Active Surveillance on the Use of Antibiotics in Children, Particularly in the Age Group from 0 to 2 Years

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Abstract

Introduction: Despite the AIFA (Italian Medicines Agency) campaigns, the consumption and prescription unsuitability of pediatric antibiotics is growing (OsMed data from 2013 to 2015) with an increase in both the adverse reactions and bacterial resistance. 70/80% infections of the respiratory tract (0-3 years) are due to a viral infection and not bacterial.

From this point a study has been foreseen to provide, on the one hand, training interventions for Family Pediatricians (FPs) and information for families on the correct use of antibiotics and possible iatrogenic diseases caused by their misuse, and on the other, which formed a territorial survey aimed at the risk-benefit balance.

Materials and methods: The study conducted by 37 Family Pediatricians (FPs) in Molise consists of three phases: 1) in the first phase (retrospective year 2013) we assessed the prevalence of antibiotic prescriptions in the 0 to 2 years age group, the type of antibiotic used and any ADRs; 2) the second phase (2014) was that of training/information to the FPs and families on prescriptive appropriateness and proper use; 3) in the third phase (year 2015) the Prevalence of prescriptions has been reassessed and the type of antibiotic used and the possible ADRs (after the training phase).

Results: The study showed, in the first phase (2013) that the prevalence of antibiotics prescribed by 37 FP from 0-2 years old (4060 children), was 83% (number of children with at least one prescription: 3339) with a number of prescriptions of 7114 (number of items prescribed: 8367). After training, the year 2015 detected a 56% prevalence (number of children 4116. number of children treated 2327) with a significant decrease (-27%) compared to 83% in 2013. In addition there has been a reduction of 2938 prescriptions (number of prescriptions 4176) and a reduction of 2975 prescribed items (number of items prescribed 5392) with savings of € 18,854.23 (60950.15 EUR in 2013 and 42095.92 EUR in 2015). Finally there was also an improvement in the appropriateness of prescriptions according to the Guide lines: Amoxicillin (38%), followed by Amoxi/clavulanate (29.3%), Macrolides (16.3%), and Cephalosporins (15.2%). There were no ADRs in the two reference years.

Conclusion: Data showed a marked reduction in the prevalence of prescribed antibiotics, a reduction in health care costs and an improvement on prescriptive appropriateness after training courses for the FPs and continuous information to the families on the proper use, and on ADRs related to the abuse of antibiotics in this age group.

Keywords: Antibiotic; Children; Surveillance; Viral infection; ADRs

Background

From the OsMed in the last three years (2012-2015), despite the campaigns undertaken by AIFA there is an increase in the consumption and prescription unsuitability for certain categories of medicines, especially antibiotics in the age group from 0 to 14 years with an increase of adverse reactions related to them. After the vaccines, in fact, antibiotics are the class of medications with higher incidences of ADRs, especially skin and allergic type, with manifestations of hypersensitivity of variable intensity, to serious reactions such as anaphylactic shock. In this class of medication, from the numerous reports of oral formulation, cefaclor and amoxicillin are prominent (particularly in combination with clavulanate potassium) while among injectable forms, ceftriaxone is the most noted [1-3].

The OsMed 2013 data show that 28% of children between 0 and 4 years old received at least one medication to the respiratory tract with the increase in consumption of 1.1% over the previous year making it a clear non-rational use of these medications is not always based on scientific evidence. Even the OsMed data of 2008 and 2009 and ARNO Observatory data in 2011 in which the calculation of frequency of use stratified according to age groups, have shown a strong, prevalent prescription of these medications in children, which amounted to above 50%. And once again an evident "over-prescription" of these medications, especially in the age group from 0 to 2 years.

Starting from the concept of prescriptive appropriateness , defined by OMS as "a treatment is appropriate if the expected benefit is greater than the possible adverse effects anticipated, with enough margin to justify its choice," defined by OsMed: a prescription medication can be considered appropriate if performed within the clinical indications for

which the medicine has been shown to be effective and, more generally, within the indicated use (dose and duration of treatment) "or simply" the right to perform on the right patient at the right time, at the right cost, "you should be aware that the overuse of antibiotics poses a risk of:

- Individual health (exposure to the risk of adverse reactions)

- Public health (development of resistance)

70-80% of infections of the respiratory tract (0-3 years) of cases have a viral cause and not bacterial, so antibiotics are not effective for treating them. Therefore, the high antibiotic prescription in the pediatric population for childhood respiratory diseases such as sore throat, cough and cold mainly caused by viruses is a recognized indicator of inappropriate prescribing [4-10].

