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Pharmacovigilance in the emergency department, results of Mereafaps Campania project year 2010-2011

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Abstract

The Emergency Division represents a strategic hospital headquarter to implement pharmacovigilance activities. The ease of access, the care availability of 24 hours to 24 and the patient's multidisciplinary approach make Emergency Division is the ideal access to health care. The data reported in this paper are from the year 2011 the project MEREAFaPS. Reporting of adverse drug reactions (ADRs) were analyzed cases from three major hospitals in the region Campania, Azienda Ospedaliera di Rilievo Nazionale "Gaetano Rummo" of Benevento, Azienda Ospedaliera di Rilievo Nazionale "San Giuseppe Moscati" of Avellino and Azienda Ospedaliera Universitaria "S. Giovanni di Dio e Ruggi D'Aragona" of Salerno.

KEY WORDS: EMERGENCY DIVISION, REPORTING, ADVERSE DRUG REACTIONS

Introduction

The Emergency Division represents a strategic hospital headquarter to implement pharmacovigilance activities.

The data reported in this paper are from the year 2010-2011 the MEREAFaPS project It is clear that the presence of the hospital pharmacist in Emergency Division is an important resource for the spontaneous reporting system. A pharmacist infact, reports and supports physician to identify ADR/ADE in Emergency Division, increasing the number of ADR/ADE report forms. The presence of pharmacist contributes so to establish a mechanism to ensure that adverse drug reactions or events are systematically reported and reviewed. Several studies confirms the importance of hospital pharmacist's figure as a pharmacovigilance monitor in Emergency Divisions including MEREAFaPS project too. [1,2]. The aim of this study is to confirm that a pharmacist who supports medical staff and nurses to signalling ADR, should be improve the national system of Pharmacovigilance involving (where possible) the patient in order to understand better the dynamics of suspected drugs use. The Emergency Division is infact an important center of immediate hospitalization of all patients with more or less serious pathological phenomena. Some specific targets (indicators) were considered: the percentage of ED visits due to ADR (adverse drug reaction) or ADE (adverse drug event), the percentage of hospital admissions due to acute ADR and ADE, suspected drugs which caused reaction and other drugs took in association, the type and frequency of observed adverse drug reactions and events, the type of population involved (age, sex, comorbidities), how many of these ADRs and ADEs are predictable and therefore preventable and their classification in severe, non severe and lifethreating. In addition, the professional role of hospital pharmacist is an useful tool to create an important network of hospital pharmacovigilance and to increase the number of ADR report forms, their quality and the awareness in safety pharmacology.

Methods

Following the work of monitoring and continuous working relationship with the medical and nursing staff of pharmacists at the hospital emergency room, the recording of ADR / ADE (coded according to MedDRA: Medical Dictionary for Drug Regulatory Activities) in PS was conducted using a single card have been reported in which the patient demographic data (initial and last name, date of birth and gender), ethnicity, medications in therapy, the duration and dosage of same, the reasons for therapy, the type of pathological changes observed (clinical and / or laboratory) and its degree of severity (according to the criteria of the EMEA), if the treatment has been prescribed by a doctor and if there is a history personal or family for previous adverse reactions to drugs.

The board also provided an indication of alternative causes (if any) to the drug / the suspect / s for the onset of the ADR / ADE, of previous reactions to medications and any comorbidities in progress, the data relating to smoking and alcohol have shown signs of clinically important for the recognition and reporting of the incident. The survey was finally completed with the recording of blood tests, when performed and available, follow-up was scheduled for more severe cases and / or requiring hospitalization, through consultations (where permitted) of medical records and detailed informational interviews with Patients (and / or their family members) and the doctors who had evaluated the clinical course. The cards have been filled by the pharmacist in charge is regularly present in PS or promptly warned by the staff of the Unit (in particular the one on duty at the triage) if he had presented a suspected ADR / ADE, either by doctors or nurses of the PS if the pharmacist had not been reached (evening shifts, night or holidays), and properly stored in a special folder in each local frame attached with the respective minutes of discharge (or admission) of the patient in question. The data reported on paper ballots were then loaded on computer, specially prepared for this project by the "Business Information Service" of the AO Niguarda

Ca' Granda. The web-based software (image ins) was shared on the Internet, without the need for loading on site, and has been used by all the companies that participated in the project, which enabled both the knowledge and the sharing of data previously recorded by part of all AO Database security was guaranteed by assigning a different password for each access code (password was sent through a text message on your mobile phone the pharmacist previously authorized and registered) in accordance with the laws on patient privacy and confidentiality of sensitive data, in addition, this software has enabled real-time statistical analysis of the collected data, allowing both a global analysis of the data that a separate analysis for each AO, So as to highlight the homologies and / or the discrepancies between the different AO. The hospital pharmacist in charge, finally, has provided monthly to exhibit at the premises of the PS, special paper reports that highlight the number of reports made during the month, the description of ADR / ADE with its triage color (red, yellow, green or white) and the suspected drugs in order to provide the medical and paramedical staff of the unit constant updates about the progress of the study and keep the attention on the subject of reports regimens.

