient). The most frequent DRPs were drug interactions (21%), untreated indications (18%), over dosages (16%)

and drugs used without a valid indication (10%). The drugs or drug classes most frequently involved were tramadol, antidepressants, acenocoumarol, calcium-vitamin D, statins, aspirin, proton pump inhibitors and paracetamol.

The following interventions were selected: no intervention (51%), verbal advice of treatment optimization (42%), and written consultation (7%). The acceptance rate of prescribers was 84% and their satisfaction was high. Pharmacotherapy expertise during medical rounds was useful and well accepted by prescribers” [7].

Appropriate therapies for commonly encountered poisonings, medication overdoses, and other toxicological emergencies are reviewed, with discussion of pharmacists' role in ensuring their ready availability and proper use. Poisoning is the second leading cause of injury-related morbidity and mortality in the United States, with more than 2.4 million toxic exposures reported each year. Recently published national consensus guidelines recommend that hospitals providing emergency care routinely stock 24 antidotes for a wide range of toxicities, including toxic-alcohol poisoning, exposure to cyanide and other industrial agents, and intentional or unintentional overdoses of prescription medications (eg. calcium-channel blockers, β -blockers, digoxin, and isoniazid). Pharmacists can help reduce morbidity and mortality due to poisonings and overdoses by [1] recognizing the signs and symptoms of various types of toxic exposure, [2] guiding emergency room staff on the appropriate use of antidotes and supportive therapies, [3] helping to ensure appropriate monitoring of patients for antidote response and adverse effects, and [4] managing the procurement and stocking of antidotes to ensure their timely availability.

Pharmacists can play a key role in reducing poisoning and overdose injuries and deaths by assisting in the early recognition of toxic exposures and guiding emergency personnel on the proper storage, selection, and use of antidotal therapies [8].

Accidental poisoning in young children is common, but severe or fatal events are rare. This study was performed to identify the number of such events occurring in the UK and the medications that were most commonly responsible. Office of National Statistics mortality data for fatal poisoning; Paediatric Intensive Care Audit Network admissions database and the National Poisons Information Service for severe non-fatal poisoning; Hospital Episode Statistics for admission data for implicated agents.

Between 2001 and 2013, there were 28 children aged 4 years and under with a death registered as due to accidental poisoning by a pharmaceutical product in England and Wales. Methadone was the responsible drug in 16 (57%) cases. In the UK, 201 children aged 4 years and under were admitted to paediatric intensive care with pharmaceutical poisoning between 2002 and 2012. The agent(s) responsible was identified in 115 cases, most commonly benzodiazepines (22/115, 19%) and methadone (20/115, 17%). Methadone is the most common pharmaceutical causing fatal poisoning and a common cause of intensive care unit admissions in young children in the UK [9,10].

This study was conducted to evaluate the availability of antidotes/key emergency drugs in tertiary care hospitals of the Punjab province, and to assess the knowledge of health care professionals in the stocking and administration of antidotes in the proper management of poisoning cases. Seventeen (n=17) tertiary care hospitals of Punjab Pakistan were selected. Two performs (A and B) were designed for 26 antidotes/key emergency drugs and given to the

hospital pharmacists and physicians respectively. It was observed that Activated Charcoal, being the universal antidote was found only in 6 hospitals (41%). Digoxin Immune Fab, Edentate Calcium disodium and Glucagon were not available in emergency department of any hospital and even not included in the formulary of any hospital. About 80% pharmacists were aware of the method of preparation of Activated Charcoal and 85% physicians were familiar with its route of administration. Data showed that tertiary care hospitals of Punjab do not stock antidotes according to national drug policy. Moreover the study strongly suggests the development of health care centers and professional by organizing antidote awareness programs, continuous education and record keeping of poisonous cases and availability of emergency drugs around the clock [11].

Insufficient stocking of cyanide antidotes in US hospitals that provide emergency care Gasco et al. “To identify the influence of catchment area, trauma center designation, hospital size, subspecialist employment, funding source, and other hospital characteristics on cyanide antidote stocking choice in US hospitals that provides emergency care. A web-based survey was sent out to pharmacy managers through two listservs; the American Society of Health-Systems Pharmacists and the American College of Clinical Pharmacy. A medical marketing company also broadcasted the survey to 2,659 individuals. We collected data on hospital characteristics (size, state, serving population, etc.) to determine what influenced the hospital's stocking choice.