Because of this excessive and sometimes improper use, in recent years there has been an observation of an increased resistance of bacterial strains. The absence of pivotal trials on antibiotics in children has led to the frequent off-label prescribing of antibiotics, with possible errors in the dosage used. From the Observatory Arno data, in fact shows that resistance to antibiotics has increased significantly: from 21% in 2003, now has exceeded to 35%.

Although the problem of the resistances regards all bacteria, including those which in recent years have complicated therapy of paediatric patients are the resistances of *Staphylococcus aureus* and *Mycobacterium tuberculosis*.

The use of products capable of eliminating the saprophyte bacterial flora also inevitably selects resistant strains. If the selection pressure is contained, as in the case in which the use of antibiotics is limited to cases in which these medications are essential, the emergence of resistance occurs slowly and accounts relatively minor on the frequency of occurrence of diseases not treatable with antibiotics become inactive. If, on the contrary, the prescription of antibiotics is extremely high, the occurrence of resistances is rapid and leads to a short time to the loss of efficacy of these medications at the appearance of little or not treatable illnesses. [11].

The misuse of antibiotics is a phenomenon highlighted by more than 40 years, which covers all medical specialties and more serious, self-prescription and the pressure exerted by the patients themselves (by parents, paediatrics) on the medical profession for the inclusion of these medications in the list of those required by any form of therapeutic intervention [11].

The difficulty of use of many antibiotics in pediatrics, for failing their official one, raises the issue of off-label use, i.e., outside the prescriptive regulatory authority rules. The pediatrician who finds that a certain antibiotic is the only possible solution for the therapy and adapts common sense regarding the dosage, by deriving it from the one normally used in the adult, with the inevitable risk of dosage errors and possible consequent lack of therapeutic effect or increased probability of occurrence of adverse events.

Pediatrics therefore remains officially often bereft of essential commodities and the pediatrician must somehow make do, hoping that there are no unforeseen damage for which he/she ends up being legally unprotected [11].

In addition to the excessive use of antibiotics, a further factor favouring the emergence of resistance is represented by the use of insufficient dosages, which determine the contact for a long time between bacteria and antibiotic concentrations lower than the minimal inhibitory [11]. See the lower dose of vancomycin-resistant strains that caused Streptococcus aureus.

Desirably that in the future the problem off-label use of antibiotics in pediatrics is exceeded with the start of a greater number of controlled clinical trials aimed at the child. It is also hoped, as the use of vectors for the intracellular transport of antibiotics or the use of different natural factors from traditional antibiotics, can develop, also in order to allow an appropriate pediatric use [11].

International and National guidelines for the Institute of Health and Clinical Excellence (NICE), 2008 affirmed that:

- In the case of a child with a sore throat, though there are other signs of infection concomitant respiratory tract (nasal discharge, cough) it is certainly a viral disease.

- All available guidelines support antibiotic therapy only for strep throat infection associated with β-hemolytic streptococcus group A (SBEA).

- In children "at risk" of complications due to the presence of a pre-existing co-morbidities, in which antibiotics are to be used for the treatment of each type of fever, suffering from: heart, lung, kidney or liver pad, diseases neuromuscular, immunosuppression, cystic fibrosis, prematurity [12-14].

New NICE 2015 Guidelines: Antimicrobial stewardship: systems and processes for effective antimicrobial use medicines recommend the effective and rational use of antibiotics in children, youth and adults.

They also suggest that physicians devote time to discussions with patients about the nature of their likely illness, on the benefits and risks of an immediate antimicrobial prescription, on alternative options such as watchful waiting and/or a delayed prescription and on the reasons why prescription an antibiotic may not be the best option for them - for example, if they have a self-limiting respiratory tract infection. It is therefore necessary for a more rational use medication, both by doctors but especially from parents who frequently administer the medication to the baby with infections of the upper respiratory tract, without consulting your pediatrician.