Results and Dscussion

The total number of alerts entered into the web-based software dell'AO Niguarda Ca' Grande during the survey period considered (April 2010 - May 2011) was of 452 suspected ADRs / ADE (Pic. 1), be distributed between the various First Aid: 154 AORN "Gaetano Rummo" (34%), 119 A.O.U. "S.Giovanni di Dio e Ruggi D'Aragona" (26%) and 179 AORN "San Giuseppe Moscati" (40%) (Pic. 2). It was not possible for technical reasons, go back to the total accesses to the emergency department during the period.

Among the reported cases, 192 (42%) were male patients, 260 (58%) patients were female (Pic. 3).

The reports concerned for the 34% of adult patients older than 65 years (154 records), 64% of adult patients under the age of 65 years (291 messages) and the remaining 2% of pediatric patients (7 messages); in the majority of reported cases (74%) did not indicate the detector, mainly because of the paucity of data, the avoidance or less of ADR / ADE (322 reports dubious), 10% (54 reports) was instead judged preventable, while 16% (76 messages) has been reported as non-preventable (Pic. 4; Pic.5).

Have been as serious by the pharmacist 168 ADR / ADE, in particular 152 led to hospitalization or prolongation hospital for short observation of the patient involved, 15 have endangered life and 1 had fatal outcome. Such death, inserted in the database of the National Network of Pharmacovigilance (RNF, card number 142631), occurred as a result of an anaphylactic shock after single intramuscular administration of one vial of ceftriaxone disodium (Rocefin® 1g / 3.5 ml) for the treatment of bronchitis ; the patient has come in PS in cardiac arrest and despite resuscitation, examinations of urgency and therapies emergency effected, died a few minutes later His medical history was highlighted how the patient presented years before another case of anaphylactic shock to an antibiotic which neither the doctor who opened the case in PS or the patient's family members were able to provide further information.

Finally 283 ADR / ADE have been identified as non-serious as of 1 recommendation has not been given any indication of the severity (Pic. 6).

67.7% of reports made as a result of a reported improvement of clinical symptoms related to the suspected ADR / ADE (306 messages) and 12.6% had complete resolution of the event (57 recommendations) 5.7% instead of the reported events (26 reports) describes a reaction unchanged or worsened after the actions taken in the emergency department. 2 ADR / ADE had a resolution with sequelae, and 1 (as shown above) has hesitated in death.

Particularly significant is the percentage concerning the non-availability of results: 13.3% (60 reports). This figure is mostly due to the objective difficulty in monitoring the patient that does not have a need for hospitalization and that, once visited at the PS, is immediately returned to the skills of the primary care physician (in most cases patients reported out in triage codes with white or green. (Pic 7)

The active ingredients involved in the onset of suspected ADR / ADE showed a peculiar predominance of β-lactam antibiotics such as amoxicillin / clavulanic acid (52 reports), amoxicillin (25 reports), ceftriaxone (24 reports) and a macrolide such as clarithromycin (25 reports) is also significant is the figure for NSAIDs such as acetylsalicylic acid (41 reports), ketoprofen lysine salt (27 reports) and nimesulide (21 messages). Below (Table 1) shows the 40 active ingredients most commonly referred to as suspect because of ADR / ADE collected.

According to the ATC classification, subject to reporting were mainly drugs of class J (antimicrobials for systemic use) with 157 reported cases, the drugs of class M (musculoskeletal system) with 103 cases and class B drugs (blood and blood-forming organs) with 101 cases. (Pic. 8)

As shown in Pic.9, the majority of ADR / ADE occurred against the skin and subcutaneous apparatus (322 cases), in particular, taking into account the classification by preferred term (PT) have been reported 95 cases of urticaria, 59 and 55 of erythema of generalized pruritus, have been reported also in large numbers, gastrointestinal disorders (225 cases, with 35 of upper abdominal pain, edema of the lips 29, 23 and 12 of vomiting of gastrointestinal bleeding), systemic diseases and administration site conditions (111 cases, including 22 of asthenia, edema of the face 15 and 13 of peripheral edema), respiratory, thoracic and mediastinal disorders (104 cases, of which 42 to 23 of epistaxis and dyspnea) and nervous system diseases (95 cases, 20 of these reported as presyncope and 13 as tremor).