The survey response rate was approximately 10% (n=286). Thirty-eight hospitals (16%) stocked at least 4 antidote kits. Safety profile, recommendations from a poison control center, and ease of use had the strongest influence on stocking decisions. Survey of 286 US hospital pharmacy managers, 38/234 (16%) hospitals had sufficient stocking of cyanide antidotes. Antidote preference was based on safety, ease of use, and recommendations by the local poison center, over cost” [12].

Adverse Effects of Common Drugs: Dietary Supplements Felix et al. “Dietary supplement-induced adverse effects often resolve quickly after discontinuation of the offending product, especially in younger patients. The potential for unwanted outcomes can be amplified in elderly patients or those taking multiple prescription drugs; especially where interactions exist with drugs metabolized by cytochrome P450 enzymes. Attributing injury or illness to a specific supplement can be challenging, especially in light of multi-ingredient products, product variability, and variability in reporting, as well as the vast underreporting of adverse drug reactions. Clinicians prescribing a new drug or evaluating a patient with a new symptom complex should inquire about use of herbal and dietary supplements as part of a comprehensive evaluation. Clinicians should report suspected supplement-related adverse effects to the local or state health department, as well as the Food and Drug Administration's Med Watch program (available at <https://www.safetyreporting.hhs.gov>). Clinicians should consider discussing suspected adverse effects involving drugs, herbal products, or dietary supplements with their community- and hospital-based pharmacists, and explore patient management options with medical or clinical toxicology subspecialists. Written permission from the American Academy of Family Physicians is required for reproduction of this material in whole or in part in any form or medium”[13].

“The paper examines the role of the clinical pharmacists as experts of excellence in drug use and its impact in ICU that will eventually reflect in not only reducing mortality rates and improving clinical

outcomes but also lowering considerably the costs of drugs, medical devices, consequential costs caused by medical errors, number of recovery days in the hospital and more. This can be obtained by using clinical pharmacist to guard, oversee, both adjust/correct therapies and take a task of using a management tool, in every day ICU's activities. Based on biomedical literature, we can observe a general improvement in different clinical outcomes and as a result a noticeable reduction in mortality rates, when a clinical pharmacist is a permanent member of the medical team. In brief words, we are here to help not only in increasing life quality of the patients in need of a functional healthcare system, but also in removing unnecessary cost burdens, which eventually prevents economy turmoil" [14,15].

Specific reversal agents for non-vitamin K antagonist oral anticoagulants are lacking. Idarucizumab, an antibody fragment, was developed to reverse the anticoagulant effects of dabigatran. "We undertook this prospective cohort study to determine the safety of 5 g of intravenous idarucizumab and its capacity to reverse the anticoagulant effects of dabigatran in patients who had serious bleeding (group A) or required an urgent procedure (group B). The primary end point was the maximum percentage reversal of the anticoagulant effect of dabigatran within 4 hours after the administration of idarucizumab, on the basis of the determination at a central laboratory of the dilute thrombin time or ecarin clotting time. A key secondary end point was the restoration of haemostasis.

This interim analysis included 90 patients who received idarucizumab (51 patients in group A and 39 in group B). Among 68 patients with an elevated dilute thrombin time and 81 with an elevated ecarin clotting time at baseline, the median maximum percentage reversal was 100% (95% confidence interval, 100 to 100). Idarucizumab normalized the test results in 88 to 98% of the patients, an effect that was evident within minutes. Concentrations of unbound dabigatran remained below 20 ng per milliliter at 24 hours in 79% of the patients. Among 35 patients in group A who could be assessed, haemostasis, as determined by local investigators, was restored at a median of 11.4 hours. Among 36 patients in group B who underwent a procedure, normal intraoperative haemostasis was reported in 33, and mildly or moderately abnormal haemostasis was reported in 2 patients and 1 patient, respectively. One thrombotic event occurred within 72 hours after idarucizumab administration in a patient in whom anticoagulants had not been reinitiated. Idarucizumab completely reversed the anticoagulant effect of dabigatran within minutes (Funded by Boehringer Ingelheim; RE-VERSE AD Clinical Trials. gov number, NCT02104947)" [16].