A study in the area showed that about 77% of family pediatricians considered insufficient their preparation insufficient on pediatric pharmacology and pharmacovigilance that 78% of them would participate in the special training courses on these subjects. From this study conducted on the territory by 552 Family Pediatricians (FPs), therefore a consideration emerges that there is a need for a training project on the proper use of antibiotics in children, which will also rely on knowledge of pediatric pharmacology, pharmacodynamics and pharmacokinetics in children as well as all acquisitions required on the concept of pharmacovigilance in pediatrics and the report of adverse events [15].

The training project on Pediatricians will spread widely to the FPs Guidelines Reference and implement skills (training of FPs) for a correct diagnosis, for an effective therapy and close follow-up of the pathologies that require the use of these medications in all children from 0 to 14 years according to their clinical severity. The training program also will provide and add to current knowledge: a) a diagnostic improvement and prescriptive appropriateness, b) the acquisition of the reference epidemiological data with the least number of possible errors, c) a reduction in the number of antibiotic prescriptions compared to the past (prevalence OsMed data and ARNO data), d) a reduction in public spending through a reduction in

both of the improper prescriptions and hospitalization, e) the fair value of ADRs related to the administration of the medication in question, f) an increase in direct reports of ADRs after FPs training.

All in order to ensure the development of the knowledge and facilitate the transfer of the best scientific evidence to the professional practice of the FPs. Finally the training project will promote a closer synergy between FPs and Families through a better and more accurate information given to families on the use of antibiotics that will lead to a reduction of the "do it yourself" and self- prescription for illnesses that are not include in GR and their use will lead for sure to a reduction in days lost from work by parents and of any hospitalizations (reduction of unnecessary hospitalization). All this will be spread through an information campaign that will include, in addition to the direct contact of the FPs with families with specific information talks, the realization of posters, referts, brochures and possibly CDs sent direct to parents and displayed in FPs surgeries (and/or delivered directly to families) on the correct use of antibiotics.

From these considerations, there was a necessity for a study to be set up in the territory that has provided on the one hand training interventions for FPs and information for families regarding the proper use of antibiotics and possible iatrogenic illnesses caused by their misuse, on the other hand that has constituted an active territorial survey on prescriptive appropriateness and safety of these medications in children aimed at the risk-benefit balance evaluation on usage. The study conducted by FP-MCRN (Family Pediatricians-Medicines for Children Research Network) [16-20], will first of all want to overcome the limits of OsMed data that foresee an inability to trace the diagnosis that underlies in the prescription, and that of a proper assessment of perscriptions in the various pediatric age groups (especially 0-2 years).

Considering the national guidelines and international ones (NICE 2008, NICE 2015, etc.) on the correct use of antibiotics in children, the possibility of recruiting close to 100% of patients, examinations at their clinics (self-help), collaboration with families and proper compliance with the protocol, the study conducted by the FPs will allow its conclusion to reach an overall improvement on prescriptive appropriateness, to have a clear picture of the epidemiological situation, to obtain effective control of the benefits of the therapy, a reduction the number of relapses (antibiotic resistance) and a proper evaluation of those that are the possible ADRs related to therapy. Finally an increase in savings of pharmaceutical expenditure by the SSN and a reduction of prescriptions (through proper diagnosis) but mainly a reduction in unnecessary hospitalization.

Materials and Methods

The study conducted by 37 Family Pediatricians (FPs) of Molise was organized in three phases:

1. In the first phase (retrospective year 2013) we assessed the prevalence of antibiotic prescriptions in the 0 to 2 years age group, the type of antibiotic used and any ADRs associated with their use; Furthermore pharmaceutical expenditure was calculated relative to the administered antibiotics.
2. The second phase of training (2014) was that of training/information to FPs and families prescriptive appropriateness and their proper use.
3. In the third phase (year 2015) the Prevalence of prescription was reassessed and the type of antibiotic used and the possible ADRs (after the training phase) and the pharmaceutical expenditure relative to the administered antibiotics.

Processing and comparison of data of the year 2013 and the year 2015 was made in order to verify if and how the training is being conducted on Family Pediatricians and families, and if it has been beneficial. The data was taken from FARMASTAT database and in particular the following prescription and consumption indicators for the evaluation of the results have been taken into consideration: the number of prescriptions, the number of pieces and the pharmaceutical expenditure.