Data on prescription from the doctor drug suspects, is quite important to establish that relationship in the occurrence of an ADR / ADE drug-related material can be related to factors such as prescribing errors, wrong patient compliance or, in the case the drug had not been prescribed to incorrect practice of self-medication (Pic. 10).

The data described below show a significant predominance of medication prescribed by a doctor as a possible cause of the onset of ADR / ADE reported (470 cases, approximately 77% of all medications reported), 72 medicines were instead taken arbitrarily by the patient without appropriate medical consultation, for 68 drugs instead it was not possible to go back to the dispensing and recruitment.

The data relating to suspected drugs for the onset of ADR / ADE demonstrate how the majority of reports concern combination therapies of two or more drugs (fig. 11), in fact the 58% of reports (260 cases) indicated as a cause of ADR / ADE a polypharmacy, while 42% of reactions reported (192 cases) is attributable to a single agent

In detail, Pic. 12 shows the numerical data of the aforementioned monotherapies suspicious and correlates the number of drugs involved in suspicious polypharmacy with the number of ADR / ADE associated with them. In particular, 87 cases of signals attributable to polypharmacy conducted with 2 drugs and 50 have been attributed to combination of 3 drugs, 37 have predicted the combination of 4 drugs. Ben 39 reports have indicated as suspicious polytherapies based seven or more drugs (for a maximum of 12 drugs).

An analysis of the number of alerts in the RNF of reality AIFA from 3 hospitals in question is clearly observed as a total of 362 ADR / ADE detected in 24 months (from 01/04/2009 to

31/03/2011), well 354 (97.8%) have been reported in the past 12 months, or during the course of the project MEREAFaPS, in front of the 8 cases reported in the 12 months prior to the project (fig. 13), showing a clear trend reversal.

Conclusion

All drugs, including those administered for treatment of pain generic trivial (common cold, to various types, etc.) have a risk of causing adverse Reactions [3]. It's important to use all the drugs that they consider their risk / benefit ratio, starting from a correct understanding of the potential adverse events and the severity of the condition for which each drug is being used. It must, therefore, make a budget on the true incidence of reactions / events that adverse drug may occur in the course of drug therapy, particularly in the division of emergency: its easy access, its availability and the patient multidisciplinary are needed to implement the strategic approach drug surveillance [4]. The Project MEREAFaPS in the years 2010-2011 [5,6] showed the validity and importance of professionalism of the hospital pharmacist for the implementation of the pharmacovigilance system and as a valuable source of information and support to the medical and paramedical staff. Following the example of project MEREAFaPS and thanks to his / her cultural background of drug, the hospital pharmacist is not identified just as a point of reference in the legislative practices of dispenses drugs (in unloading or departments) but as a consummate professional for prescription appropriateness, for interactions and toxicity of drugs, for pharmacovigilance practices and active medical device vigilance too. These dynamics have was favored by specific hospital guidelines pharmacist with the aim of involving physicians and paramedical personnel in PS and highlight how good and the work of the charity hospital pharmacist had undertaken with a view to improving the quality of patient care.

Hospital pharmacist supports medical and paramedical staff with the recent scientific literature, EMEA AIFA and updates that may resolve all suspected cases of ADR / ADE. Adverse reactions not only affect the health of the population, but also a high economic cost. In light of the obtained project results MEREAFaPS, it is possible conclude that the implementation of an efficient structure and culture of pharmacovigilance and professional competence of the pharmacist in the hospital can open and encourage many future scenarios. In fact, creating a dense monitoring network, we able to improve the appropriateness of drug use to all the Italian territory to protect the life of the population and to save on hospital costs related to ADR / ADE. Pharmacovigilance is an essential source for reporting the inadequacy of the pharmacokinetic / pharmacodynamic characteristics of all medications that are on the market, but which are not observed during the earlier stages of clinical trials.