Diagnosis and treatment of polonium poisoning. Jefferson RD1, Goans RE, Blain PG, Thomas SH. Interest in the clinical toxicology of (210) polonium ((210) Po) has been stimulated by the poisoning of Alexander Litvinenko in 2006. This article reviews the clinical features, diagnosis, and treatment of acute radiation syndrome (ARS) resulting from the ingestion of (210) Po. PHYSICAL CHARACTERISTICS: (210)Po is a high-energy alpha-emitter (radioactive half-life 138 days) that presents a radiation hazard only if taken into the body, for example, by ingestion, because of the low range of alpha particles in biological tissues. As a result, external contamination does not cause radiation sickness.

Ingested (210) Po is concentrated initially in red blood cells and then the liver, kidneys, spleen, bone marrow, gastrointestinal (GI) tract, and gonads. (210) Po is excreted in urine, bile, sweat, and (possibly) breathes and is also deposited in hair. After ingestion, unabsorbed (210) Po is present in the faeces. The elimination half-life in man is

approximately 30-50 days. In the absence of medical treatment, the fatal oral amount is probably in the order of 10-30 microorganisms.

If the absorbed dose is sufficiently large (e.g., >0.7 Gy), (210) Po can cause ARS. This is characterized by a prodromal phase, in which nausea, vomiting, anorexia, lymphopenia, and sometimes diarrhoea develop after exposure. Higher radiation doses cause a more rapid onset of symptoms and a more rapid reduction in lymphocyte count. The prodromal phase may be followed by a latent phase during which there is some clinical improvement. Subsequently, the characteristic bone marrow (0.7-10 Gy), GI (8-10 Gy), or cardiovascular/central nervous system syndromes (>20 Gy) develop, with the timing and pattern of features dependent on the systemic dose. The triad of early emesis followed by hair loss and bone marrow failure is typical of ARS. Those patients who do not recover die within weeks to months, whereas in those who survive, full recovery can take many months.

Serial blood counts are important for assessing the rate of reduction in lymphocyte counts. Chromosome analysis, especially the dicentric count, may establish radiation effects and provides an estimation of dose. The diagnosis of (210) Po poisoning is established by the presence of (210) Po in urine and faeces and the exclusion of other possible causes. In the absence of a history of exposure, diagnosis is very difficult as clinical features are similar to those of much more common conditions, such as GI infections and bone marrow failure caused, for example, by drugs, other toxins, or infections.

Good supportive care is essential and should be directed at controlling symptoms, preventing infections but treating those that do arise, and transfusion of blood and platelets as appropriate. Gastric aspiration or lavage may be useful if performed soon after ingestion. Chelation therapy is also likely to be beneficial, with research in animals suggesting reduced retention in the body and improvements in survival, although increased activity in some radiosensitive organs has also been reported with some chelating agents. Dimercaprol (British Anti-Lewisite) (with penicillamine as an alternative) is currently recommended for (210)Po poisoning, but animal models also indicate efficacy for 2,3,-dimercapto-1-propanesulfonic acid, meso-dimercaptosuccinic acid, or N, N-dihydroxyethylethelene-diamine-N, N-bis-dithiocarbamate.

Results

We observe the activity of clinical pharmacist in ICU: Poison event are managed often by ICU team and ASHP Guidelines "Pharmacist should function a liaison between pharmacy and staff including anaesthesiology, surgery, antibiotic use." Surgery wards setting, anaesthesiology Pharma. Service is relevant working place for clinical pharmacists and in this setting clinical pharmacist participates in:

