



Administration

Effects of the implementation of a preventive interventions program on the reduction of medication errors in critically ill adult patients ☆,☆☆

Carlos M. Romero MD, FCCM^a, Nicole Salazar PharmD^{a,b}, Lorena Rojas PharmD^b, Leslie Escobar PharmD^b, Héctor Griñén PharmD^b, María Angélica Berasaín RN^a, Eduardo Tobar MD, FCCM^a, Marcela Jirón PharmD, PhD, MSc^{b,*}

^aUnidad de Pacientes Críticos, Departamento de Medicina, Hospital Clínico Universidad de Chile, Santiago de Chile, Chile

^bFarmacia Clínica, Departamento de Ciencias y Tecnologías Farmacéuticas, Facultad de Ciencias Químicas y Farmacéuticas, Universidad de Chile. Santiago de Chile, Chile

Keywords:

Medication errors;
Pharmacist;
Safety;
Quality;
Multidisciplinary team;
ICU

Abstract

Purpose: Medication errors (MEs) are a major factor limiting the effectiveness and safety of pharmacological therapies in critically ill patients. The purpose was to determine if a preventive interventions program (PIP) is associated with a significant reduction on prevalence of patients with MEs in intensive care unit (ICU).

Methods: A prospective before-after study was conducted in a random sample of adult patients in a medical-surgical ICU. Between 2 observational phases, a PIP (bundle of interventions to reduce MEs) was implemented by a multidisciplinary team. Direct observation was used to detect MEs at baseline and postintervention. Each medication process, that is, prescription, transcription, dispensing, preparation, and administration, was compared with what the prescriber ordered; if there was a difference, the error was described and categorized. Medication errors were defined according to the National Coordinating Council for Medication Error Reporting and Prevention.

Results: A total of 410 medications for 278 patients were evaluated. A 31.7% decrease on the prevalence of patients with MEs (41.9%-28.6%; $P < .05$) was seen. Main variations occurred in anti-infectives for systemic use and prescription and administration stage.

Conclusions: The implementation of PIP by a multidisciplinary team resulted in a significant reduction on the prevalence of patients with ME at an adult ICU.

© 2013 Elsevier Inc. All rights reserved.

☆ Disclosure: The authors declare no conflicts of interest.

☆☆ Funding: This study was not funded.

* Corresponding author. Tel.: +56 2 29782838; fax: +56 2 29782990.

E-mail address: mjiron@ciq.uchile.cl (M. Jirón).

1. Introduction

Medication errors (MEs) are the most common clinical error and account for 78% of serious clinical errors in the ICU [1]. In addition, MEs represent the main factor limiting the effectiveness and safety of pharmacotherapy [2]. Such errors may occur at any stage of the medication use procedure, namely, during prescription, transcription, preparation, dispensing, or administration [3].

It is known that patients in intensive care units (ICUs) experience approximately 1.7 clinical errors every day and many of them are exposed to potentially fatal errors during hospital stay [3].

Patient safety is critical in the ICU, but the complexity of processes and the medical conditions of patients make them more vulnerable to errors [4]. Indeed, ICU patients normally use twice as many medications as those with less complex problems. In addition, medications are administered mainly through parenteral routes and often require complicated mathematical calculations to establish optimal doses, which increase the potential for MEs [5].

Several international studies have assessed MEs prevalence in the ICU, and results vary widely [6-9], mainly due to differences in methodology, ME definitions, and reporting [8]. Recently, a multinational study reported a 33% of MEs prevalence over parenteral drug administration using voluntary reporting [7].

Availability of ME-related information enables the assessment of processes more prone for generating errors [9,10]. Only a few studies conducted in Latin American countries allow the identification of part of the processes and causes most responsible for errors. Those studies have been carried out in hospitalized patients in Brazil [11-13], Mexico [14], Uruguay [15], and Argentina [16], reporting ME rates to a specific stage of medication process and different setting than adult ICU. In addition, medical record review has been the method mainly used for detecting MEs [17]. Direct observation has demonstrated being the best method for detecting and counting the frequency of MEs [18].

In Chile, there are no data published on MEs. In addition, multidisciplinary interventions including pharmacist and related to medication use practices are infrequent due to pharmacists are not included as a permanent staff of the ICU or an active participant in clinical rounds.