Results

Development of prescriptive data of antibiotics in the age 0-2 years (year 2013)

In the first phase of the project prescriptive data of the antibiotics used in children in the age group 0-2 years as related to 2013 (the previous year of study) were procured and processed in order to get a clear picture of prescriptions in the Molise Region (MR). The number of patients was also assessed in order to be able to calculate the prevalence of use of antibiotics in children 0-2 years as prescriptive appropriateness indicators.

The results show that the number of antibiotic prescriptions made by 37 FPs of the MR (Table 1) for children aged 0 to 2 years were 7,114 corresponding to a prescribed number of 8,367 pieces (Table 2).

Area/District	Family Pediatricians
Agnone	1
Isernia	6
Venafro	4
Bojano	4
Campobasso	11
Larino	3
Termoli	8
TOTAL	37

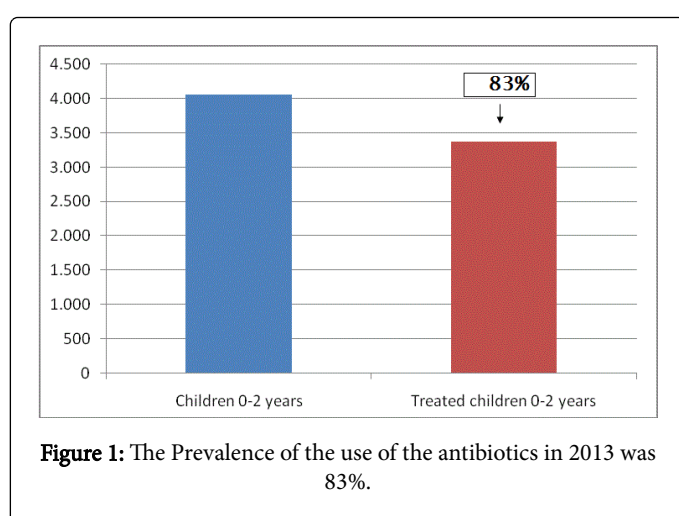**Table 1:** Family pediatricians of the Molise region divided by area/district.

The consumption data according to area/district, amounting to a total of €60,950.16 for the prescription of antibiotics, (in the age group 0-2 years), during the year 2013 in the MR (Table 2).

Zone/District	Prescriptions	Pieces	Expenditures (euro)
Agnone	104	109	931,85
Isernia	1361	1766	12.027,97
Venafro	543	749	4.412,98
Bojano	775	860	5.268,95
Campobasso	1925	2259	15.258,13
Larino	587	653	5.318,99
Termoli	1819	1971	17.731,29
TOTAL	7.114	8367	60.950,16

Table 2: Prescription indicators and expenditures 2013.

The number of the children 0-2 years treated with antibiotics for each zone/district were also analysed in order to be able to calculate the data of prevalence of use.

As is known, the indications of appropriateness of prescribing specialized medicine are expressed in terms of prevalence of use (P=n° subjects/population ^{*100}). Whereas the number of children 0-2 years in the MR for the year 2013 was 4,060 and the number of children 0-2 years who received at least one antibiotic prescription during the annuity in question was 3369, it follows that the prevalence of use (P = 3369 / 4060 * 100) of the antibiotics prescribed in the age group 0-2 years by Pediatricians for the MR (in the year-end 2013) was 83% (Figure 1).

Figure 1: The Prevalence of the use of the antibiotics in 2013 was 83%.

Finally we were used prevalence data of antibiotics used in the age of 0-2 years in the year 2013 according to the active principle. The association Amoxicillin+clavulanic acid proved to be the most prescribed (33%), followed by Amoxicillin (24.3%), Macrolides (22.3%), Cephalosporins (18.2%) and others (phosphonic acids, aminoglycosides, fluoroquinolones, Lincosamides, Sulfa drugs: 2.2%).

Development of prescriptive data of antibiotics in the age 0-2 year (year: 2015)

The third phase of the project involved the development and comparison of prescriptive data of antibiotics used in the age group 0-2 years, in the year 2013 and 2015, in order to evaluate a possible improvement in prescribing following training events/information.

All this in order to evaluate the improvement of appropriateness prescriptive in the next year to the training/information events, by monitoring the prescription of drugs object data in the year 2015.