Recommendations regarding medication regimen review, appropriate antibiotic therapy and duration, drip rates and titration for vasopressor agents, IV compatibility, stability, anticoagulants and fluids (electrolytes and colloids) pharmaceutical anamnestic data collection, allergy evaluation antimicrobial surgery prophylaxis, infectious disease therapy: severe sepsis, septic shock protocols. Analgesia, anaesthesia, trombofropylaxis, emergency drugs list. Risk assessment, ADR reporting medication to stop, switch ev/os Post-operative complication, need of therapy changes drug and med.devices information service ,monitoring ADR, patient care rounds. Toxicologic emergencies, antidotes, support therapies, decontaminations measures toxicology lab, target organ specific toxicity Identify prescribing errors, evaluations most critical conditions, priority actions

clinical and economical evaluations of therapy errors. Preventive actions, risk management culture, Incident reporting, near miss Fmea-Fmeca, clinical audit-Root cause analysis, monitoring, documenting activities drugs and Med. Devices information, education and consulting activity (pharmaceutical and clinical pharmacy approach), updating procedure, protocols and guideline observance, development, ministerial advices following pharmaceutical anamnestic activities, allergy conditions

Technologies support: Validation therapy systems, alert, interaction, side effect, dose verify patient identification systems (RFID), dose units systems, informatic order compounding unit (aseptic, robotized, standardized, quality assurance).

Prontuaries policy: Rationalization.

High attention drugs procedures: Concentrated electrolytes, oncological therapy, immunosuppressive drugs, nephrotoxic antimicrobial etc. double control in critical drug therapy or in high risk drug use checklist use (emergency drugs, antidotes, haemoderivates) dose verify in magistral formula equip accountability, individual and organizative responsibilities, legal implications regulatory organization role, advices, registered name, limitation prescription policy electronic clinical data system ebm approach, biomedical literature collaborative team working (assessment, causes, modify in procedure) in errors management: medical team, central pharmacy, general hospital management, insurance companies, patient organizations tdm therapeutic drug monitoring, laboratory results stressing working conditions (RISK MANAGEMENT) expiration data drugs control, right storage conditions shared acronyms wrong dose, too low, too high, wrong route, pharmaceutical form, patient, frequency, omission dose, in understanding, no indication for therapy to start: ex. antimicrobial surgical prophylaxis therapy to stop, duplicates in therapy toxicity too high, labelling, dilution, compatibility acronymus, verbal ordering, decimal point and zero number calculation errors, unity of measurement LASA Look-alike/Sound-like low level in equipe communication low level in updating risk management, PDCA, root causes analysis, Ishikawa diagram, project management.

The bibliography cited in this paper (as well as other not reported in this work) shows that:

Often also drugs may be responsible in poisoning.

The stokes of some antidote as towards cyanide can be inappropriate.

That clinical pharmacist in medical team gives general improvement in clinical outcomes and that they can play a relevant crucial role.

That poisoning is a very specialistic discipline that can involve an example verbal product (but also in many products from biological to chemistry, from organic and inorganic world, microbes, bites et other).

That a discipline named clinical pharmaceutical care can be the right one discipline to be added in toxicological medical team.

That hospital pharmacist must have an active role in antidotes stokes management (quali quantitative analysis).

That also for new drugs antidotes play a relevant aspect (idaracizumab).

That sometimes poisoning is a very complex therapy (as polonium) and we think the collaboration with clinical pharmacist can give more chances than without.

Discussion and conclusion

Poisoning is a rare event often, but in some cases whit critical consequences and so the right diagnosis and therapy is a golden endpoint. The toxicology medical equip must be multi-professional. Observing the results of bibliography cited in this works and some university toxicology programs for pharmacists when observe that the clinical pharmacist presence in stabile way in toxicologist medical team give improving in clinical outcomes.

Antidotes are used not often but rarely, and physicians need rapid information also in medicinal chemistry and toxicology field. The management of the systems must involve clinical and logistic pharmacist. The pathology, toxicology, pharmacology and medicinal chemistry competence of clinical pharmacist added to the emergency and ICU physician's competences can be the right keywords. The skills requested to the clinical pharmacist in order to works in efficiently way in toxicological medical team are: proactivity, learn about error, critical thinking, collaborative, approach, management ability, problem solving risk management (therapy errors management, some example and causes. illegible handwriting), we think that in order to have a more and efficacy inclusion of clinical pharmacist in the toxicologist equip also psychological and behaviour specific skill are useful instruments (Luisetto 2016 ijppr) [17].

New instruments as professional social media can give more opportunity to meet researcher in healthcare field. Luisetto et al int. journal of economics and management sciences 2016 [18,19], Instrument to rapid share the information between healthcare professionals and to transfer research activities to practical settings.

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