Until now, there are no data from Latin American countries estimating the prevalence of patients with MEs and MEs rate in every stage of process of medication use. The purpose of this study was to determine if the implementation of formal, structured preventive intervention program (PIP) by a multidisciplinary team to improve medication use in an ICU is in fact associated with a significant reduction on the prevalence of patients with MEs.

2. Methods

Hospital Clínico Universidad de Chile is a tertiary care teaching hospital (600 beds) located in Santiago, capital of Chile, a developing country in Latin America. In this hospital, drugs are dispensed from the pharmacy using unit-dose drug distribution system, and once drugs are received by the nursing staff, any additional preparation process is performed by them before administration. The present study was carried out in the medical-surgical adult ICU (12 beds) where approximately 500 patients are admitted annually.

A prospective before-after study was conducted between March 2009 and July 2011 to determine the effect of a bundle of interventions on MEs in the ICU. Prevalence of patients with MEs was determined at baseline and post-intervention; after baseline assessment, a PIP to reduce MEs in the ICU was developed and implemented.

An *ME* was defined as a failure in the treatment process that leads to or has the potential to lead to harm to the patient [19]. It is included any error occurring during medication use procedure of a patient, that is, prescription, transcription, preparation, dispensing, and administration stages, regardless of having an adverse consequence or not [20]. Therefore, not all MEs cause an adverse event [19].

Each ME detected was classified according to criteria adapted from the National Coordinating Council for Medication Error Reporting and Prevention [21] (Appendix E1).

2.1. Prevalence of patient with ME: before and after PIP

Prospective observational monitoring of each medication use-related process was conducted by external and previously trained pharmacists.

Prevalence of patients with at least 1 ME detected was estimated during a given period studied as follows: [(number of patients with at least one ME detected)/(total number of patients studied)] \times 100.

In addition, the ME rate was calculated as follows: [(number of MEs detected)/(total number of observations)] \times 100.

2.1.1. Sample size and selection

At baseline, a random sample of 124 patients in ICU was calculated based on the 33% of prevalence reported on the international literature [7], with a significance level of 95%. Each patient was selected using a random number generator, based on bed number assigned in the ICU, administration time schedule, and day of week. In case of requiring a replacement (patient with no medication at the time schedule selected or bed with no patient), the next bed in a clockwise direction was selected, until achieving the required assessment.

Patients were included if they were prescribed medications in a day-bed-randomized time schedule, during daytime, and

Monday to Friday over a 3-month period each phase of study. The 5 most common time schedules were assessed, and only patients being administered enteral or parenteral medications were studied. Inhalers and drugs administered through continuous infusion pumps were excluded.

2.1.2. Procedures and data collection

Direct observation was used to detect MEs based on the method of Barker and McConnell [22]. On each day of observation, pharmacists arrived on the ICU in time to attend to clinical rounds, being witness of medication use process, that is, prescription, transcription, preparation, dispensing, and administration stages. Pharmacists watched the actual medication process and wrote down exactly what subject did, including all details about the medication and the patient selected. Each medication process was compared with what the prescriber ordered; if there was a difference, the error was described and categorized. Near misses events and close calls were considered as an ME.

Similarly to the reports by Kopp et al [23], only the error considered as the origin of the problem was documented as a ME. For instance, if a physician placed an incorrect order, which resulted in other MEs, the root of the problem consists of the prescription error, even if additional errors had occurred after the initial event.

A form and its protocol of use were specially designed and validated by iterative sampling up to reach saturation for data collection [24]. The validation of the form was performed before the study was begun. This form included medication characteristics, error type and subtype, time schedule, day of the week, type and number of medications at the same time schedule, patient demographic data, diagnosis upon admission to ICU, and Acute Physiology and Chronic Health Evaluation (APACHE) II score. Drugs were classified using Anatomic Therapeutic Chemical classification system [25].

2.1.3. Information quality

Ten percent of the patients randomly selected were followed up by an external and independent supervisor, who witnessed the medication use process. Medical error detection was performed using the same method used by pharmacists. Supervisor filled out her own forms, and data recorded were compared with what the pharmacist recorded. No differences were found between supervisor and pharmacist records. There was no interrater reliability assessment.