In fact, in this phase of the project the prescriptive data of antibiotics for pediatric use in the age 0-2 years for the year end 2015 were retrieved and processed, in order to get a clear picture of data of the antibiotic prescriptions in the MR after training and proper attention to the use of antibiotics by the Family Pediatricians.

As for the structures involved, 37 FPs of the MR (Table 1) divided by area/district participated in the study.
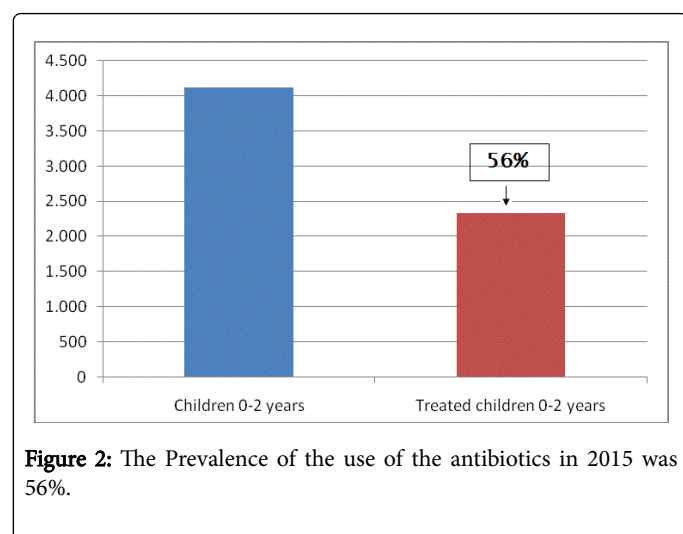
The results are shown in Table 3 and highlighted showing the number of antibiotic prescriptions made by FP of the MR for children aged 0 to 2 years was 4176 corresponding to a prescribed number of 5392 pieces. The data was analysed for each zone/district. There are also the consumption data broken down by area/district, amounting to a total of € 42,095.93 for the prescription of antibiotics, in the age group 0-2 years, during the year 2015 in the MR.

District	Family Pediatricians	Children 0-2 years	Treated children 0-2 years	Total prescriptions	Total pieces	Expenditure (euro)
Agnone	1	149	65	76	98	1.175,85
Isernia	6	580	451	880	980	8.158,59
Venafro	4	415	182	378	595	3.292,38
Bojano	4	450	283	532	768	5.119,97
Campobasso	11	1201	573	986	1.286	10.365,57
Larino	3	345	208	348	523	3.762,72
Termoli	8	976	565	976	1.142	10.220,85
Total	37	4.116	2.327	4.176	5.392	42.095,93

Table 3: Prescription indicators and expenditures 2015.

It was also analysed the number of the children (0-2 years) treated with antibiotics for each zone/district, in order to be able to calculate the data of prevalence of use.

As is known, the appropriateness of prescribing indicators in specialized medicine are expressed in terms of prevalence of use (P=n° subjects/population ^{*100}). Whereas the number of children 0-2 years in the MR in the year 2015 was 4116, the number of children 0-2 years who received at least one antibiotic prescription during the annuity in question was 2327, it follows that the prevalence of use (P = 2327 / 4116 * 100) of the antibiotics prescribed in the age group 0-2 years by FP for the MR in the year 2015 was 56% (Figure 2).

Figure 2: The Prevalence of the use of the antibiotics in 2015 was 56%.

Finally we analysed the prevalence data of the antibiotics used in the age 0-2 years old in 2015 divided by the active ingredient. L Amoxicillin proved to be the most prescribed (38%), followed by Amoxicillin+Clavulanic acid (29.3%), Macrolides (16.3%), Cephalosporins (15.2%) and others (phosphonic acids, aminoglycosides, fluoroquinolones, Lincosamides, Sulfa drugs: 1.2%).

Discussion

The study "Active surveillance on the use of antibiotics in children, particularly in the age group from 0 to 2 years", is the first regional pharmacovigilance project presented by the Molise Region in the pediatric field.

Taking into account that the AIFA places particular relevance to projects focused on special populations such as the pediatric population, the elderly with poles diseases, institutionalized patients and pregnant women and/or breastfeeding women.