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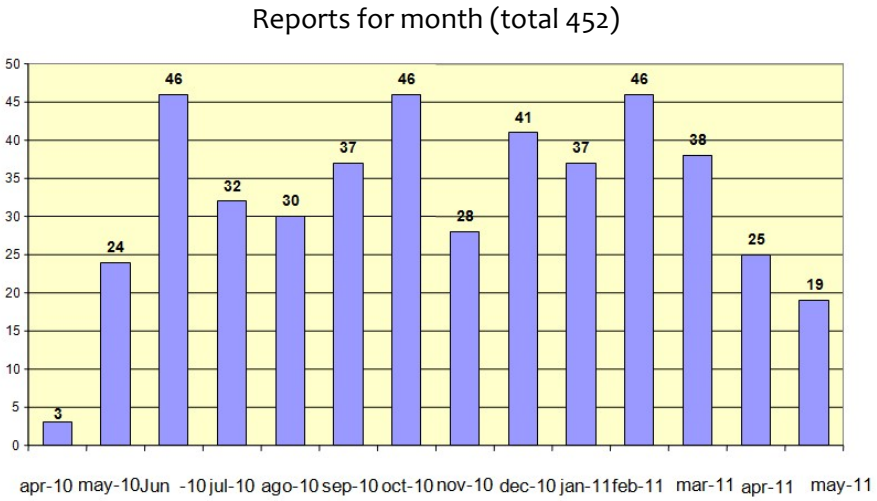
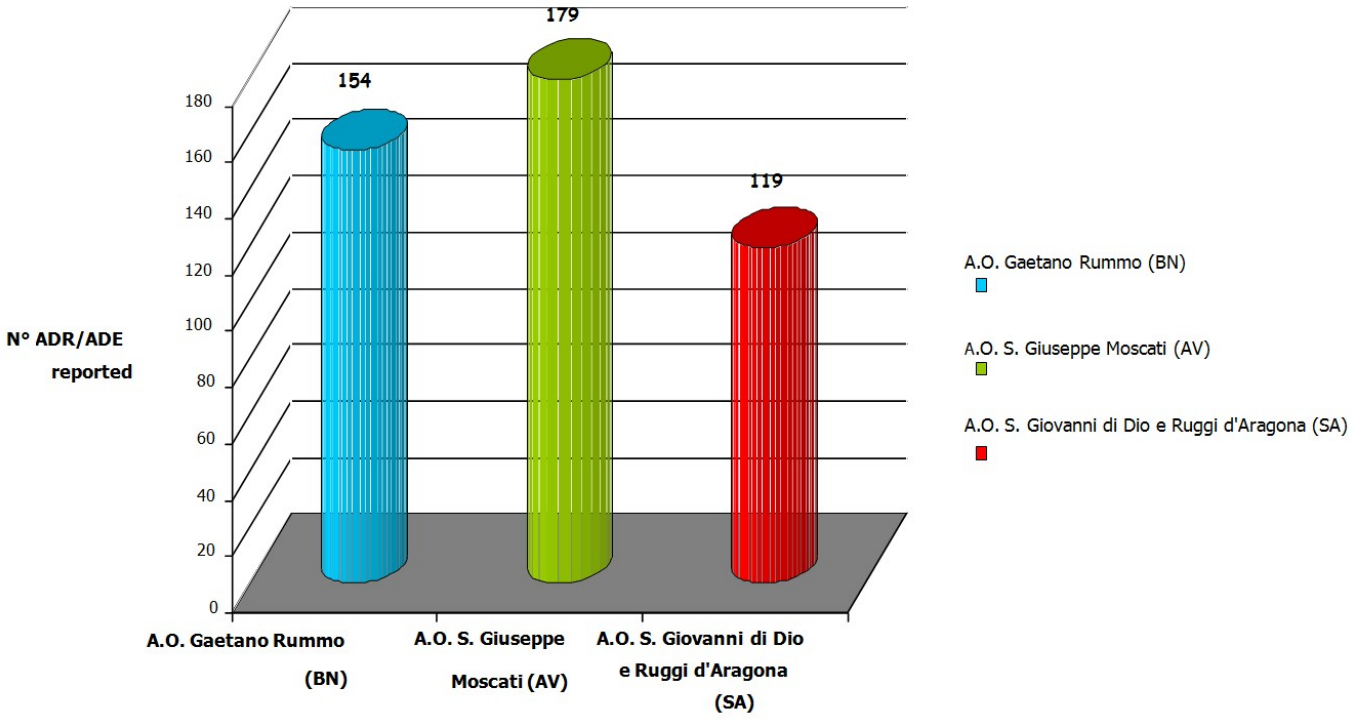
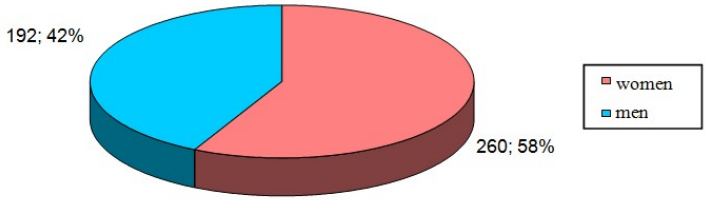


