

## The Beneficial Effects of Medication Reconciliation on Paediatric Patients

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### Abstract

**What is known and Objective:** Information on the safety of paediatric drug therapy is still limited in particular with regard to patients with chronic treatment and in polytherapy. This study aimed to identify drug-drug interactions (PDDIs) in a strategy that can guarantee the safety of drug therapy through medication reconciliation, an important tool for personalised treatment of paediatric patients.

**Methods:** This was a multicentre pilot study including a total of 138 paediatric patients across different hospitals. Patient demographics and therapy were evaluated. The analysis of collected data was performed by two clinical pharmacists and one paediatrician. The PDDIs were identified using Micromedex<sup>®</sup> and Clinical Pharmacology<sup>®</sup>.

**Results and discussion:** The pharmacological analysis identified 227 PDDIs: 94 (74.5%) were defined as major and moderate interactions. Only 1 case showed a contraindicated drug association. No interaction was detected in 77 cases (25.3%). Evidence of the beneficial consequence of medication reconciliation is provided.

**What is new and Conclusion:** Despite limited data our study is the first to be performed in Italy to collect data on PDDIs in the paediatric population. Our data show that PDDIs are a major issue in paediatric patients that can be limited by medication reconciliation.

**Keywords:** Medication reconciliation, ADRs, Drug-drug interactions, Rehabilitation.

### What is known and Objective

Medication errors affect the whole process of drug management. They occur most frequently during care transition: hospitalisation of the patient in hospital and discharge, transfer of the patient between departments of the same structure or between different health facilities. They are often related to unintended discrepancies, which can cause damage prolonged hospitalisation or use of additional health resources. Upon admission to the hospital, according to the literature, 67% of patients suffer from unintended discrepancies in the therapy [1]. Following discharge, an inaccurate or incomplete communication between professionals as well as between professionals and patients and family / caregiver is indicated as a determining factor in the occurrence of adverse events since it influences adherence to therapy. The aging of the population and the increase in chronic diseases and the polytherapy both increase the risk of medication errors. They may account for up to 33% of all hospital errors [2], and unintended medication discrepancies occur in ~33 to 66% of hospital admissions [3]. For this reason, World Health Organization (WHO) recommended the adoption of medication reconciliation to evaluate carefully the safety and appropriateness of drug therapy for a given patient and to prevent discrepancies and potential adverse drug reactions (ADRs) [4]. Following these indications, the Italian Ministry of Health has issued Recommendation number 17, which regulates the process of therapeutic reconciliation in the various care settings in Italy [5].

Medication reconciliation is a multistep process involving two phases: recognition and reconciliation. In the first phase data concerning the patient and the drugs taken, whether they are Rx, without prescriptions or over the counter (OTC), are collected. The second phase, the reconciliation, provides a comparison between the therapy followed and the one to be set. The information collected is then made available to the stakeholders involved in the process of registration/transmission/use of the data.

The objective of this study was to promote therapeutic reconciliation in the departments dealing with paediatric patients to assess the impact of a clinical pharmacist in wards. Our specific focus was the identification of potential drug-drug interactions (PDDIs) and the optimisation of drug dosage regimens by medication reconciliation, in paediatric hospital settings across the Lombardy Region.

## Methods

We designed an observational pilot project of medication reconciliation activity, which was started in March 2017 focussing on the inpatient paediatric population. The study encompassed patients hospitalised in 10 participating Hospital Units distributed across the Lombardy Region, of which 7 Paediatric Units, 1 Neurologic Paediatric Units, 1 Paediatric Oncology Unit, 1 Paediatric Nephrology Unit and 1 Paediatric Intensive Care Unit, representing nearly 18% of all paediatric units in the region.

We enrolled all patients, aged 0-18 years, during their

hospitalisation, if treated with 2 or more pharmacological drugs simultaneously, independently of the clinical indication of the prescriptions.

A medication reconciliation data sheet was designed ad hoc according to the guidelines of the Italian Ministry of Health. The data sheet was divided into two sections: recognition and reconciliation (Figure 1). The recognition section was designed to collect patient personal data, concomitant and/or chronic diseases if present. The clinicians had also to register the list of drugs, including their dose, the frequency and route of administration and whether it was an occasional or chronic use. The completed data sheet was then electronically transferred to the clinical pharmacist who analysed the PDDIs, controls dosages and prescriptive appropriateness. Thereafter, the clinical pharmacist filled in a report, containing the indication of the existence of PDDIs and their severity level, according to Micromedex® and Clinical Pharmacology® [6,7] and possible therapy adjustments. Pharmacological interactions had to be classified by gravity:

**Specify other reason (s) for the counselling request (if applicable):**

- adverse event in progress
- adverse event prevention
- dosage adjustment

**THERAPIES**

RECOGNITION			RECONCILIATION				
Drug name (generic or branded)	Dose / Frequency	route of administration	Stop	Modify	Going on	New drug	Notes

**PHARMACOLOGICAL ANALYSIS (by the Pharmacovigilance Service ASST-FBF-Sacco, Milan):**

**SECTION 2 (by the reporting Doctor)**

**TO COMPLETE AS A RESULT OF RECEIVING PHARMACOLOGICAL ANALYSIS (IF APPROPRIATE) AND RE-START THERAPIES**

**THERAPIES**

RECOGNITION			RECONCILIATION				
Drug name (generic or branded)	Dose / Frequency	route of administration	Stop	Modify	Going on	New drug	Notes

**PHARMACOLOGICAL ANALYSIS (by the Pharmacovigilance Service ASST-FBF-Sacco, Milan)**

Figure 1: Medication reconciliation Data Sheet.

“contraindicated”, when co-administration endangers the life of the patient; “major” when the interaction could be potentially lethal and/or require medical intervention to minimise or prevent serious adverse effects, “moderate”, when the interaction could cause a deterioration of the patient’s condition and/or require a modification of therapy; “minor” when the drug interaction would not usually result in clinically significant effects and not requiring alteration in therapy or further monitoring. Finally, information on the possible advantage of pharmacokinetics or pharmacogenetics test was included. The data sheet was finally returned to the clinicians. It was not necessary to make any request for ethical approval because the results derive from daily clinical practice.

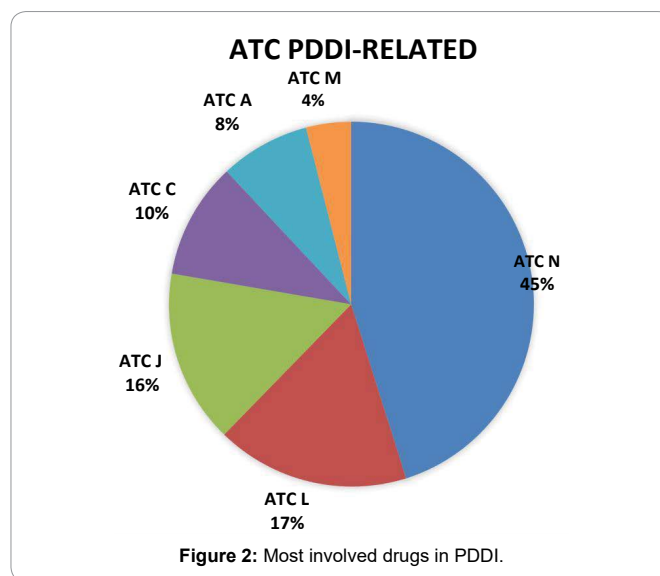
## Results and discussion

During a six-month period, 138 medication reconciliation reports were generated in the various hospitals on multidrug-treated paediatric patients (0-18 years). Medium age of patients was 7 years (+/- 6.6 standard deviation); 51.4% were males and 43.5% were females.

The reports in which at least one drug interaction had been identified were 61 (44.2%), for a total of 227 PDDIs: of these 0.4% were of the contraindicated type, 41.2% were major and 58.3% were moderate. Table 1 shows the list of wards that took part in the pilot project: for each wards a number of identified PDDIs was reported, the corresponding number of medication reconciliation reports within which they were identified and the total number of reports requested.

Figure 2 shows the frequency of the drugs involvement in the reported PDDIs, classified according to the Anatomical Therapeutic Chemical Classification system (ATC). In particular, the most involved drugs in PDDI were furosemide (ATC C 9.4%), followed by phenobarbital (ATC N 8.9%), clarithromycin (ATC J 8.4%), fluconazole (ATC J 6.8%), tacrolimus (ATC L 6.2%), phenytoin (ATC N 5.2%), morphine (ATC N 4.7%).

We then assessed the relevance of medication reconciliation in the resolution of the ADRs. We found that in 44.2% of cases the counselling approach resolved the existing ADR leading to a better therapeutic regimen without impact on efficacy. The most significant example of pharmacological analysis comes from the PICU of Buzzi Hospital, in which not only the number of molecules prescribed to each patient, but also the severity of clinical manifestations made the synergy between clinicians and pharmacologists an excellent strategy. In this regard, we report two clinically significant examples: the first is the case of a 5 years-old female patient affected by congenital epilepsy, chronically treated with valproic acid. After receiving a diagnosis of pharyngitis clarithromycin was prescribed. On the fourth day of treatment the girl experienced alopecia. It is presumed that the adverse



event can be justified by the inhibition of P glycoproteins, efflux transporter, involved in the process of elimination of valproic acid, performed by clarithromycin [8]. The increase in serum valproic acid concentration was closely related to an increased risk of toxicity related to it: alopecia in our case. The ADR completely resolved when the macrolide therapy was suspended.