Specifically the study was a phase IV research project, coordinated by a FP-MCRN (Family Pediatrician-Medicines for Children Research Network), which on the one hand provided training and information regarding the proper use of antibiotics in children and possible iatrogenic diseases caused by their misuse, on the other hand setting up a territorial active survey on prescriptive appropriateness and safety of these medications in children aimed at the risk-benefit balance on usage.

The project's aim is to improve prescriptive awareness, giving an accurate diagnosis and attaining a reduction in pharmaceutical expenditures related to antibiotic use from 0-2 years.

The study wanted firstly to overcome the limits of OsMed data, which they see as an inability to trace the diagnosis that underlies the prescription, on a proper assessment of the requirements in the age group that ranges from 0 to 2 years.

Considering the national guidelines and international ones (NICE 2008-NICE 2015, etc.) on the correct use of antibiotics in children, the possibility of recruiting close to 100% of patients, examinations at their clinics (self-help), collaboration with families and proper compliance with the protocol, the study conducted by the FP-MCRN has allowed the conclusion to achieve an overall improvement of prescriptive appropriateness, to have a clear picture of the epidemiological situation, to obtain effective control of the benefits, a reduction in the number of relapses (antibiotic resistance) and a proper evaluation of those that are the possible ADRs related to therapy.

More specifically, therefore, the project is proposed as objectives the improvement of diagnostic and prescriptive appropriateness, reducing unnecessary hospitalization in pediatrics and achieving reduction in pharmaceutical expenditure relating to the use of antibiotics in the range of ages 0-2 years.

The activities pursued under the aforesaid project have been divided into three time steps:

1. Development of prescriptive data of antibiotics in the 0-2 age group (year 2013).
2. Training/information events on pediatricians and families on the proper use of antibiotics.
3. Development of prescriptive data of antibiotics in the age 0-2 age group (2015) compared with those of 2013.

In the first phase of the project, as revealed in the results, prescriptive data of the antibiotics used in children in the age group 0-2 have been found and processed as related to 2013, and the previous years in order to have a clear picture of prescriptions in the Molise Region.

The results showed that the number of antibiotic prescriptions made by paediatricians of the Molise region for children aged 0 to 2 years is 7,114 corresponding to a prescribed number of 8,367 pieces.

Also presented was the consumption data broken down by area/district, amounting to a total of €60,950.16 for the prescription of antibiotics, in the age group 0-2 years, during the year 2013 in the MR. Also analyzed was the number of the assisted 0-2 years treated with antibiotics for each zone/district, in order to be able to calculate the data of prevalence of use.

Whereas the number of assisted 0-2 years in the Molise region for the year 2013 is 4,060 and the number of children 0-2 years who received at least one antibiotic prescription during the annuity in question is 3369, it shows that the prevalence of use (P = 3369 / 4060 * 100) of the antibiotics prescribed in the age group 0-2 years by Pediatricians for the Molise Region family in the year-end 2013 is 83%.

Finally we analysed the prevalence data of the antibiotics used in the age 0-2 year-olds in the year 2013 according to the principle factor. The association Amoxicillin+clavulanic acid proved to be the most prescribed (33%), followed by Amoxicillin (24.3%), Macrolides (22.3%), Cephalosporins (18.2%) and others (phosphonic acids, aminoglycosides, fluoroquinolones, Lincosamides, Sulfa drugs: 2.2%).

The processing of prescription data of antibiotics in children, particularly in the age group 0-2 years has shown a strong prescriptive critical activity in the Molise region in the year 2013 examined.

Therefore, in light of the results before mentioned, there was a clear necessity to undertake an information campaign on the appropriate use of this class of medication, either through the organization of training/information events, and through the dissemination of national and international guidelines on the correct antibiotic use in therapy.

As it is known, in fact, an inappropriate use of antibiotics is a potential risk not only for individual health, with an increase in exposure to the risk of adverse reactions, but also for public health

resulting in development of resistance, and the problem of costs to the National Health Service.

Among the main unjustified use of antibiotics, highlighted is the fact of the high use of this class of medication for the treatment of colds, flu and other respiratory infections, which for 80% of cases are due to viral and not bacterial, especially in the 0 to 2 years age group, and therefore antibiotics are not effective for treating them.