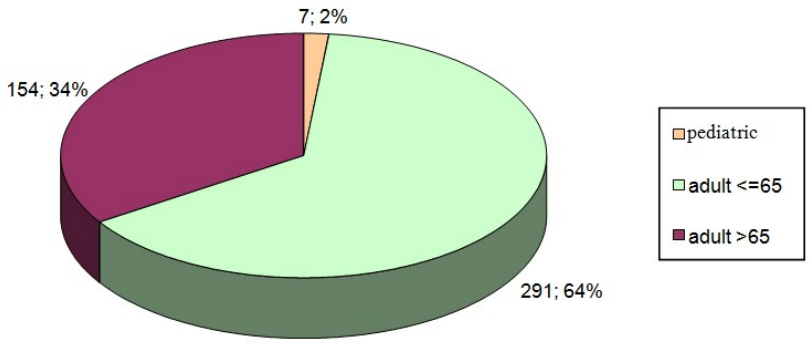
Pic. 1: Reports MEREAFaPS made in Campania in the period April 2010 - May 2011



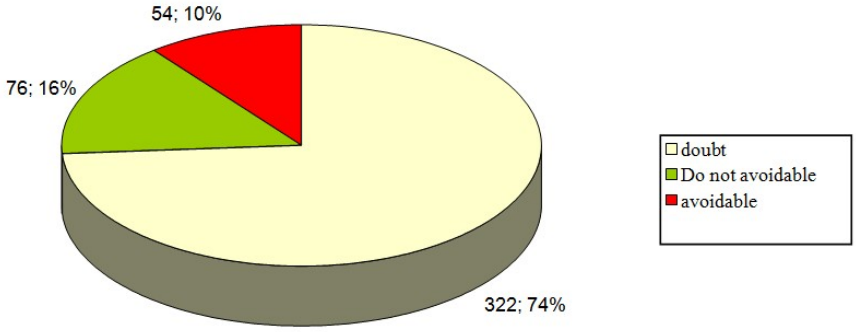
Pic. 2: Reports MEREAFaPS made in Campania (April 2010 - May 2011) distributed by individual Hospital



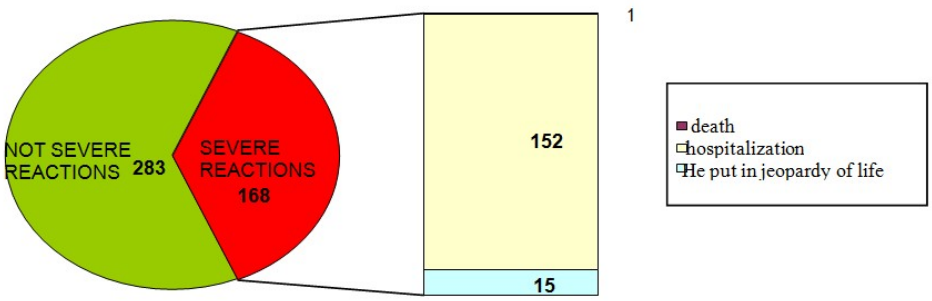
Pic. 3: Patients reported for suspected ADR / ADE broken down by gender