The ICU staff was blinded of the study to avoid influencing their usual behavior. However, when an ME was detected that might be life threatening to the patient, the staff in charge of providing care to that patient was immediately informed so as to assure patient safety.

The present study does not include reports of the frequency, the capacity of being intercepted, or the seriousness of adverse events.

2.2. Design and implementation of PIP

Preventive intervention program development began after baseline assessment. Each strategy to be implemented was selected based on types and causes of MEs detected during the baseline period.

Finally, a multidisciplinary team including physicians, nurses, and pharmacists developed and implemented a PIP over a period of 6 months, which included the following (Appendix E2):

2.2.1. Incorporation of a clinical pharmacist into the ICU

The specially trained clinical pharmacist was placed in charge of direct supervision and monitoring of the stages of prescription and transcription, coordination, and logistics within the hospital pharmacy (dispensing) and maintained an active participation during daily morning clinical rounds and educational activities. Clinical pharmacist main responsibilities were focused on evaluate appropriate drug, dose, route, dosage form and dosing intervals, monitoring efficacy and safety, providing pharmacokinetics monitoring and consultation, participate in the development and implementation of drug related policy, procedure and guidelines, and participate on quality improvement activities.

2.2.2. Standardization of medication use

Standard operating procedures (SOPs) were created for enteral and parenteral medication use (preparation and administration) based on supplier information and scientific literature regarding drug incompatibilities and drug formulations, among others. In addition, there was a reorganization of medication administration to reduce the number of medications concurrently.

2.2.3. Training and motivation

An organized educational program was made by the clinical pharmacist incorporated into the ICU health care team (residents, interns, nursing staff, and physical therapists). This program included workshops and conferences on the culture of safety in the ICU, medication use system, and SOPs to be implemented. In addition, motivational conferences were provided to show the achievements in other areas of safety and quality in the ICU, such as reduction in nosocomial infection rates: ventilator-associated pneumonia, catheter-related bloodstream infection, and urinary tract infection.

2.2.4. Creation of a MEs reporting system

Specially designed mailboxes and report forms were placed in the ICU, intended to receive staff self-reporting. Reporting included basic information related to the error or near miss, to allow learning from the error or risk situation, to generate preventive interventions. The report was voluntary, anonymous, and nonpunitive.

Table 1 Sample characteristics before and after a PIP to reduce ME in an ICU

| Characteristic | Control | Postintervention | <i>P</i> |
|---|-------------|------------------|---------------------|
| n | 124 | 154 | |
| Male, n (%) | 85 (68.5) | 89 (57.8) | .0654 ^a |
| Age, mean (y) ± SD | 51.1 ± 17.8 | 60.9 ± 15.0 | <.0001 ^b |
| APACHE II, mean ± SD | 20 ± 2 | 21 ± 6 | .0774 ^b |
| Nurse:patient ratio | 1:2.5 | 1:2.5 | |
| Admission diagnosis, n (%) | | | .0026 ^a |
| Septic shock/ARDS | 67 (54.0) | 59 (38.3) | |
| Pancreatitis | 8 (6.5) | 3 (1.9) | |
| TBI | 6 (4.8) | 0 (0.0) | |
| SAH | 5 (4.0) | 16 (10.4) | |
| Hemorrhagic shock | 3 (2.4) | 14 (9.1) | |
| OLT | 2 (1.6) | 7 (4.5) | |
| Postneurosurgery | 0 (0.0) | 7 (4.5) | |
| Other ^c | 33 (26.6) | 48 (31.2) | |
| Therapeutic groups, n ^d (%) | | | <.0001 ^a |
| Anti-infectives for systemic use | 41 (21.1) | 71 (32.9) | |
| Nervous System | 30 (15.5) | 46 (21.3) | |
| Blood and blood forming agents | 26 (13.4) | 21 (9.7) | |
| Cardiovascular system | 26 (13.4) | 31 (14.4) | |
| Others | 71 (57.3) | 47 (30.5) | |
| Time schedule, n (%) | | | .7207 ^a |
| 9 AM | 46 (37.1) | 59 (38.3) | |
| 12 AM | 18 (14.5) | 27 (17.5) | |
| 13 PM | 18 (14.5) | 21 (13.6) | |
| 16 PM | 18 (14.5) | 26 (16.9) | |
| 17 PM | 24 (19.4) | 21 (13.6) | |
| Days of the week, n (%) | | | .7997 ^a |
| Monday | 26 (21.0) | 27 (17.5) | |
| Tuesday | 30 (24.2) | 33 (21.4) | |
| Wednesday | 27 (21.8) | 32 (20.8) | |
| Thursday | 20 (16.1) | 30 (19.5) | |
| Friday | 21 (17.0) | 32 (20.8) | |
| No. of medications at the same time schedule, n (%) | | | .2652 ^a |
| 1 | 84 (67.7) | 104 (67.5) | |
| 2 | 24 (19.4) | 38 (24.7) | |
| ≥ 3 | 16 (12.9) | 12 (7.8) | |
| Dosage forms used, n ^d (%) | | | .0003 ^a |
| Tablets | 58 (29.9) | 89 (41.2) | |
| Parenteral solutions | 43 (22.2) | 18 (8.3) | |
| Ampoules | 41 (21.1) | 50 (23.1) | |
| Lyophilized powder for IV reconstitution | 12 (6.2) | 12 (5.6) | |
| Viaflex | 15 (7.7) | 30 (13.9) | |
| Vial | 25 (12.9) | 17 (7.9) | |
| Others | | | |
| Route of administration, n ^d (%) | | | <.0001 ^a |
| Intravenous | | | |
| CVA | 103 (53.1) | 103 (47.7) | |
| PVA | 6 (3.1) | 4 (1.9) | |
| Enteral | | | |
| NGT | 65 (33.4) | 50 (23.1) | |
| NJT | 14 (7.2) | 14 (6.5) | |
| Oral | 1 (0.5) | 25 (11.6) | |
| Other | 5 (2.6) | 20 (9.2) | |