The high prescription of antibiotics in the pediatric population for childhood respiratory diseases such as strep throat, acute cough and cold mainly caused by viruses is a recognized indicator of inappropriate prescribing. It then proceeded to give relief to these aspects of inappropriateness prescriptive disseminating the main aspects of national and international guidelines for paediatricians. In particular, it was forwarded, as shown in the international guidelines (NICE 2008-2015), in the case of a child with a sore throat, though there are other sign of infection concomitant respiratory tract (nasal discharge, cough) is certainly a viral disease. In addition, another important aspect is that it is reasonable to delay antibiotic therapy for a few days, waiting for proper diagnosis and ascertained through use of instrumental tests at its clinics (self-help quick test to SBEA, urine stick, etc.) or performed in the laboratory, in all mild cases of upper respiratory tract infection. In this regard, we note that several studies have addressed the problem of early treatment compared to delayed therapy in children, this shows that a delay of antibiotics until 9 days after onset of symptoms does not involve any increase in the risk of complications or treatment failure or recurrence.

Finally, information about justified use of antibiotics in pediatrics were made known. In particular, in regard to the management of pharyngitis in pediatric age (which represents one of the main clinical conditions in which the use of antibiotics is most frequent) guidelines (national and international) support available antibiotic therapy exclusively for pharyngotonsillitis associated with infection by Streptococcus β-hemolytic group A. Moreover antibiotics should be used in so called children at "risk", or for the processing of each type of fever in case of co-morbidity for pre-existing cardiac, pulmonary, significant renal or hepatic, neuromuscular diseases, immunosuppression, cystic fibrosis and prematurity, given the high risk of complications.

Attention has been drawn to November 15, 2014, c/o to the Department of Medicine and Health Sciences of the University of Molise, a training/information event was organized and directed to family pediatricians in the MR, in context of the presentation of CRFV "regional initiatives for prevention and health protection-Establishment of the regional Pharmacovigilance Centre."

The event has paid particular attention to the importance of promoting research and pharmacological trial culture, by building an even higher skill aimed especially at protecting the most vulnerable as the pediatric population, and its attention to the culture of iatrogenic disease for a careful analysis of the risk/benefit ratio of medication for use in children. Also pediatrician's colleagues were stimulated to major reporting of adverse reactions in children.

The aims of the project were illustrated and announced, first the data of the pediatric antibiotic prescriptions, promoting awareness on appropriateness of prescription through the communication of the above mentioned national and international guidelines.

Previously, a meeting had been established to present the research project by the Scientific Coordinator of the project with the Molise Family Pediatricians who then followed the electronic transmission of the data collected in order to have the involvement of all the pediatricians in the Molise region.

A further meeting was set up on of briefing by the Scientific Coordinator of the project with the Family Pediatricians of Molise in order to confirm the concept of the use of appropriate antibiotics in pediatrics.

Furthermore, the Scientific Coordinator of the project periodically sent e-mails to family pediatrician of Molise on the focus of the study's objectives with particular regard to the correct use of antibiotics in the age group from 0 to 2 years.

Finally it highlights the information/training work done by Family Pediatricians with the families of their patients to stress the concept of the proper use of medicines in children, and in particular of antibiotics in the most vulnerable age group, avoiding the "do it yourself" by families , that expose children to the risk of adverse symptoms.

The final phase of the project involved the development and comparison of prescriptive data of antibiotics used in the age group 0-2 years, in the year 2013 and 2015, in order to evaluate a possible improvement in prescribing, following training/information events.

All in all to evaluate the improvement of prescriptive appropriateness in the next year to the training/information events, by monitoring the prescription of medication as object data in the year 2015.

In fact, in this third phase of the project the prescriptive data of antibiotics for pediatric use in the age 0-2 years for the year end 2015 were retrieved and processed, in order to get a clear picture of prescriptions in the Molise region after training and proper attention to the use of antibiotics by the Family Pediatricians.

As for the structures involved, 37 FP of the MR divided by area/district, participated.

The figures were taken from FARMASTAT database and in particular the following has been taken into consideration, prescription and consumption indicators for the evaluation of the results: the number of prescriptions, number of items and pharmaceutical expenditure. The number of patients assessed in order to be able to calculate the prevalence of use of antibiotics in children 0-2 years as a prescriptive appropriateness indicator.