Pic. 4: Reports ADE / ADR divided by age of the patient



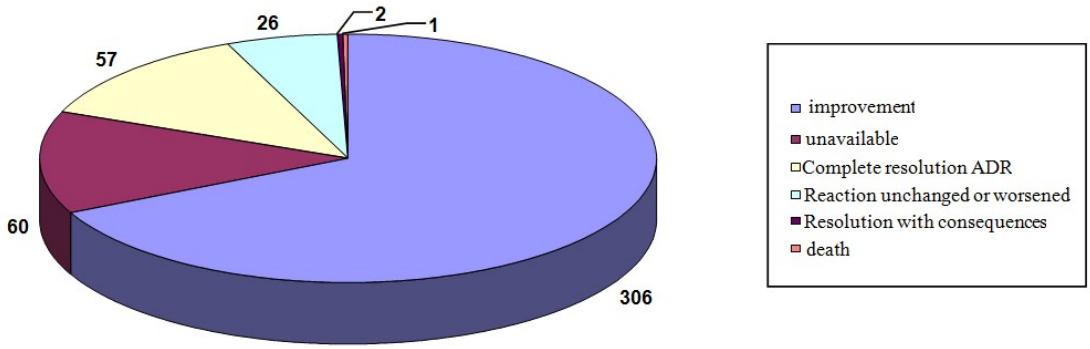
Pic. 5: Avoidance of ADR / ADE reported



Pic. 6: Classification by severity of ADR/ADE reporteds

The active substance suspect	N. reporting
Amoxicillin / clavulanic acid	52
acetylsalicylic acid	41
Ketoprofen lysine salt	27
amoxicillin	25
warfarin	25
ceftriaxone	24
nimesulide	21
clarithromycin	17
Acetylsalicylic acid / ascorbic acid	11
ticlopidine	11
clopidogrel	9
ketorolac	8
acetaminophen	7
Diclofenac	6
ibuprofen	6
levofloxacin	6
omeprazole	6
thiocolchicoside	6
tramadol	6
acenocoumarol	5
allopurinol	5