The second is the case of 8 years old boy, affected by a congenital form of epilepsy chronically treated with levetiracetam, whose symptomatology was completely under control and the plasma level of levetiracetam was in range. After appearance of cough, possibly attributed to gastroesophageal reflux, an anti-reflux syrup containing magnesium alginate, althaea officinalis, sodium bicarbonate, sodium hydroxide was introduced into therapy. The patient was hospitalised in PICU, due to relapse of seizures: plasma levetiracetam concentration was below the reference ranges. Antacid substances, altering the pH of the gastrointestinal tract had probably compromised the absorption of levetiracetam, reducing its effectiveness. Removal of the antiacids normalised the patient condition and levetiracetam levels.

The paediatric population is not exempt from medication errors including PDDIs [9] also because of the peculiar pharmacokinetic characteristics of drugs in these patients [10], the extensive use of off-label therapies [11] and the increase in chronic paediatric diseases [12,13] and the involvement of clinical pharmacists in the paediatric setting has a documented impact on paediatric patient safety, quality of life, and economic outcomes [14]. In a large US study conducted in 2006, data collected on 491,451 hospitalisations in 52 children’s hospitals, and in 411 general hospitals revealed that a considerable fraction of patients was exposed to numerous

Departments/ward	Number of PDDI identified, (Number of counselling data sheet)	Total of counselling data sheet required
PAEDIATRIC UNITS (7)	53 (23)	94
PICU BUZZI HOSPITAL	99(17)	19
CLINICAL PAEDIATRIC NEPHROLOGY UNIT -DE MARCHI	27 (11)	13
PAEDIATRIC NEUROLOGY UNIT-BUZZI HOSPITAL	9 (5)	12
PAEDIATRIC UNIT- ISTITUTO TUMORI OF MILAN	5 (1)	1

Table 1: Wards took part in the pilot project

medications; moreover, in both paediatric and generic hospitals, the median number of different drugs received by infants and children during hospitalisations tended to increase from day 1 to day 7 of hospitalisation, even reaching 35 different drug, in infants aged less than 1 year, hospitalised in children's hospitals [15].

PDDIs were found to be frequent during polytherapy approaches. In US children's hospitals PDDIs of any severity were found in 49% of patients; in 28% of cases PDDIs were classified as moderate, and in 41% of cases as major [9]. Rates of PDDIs were even higher in Intensive Care Units, where as much as 75% of patients was exposed to 1 or more PDDIs. In those patients, PDDIs were classified as moderate or major in 69% and in 57% of cases, respectively [10]. According with this information we found in our setting that 75% of PDDIs were major or moderate and 25% were free from pharmacological interactions.

Our pilot study revealed that PDDIs are a frequent occurrence in a paediatric setting in Italy. We also show that in 44.2% of the cases examined, medication reconciliation played an important role with substantial benefits for patients in terms of therapy optimisation. We also found that it represented an important tool in the diagnostic process, allowing to determine whether specific clinical aspects were of iatrogenic nature. The involvement of the clinical pharmacists in the paediatric setting is scant in Italy and its efficacy remained thus far largely undocumented. Our study confirms previous experience on other countries on the benefits arising from the application of medication reconciliation, particularly relevant in a paediatric setting because of the frequent use of off label therapies. We suggest that such an approach could be optimised and made simpler if a centralised team to this scope could be set up to serve different hospitals.

These would require a common electronic record system to handle patients' information. In our study, the lack of such a common system has slowed the study and made less simple the interaction between the team responsible for the reconciliation and the paediatricians in charge of the patients.

## What is new and Conclusion

Despite limited data, our study is the first to be performed in Italy to collect data on PDDIs in the paediatric population

and assess the impact of medication reconciliation on them. Our study underlines the importance of a clinical pharmacist performing an individualised pharmacological analysis, to help clinicians in making the best therapeutic choices for their patients reaching the best result of care and preventing harm. It thus adds to the relatively limited literature on reconciliation in a paediatric setting. This would also benefit the National Health System minimising unnecessary bed occupancy and optimising rehabilitation procedures of complex patients.

## Pharmacological Counselling Group

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## Conflicts of interest

The authors have no conflicts of Interest to disclose.

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