The results showed that the number of antibiotic prescriptions made by FP of the MR for children aged 0 to 2 years is 4176 corresponding to a prescribed number of 5392 items. The data was analysed for each zone/district, the consumption data broken down by area/district, amounting to a total of € 42,095.93 for the prescription of antibiotics, in the age group 0-2 years, during the year 2015 in the MR are also presented.

Analyzed was the number of the children 0-2 years treated with antibiotics for each zone/district, in order to be able to calculate the data of prevalence of use. Whereas the number of children 0-2 years in the MR in the year 2015 was 4116, the number of children 0-2 years who received at least one antibiotic prescription during the annuity in question was 2327, shows the prevalence of use (P=2327/4116 *100) of the antibiotics prescribed in the age group 0-2 years by FP of the MR in the year 2015 was 56%.

Finally we analyzed the prevalence data of the antibiotics used in the age 0-2 year-olds in 2015 divided by the active ingredient. L

Amoxicillin proved to be the most prescribed (38%), followed by Amoxicillin+clavulanic acid (29.3%), Macrolides (16.3%), Cephalosporins (15.2%) and others (phosphonic acids, aminoglycosides, fluoroquinolones, Lincosamides, Sulfa drugs: 1.2%).

By comparing prescription data of 2013 and 2015 after the formation of Family Pediatricians and the information to families on the proper use of antibiotics and of any adverse events related to their misuse, the first thing that emerges is the prevalence of prescriptions has gone from 83% (Year 2013) to 56% (Year 2015) with a significant decline of 27%.

This indicates two things: the first is that the prevalence in 2013 of 83% is very high and the second things is that through proper training/information to pediatricians and families, huge results can be obtained which can be seen from the response to the prevalence decrease of 56% in 2015.

Maintaining almost unchanged the number of children, age group of 0-2 in the two years considered, (specifically for 2013 children 4060 and for the year 2015 children 4116), there has been a reduction in the number of prescriptions amounting to 2938 (number 7114 in year 2013 to number 4176 in year 2015) and a reduction in the number of prescription pieces equal to 2975 (number prescribed for year 2013 was 8367 and number of items prescribed for year 2015 was 5392 .If we want to consider the expenditure incurred by the Region of Molise, there has been a saving expenditure of EUR 18,854.23 by comparing the costs incurred in the years 2013 and 2015 (EUR 60,950.16 in the year 2013 to 42,095.93 in the year 2015).

Assessing any adverse events that occurred in the two reference years in children aged 0 to 2 years after medication treatment with antibiotics, have not revealed any adverse events, even gastro enteric disorders.

Finally, there has been an improvement on prescription appropriateness according to reference guidelines: in fact, while for the year 2013 the association Amoxicillin+clavulanic acid proved to be the most prescribed (33%), followed by Amoxicillin (24.3%) , Macrolides (22.3%), cephalosporins (18.2%), for 2015 the most prescribed was the Amoxicillin (38%), followed by Amoxicillin+clavulanic acid (29.3%), MACROLIDES (16, 3%), and the cephalosporins (15.2%) as suggested by the reference guidelines.

Conclusion

The following emerges after a comparison of prescriptive data of 2013 and the year 2015 after the formation of Family Pediatricians and the information to families on the proper use of antibiotics and of any adverse events related to their misuse:

1. The data of the prevalence of prescriptions has gone from 83% (2013) to 56% (2015) with a significant decline of 27%.

2. There was a reduction in the number of prescriptions equal to 2938 and a reduction of the number of pieces prescribed equal to 2975, maintaining almost unchanged the number of assisted of 0-2 years in the two years under review.

3. There have been saving expenses of EUR 18,854.23.

4. There were no ADRs in the two reference years.

5. Improving prescriptive appropriateness according to guidelines: The most prescribed was Amoxicillin (38%), followed by Amoxicillin+clavulanic acid (29.3%), Macrolides (16.3%), and the Cephalosporins (15.2%).

Overall, the importance of proper training is clear for paediatrician's appropriateness of prescribing antibiotics for this vulnerable class of children, correct information for families on knowledge and experience of pediatric medication and the importance of always consulting the pediatrician before "misuse" of medication that do not resolve the clinical solution but rather expose these young patients at risk.

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