ARDS indicates acute respiratory distress syndrome; TBI, traumatic brain injury; SAH, subarachnoid hemorrhage; OLT, orthotopic liver transplantation; NGT, nasogastric tube; NJT, nasojejunal tube; CVA, central venous access; PVA, peripheral venous access; IV, intravenous.

^a χ^2 test.

^b Student *t* test.

^c Other: status epilepticus, status asthmaticus, polytraumatized patient, acute liver failure among others.

^d Data calculated based on number of observations n = 194 (control) and n = 216 (postintervention).

2.3. PIP assessment

The same study design was used to determine the prevalence of patients with at least one ME before and after PIP over the same 3-calendar-months period each time. The PIP was assessed 6 months after the implementation of the whole preventive measures (“bundle”). After PIP, all patients received the PIP bundle; however, only randomized patients were selected to determine the prevalence of patients with at least 1 ME and MEs rate postintervention.

A postinterventional sample size of 154 patients was calculated, considering an expected reduction on 30% of the prevalence of patients with at least 1 ME found at baseline, a significance level of 95%.

Continuous data were reported as mean \pm SD, and the Student *t* test was used when comparisons were made for parametric data. Categorical variables were reported as frequency distributions, and χ^2 or Fisher exact tests were used to test whether differences existed between groups. All tests were 2 tailed, and an $\alpha < .05$ was predetermined to represent statistical significance. Analyses were done using the STATA 10.1 (Texas, USA) software package.

Confidentiality of data was safeguarded by the use of a numeric system code, known only by the principal investigator. The present study was approved by the institutional ethics committee that exempted it from the informed consent.

3. Results

A total of 278 patients were assessed, of whom 124 (44.6%) were included in the sample selected at baseline in 2009, and 154 (55.4%) patients at the postintervention assessment in 2011. When comparing the study samples (control and postintervention groups), statistically significant differences were noted with the mean age (51.1 vs 60.9 years, $P < .05$). There were no significant differences for the other variables. Demographic data concerning morbidity for each assessment year are shown in Table 1.

Table 1 also shows pharmacotherapy characteristics of samples studied before and after PIP. Anti-infectives for systemic use were the therapeutic group more prescribed; administration time schedule was mainly at 9 AM in control and postintervention group. The route of administration most used was intravenous, mainly by central venous access. There were no significant differences among groups related to day of week, time schedule, and number of medications at the same time schedule before and after PIP.