amiodarone	5
atorvastatin	5
furosemide	5
metformin	5
prednisone	5
ramipril	5
temozolomide	5
azithromycin	4
enoxaparin	4
Indomethacin / caffeine / prochlorperazine	4
ketoprofen	4
Paracetamol / codeine	4
piroxicam	4
Trimethoprim / sulfamethoxazole	4
Lysine acetylsalicylate	3
amlodipine	3
betamethasone	3
carvedilol	3
ciprofloxacin	3

Tab.1: The active substances associated with ADR / ADE in order of frequency (shows the first 40)



Pic.7: Outcome of ADR / ADE reported

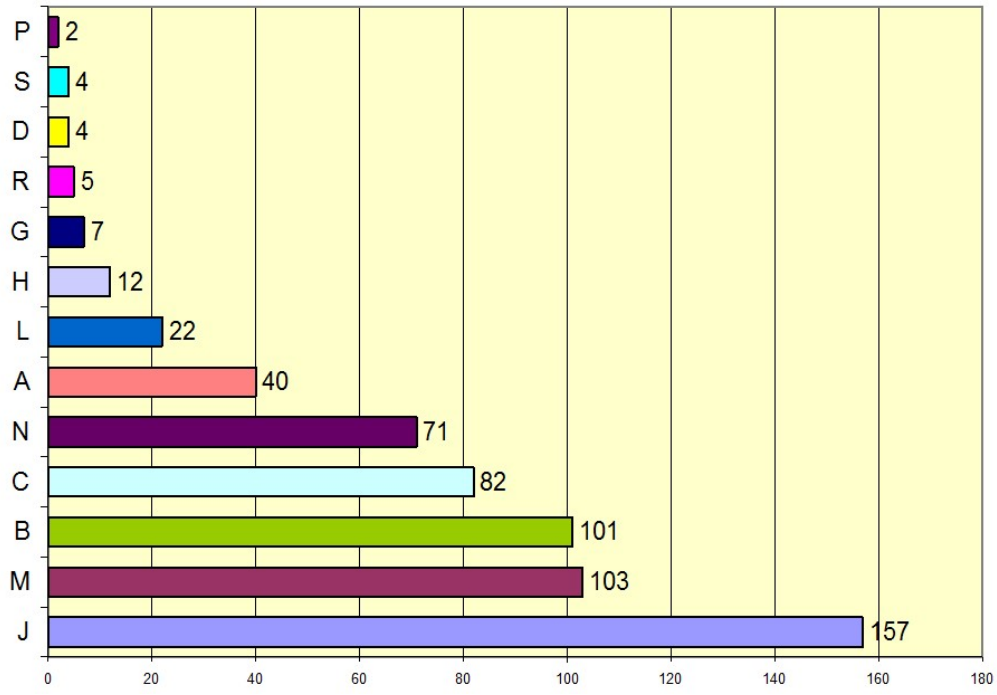
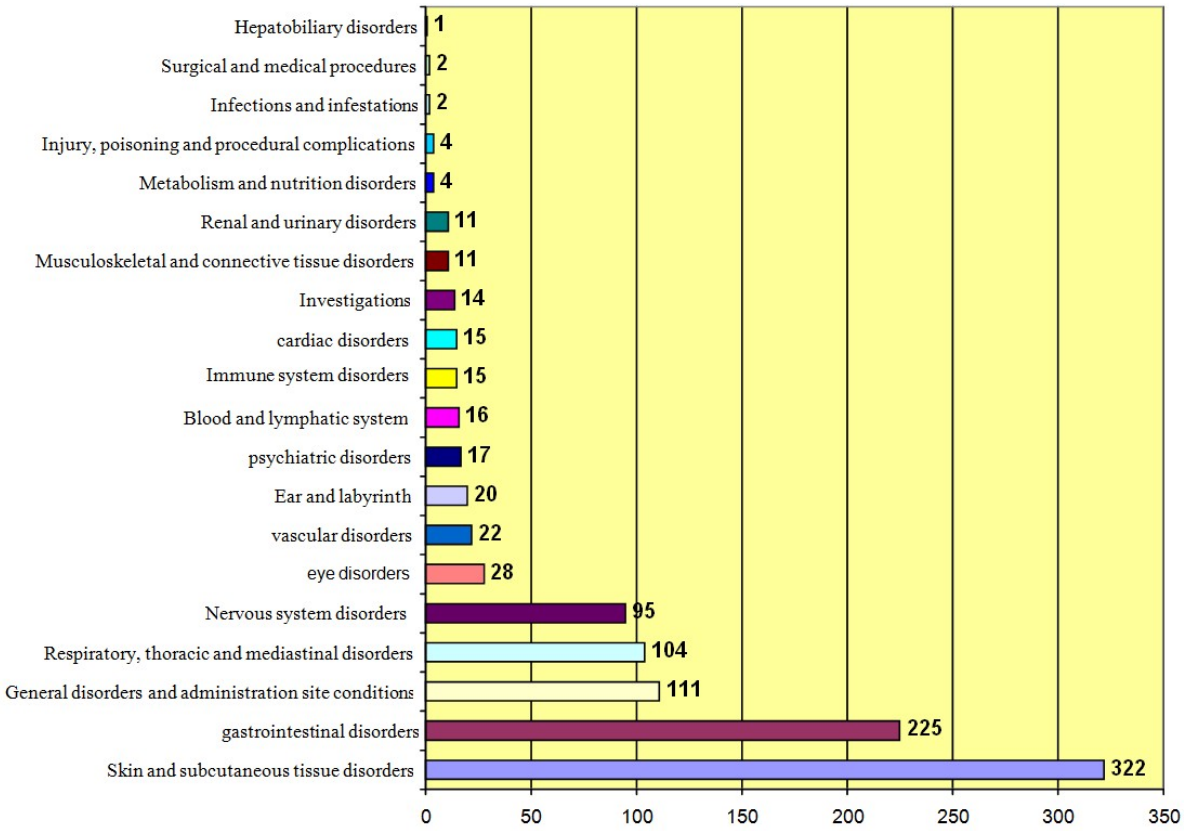
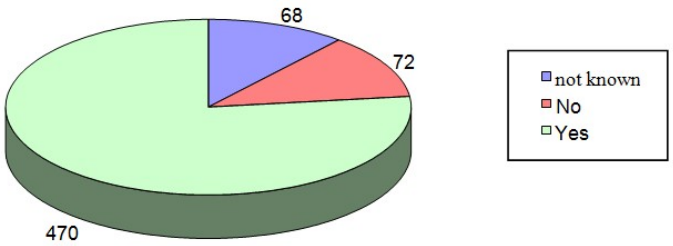