3.1. Medication errors and PIP

Over the study period, the implementation of PIP was associated with a significantly lower prevalence of patients with at least 1 ME in ICU, reducing by 31.7% (41.9%-28.6%; $P < .05$) between 2009 and 2011. Medical error rate decreased 25% (34.0%-25.5%, $P = .058$). At baseline, 52 patients

(41.9%) were exposed to at least 1 ME, whereas postintervention, this value was 44 (28.6%). A total of 410 medications were assessed (194 before PIP and 216 after PIP).

The highest differences at the prevalence of patients with ME before and after PIP were seen at the prescription and administration processes, representing 50% lower prevalence at each of such stages (Fig. 1).

Among common causes of MEs seen at baseline were as follow:

- Lack of SOPs related to preparation and administration of drugs in ICU (wrong preparation and wrong time schedule).
- Insufficient knowledge on safety and quality of care related to MEs and their consequences by the health care team. No other training on these topics existed before PIP in this ICU.
- Insufficient monitoring of medication use procedure and preventive strategies for MEs detection, such as proactive interventions.
- Prescription errors were due to missing data and inappropriate dosage form for the selected route of administration. For instance, modified-release tablets through a nasogastric tube.

Table 2 shows ME occurrence before and after PIP by characteristics studied. There was a significant decrease on the ME rate on Thursday and Friday, no special explanations for these results. In addition, a significant decrease on ME rate at 12 PM and 16 PM was seen, mainly due to antibacterial administrations have been scheduled at those time schedules at this ICU.

On the other hand, the prevalence of patients with at least 1 ME was higher when the number of medications administered at the same time schedule increased (Table 2), but this was not statistically significant. In addition, during postintervention period, an increase of MEs rate was seen among albumin users due to wrong manipulation of a new container of a different supplier.

Anti-infectives for systemic use was the therapeutic group with the highest MEs rate at baseline (65.9%), mainly due to errors during administration process in association with problems with doses administered or wrong time schedule. Nevertheless, after the PIP, a statistically significant decrease of 50.8% on MEs rate was seen (65.9%-32.4%) (Table 2).

4. Discussion

It has been reported that critical patients have a higher risk of MEs by virtue of (a) usually being under sedation, making it more difficult for the provider to detect possible adverse event due to error; (b) receiving a large numbers of different medications; and (c) receiving mainly parenteral medications, requiring calculations for their administration [26]. Therefore, safe management of medication is

Table 2 Prevalence of patients with at least 1 ME and ME rate before and after the PIP by studied characteristic

| Characteristic | Control n = 194 observations, 124 patients | | | | Postintervention n = 216 observations, 154 patients | | | |
|-------------------------------------|---|-------------|---------------|-------------------------------------|--|-------------|---------------|-------------------------------------|
| | No. of errors | No. of Obs. | Error rate, % | % Patients ≥ 1 ME ^a | No. of errors | No. of Obs. | Error rate, % | % Patients ≥ 1 ME ^a |
| Day | | | | | | | | |
| Monday | 11 | 39 | 28.2 | 34.6 | 11 | 42 | 26.2 | 33.3 |
| Tuesday | 12 | 53 | 22.6 | 26.7 | 13 | 43 | 30.2 | 27.3 |
| Wednesday | 18 | 41 | 43.9 | 59.3 | 16 | 45 | 35.6 | 40.6 |
| Thursday | 10 | 31 | 32.6 | 45.0 | 5 | 43 | 11.6 * | 16.7 * |
| Friday | 15 | 30 | 50.0 | 47.6 | 10 | 43 | 23.3 * | 25.0 |
| Administration time schedule | | | | | | | | |
| 9:00 AM | 21 | 86 | 24.4 | 34.8 | 20 | 85 | 23.5 | 27.1 |
| 12:00 PM | 13 | 18 | 72.2 | 61.1 | 10 | 35 | 28.6 * | 29.6 * |
| 13:00 PM | 7 | 23 | 30.4 | 38.9 | 5 | 30 | 16.7 | 23.8 |
| 16:00 PM | 12 | 18 | 66.7 | 55.6 | 12 | 35 | 34.3 * | 38.5 |
| 17:00 PM | 13 | 49 | 26.5 | 33.3 | 8 | 31 | 25.8 | 23.8 |
| No. of medications | | | | | | | | |
| 1 or 2 | 51 | 132 | 38.6 | 38.9 | 49 | 180 | 27.2 | 27.5 |
| ≥ 3 | 15 | 62 | 24.2 | 62.5 | 6 | 36 | 16.7 | 41.7 |
| Therapeutic group | | | | | | | | |
| Anti-infectives | 27 | 41 | 65.9 | 54.3 | 23 | 71 | 32.4 * | 36.2 |
| Nervous system | 9 | 30 | 30.0 | 40.0 | 6 | 46 | 13.0 | 18.8 |
| Blood agents | 9 | 26 | 34.6 | 36.8 | 8 | 21 | 38.1 | 42.9 |
| CV system | 9 | 26 | 34.6 | 42.9 | 4 | 31 | 12.9 | 17.4 |
| Others | 12 | 71 | 16.9 | 26.7 | 14 | 47 | 29.8 | 25.9 |
| Total | 66 | 194 | 34.0 | 41.9 | 55 | 216 | 25.5 | 28.6 |