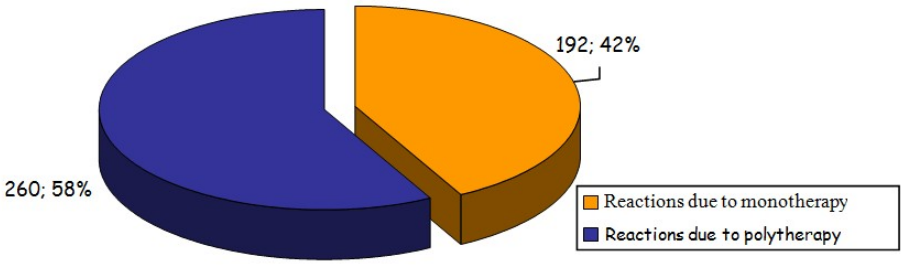
Fig.8: Suspected drugs classified by ATC (1st level)



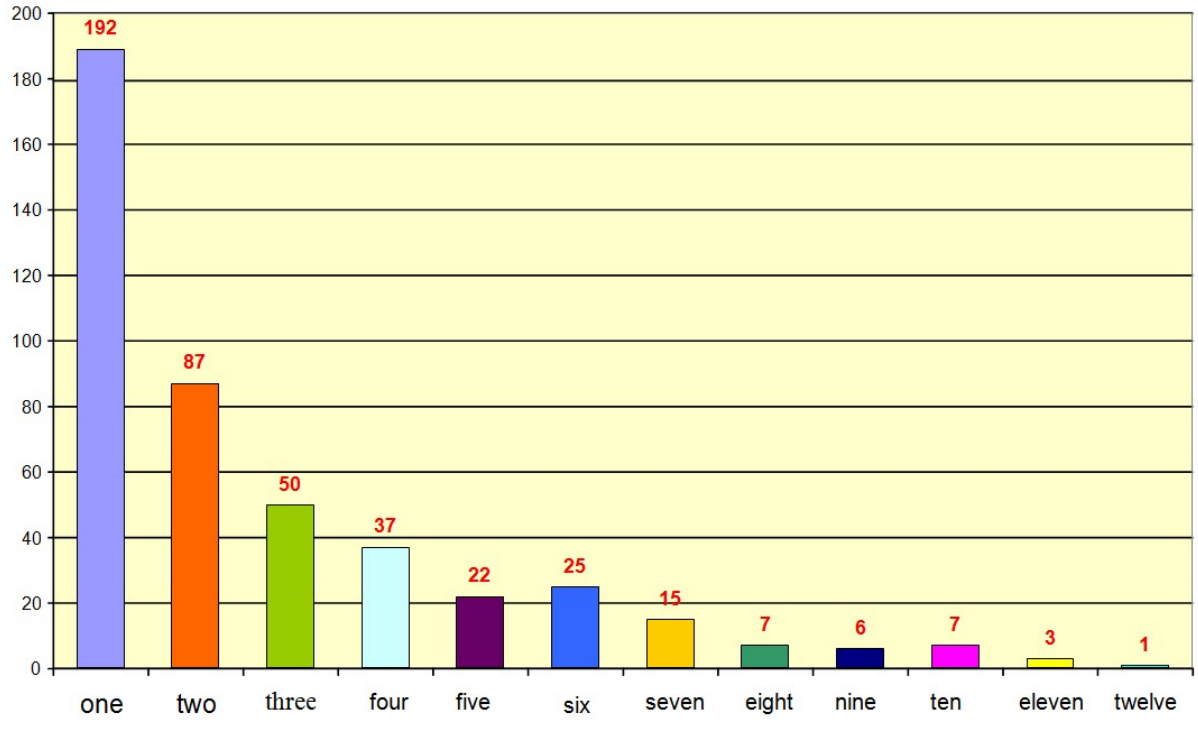
Pic. 9: type of ADR / ADE reported terminology classified according to System Organ Class (SOC)



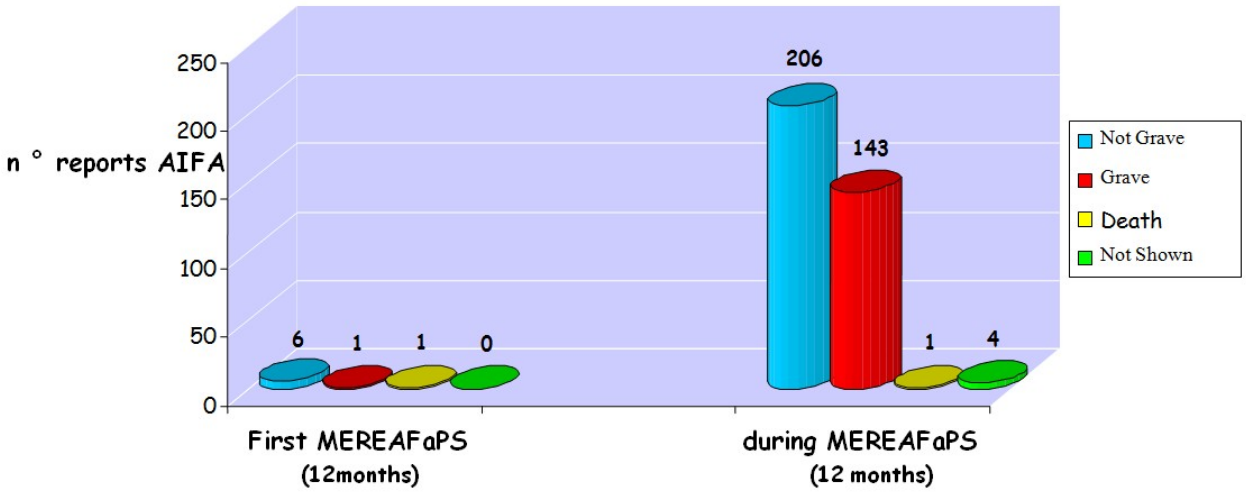
Pic. 10: Suspected drugs unless prescribed by a doctor



Pic.11: distribution reactions monotherapy polypharmacy



Pic.12 Distribution ADR / ADE for number of drugs



Pic.13 Comparison of the number of alerts in the RNF AIFA between 12 months prior the MEREAFaPS and the first 12 months of the project.