Obs indicates observations; no. of medications, number of medications on the same time schedule; anti-infectives, anti-infectives for systemic use; blood agents, blood and blood forming agents; CV, cardiovascular; others included alimentary tract and metabolism drugs; systemic hormonal preparations, excluded sex hormones and insulins; respiratory system drugs; sensory organs drugs; various.

* $P < .05$, χ^2 test.

^a Prevalence of patients with at least 1 ME.

particularly challenging because of the complexity of the different stages involved in their use. Thus, the administration of a single dose of a medication at a hospital may require the appropriate undertaking of between 80 and 200 steps [27] increasing the opportunity for many errors.

The present study is the first in Latin America to assess every stage of medication use procedure in an adult ICU.

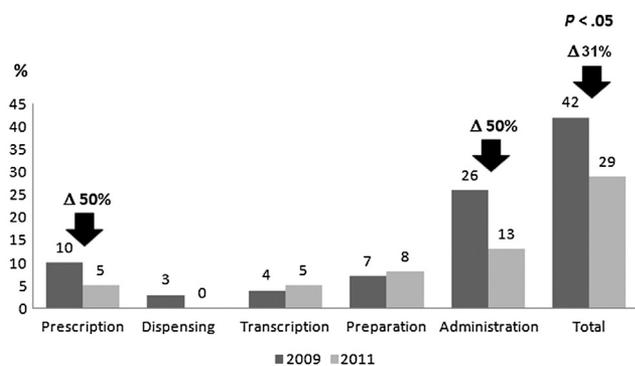


Fig. 1 Prevalence of patients with at least 1 ME before and after the PIP by stage of the medication use process. $P < .05$, χ^2 test. Differences were significant only for the total. There were no significant differences at the analysis by stage.

Our study has shown that a bundle of multidisciplinary nontechnological interventions reduced significantly the prevalence of patients with at least 1 ME (from 41.9% before to 28.6% after PIP). The most common MEs at baseline occurred during administration stage, accounted for half of the MEs detected. The subtypes were mainly wrong time schedules and to the administration technique. Several international studies have reported similar prevalence and causes mentioned at present research, using different methods [28-30].

Systematic evaluation of every stage of medication use enabled the identification of causes of MEs at our ICU. Work overload as a result of inadequate organization, inappropriate standardization of medication preparation and administration, lack of coordination between the ICU and the pharmacy, and the simultaneous administration of medication at the same time schedule were some of the causes identified, as was reported by other authors [31].

We also learned that lower prevalence of patient with MEs found at the dispensing stage might be explained by the availability of ICU staff in charge of reviewing each delivery from and to the pharmacy. Delivery revision from and to the pharmacy was a regular procedure at this ICU before the study was conducted. Therefore, it was not considered part

of the PIP. In addition, this strategy may underestimate dispensing errors prevalence.

Baseline information was critical for the development of the PIP. The constitution of multidisciplinary teams in the ICUs has been shown to improve the quality and the safety of critical patient care and to generate a positive impact on clinical outcomes [32-34].

Monitoring, measurement, and improvement of safety and quality represent a great challenge to the health care staffs in charge of providing care to critically ill patients [35]. Many authors have reported a significant decrease of MEs prevalence when individual preventive interventions are implemented, such as medication standardization [36], education and training programs for the health care team [23], voluntary MEs reporting [37], and the incorporation of a pharmacist into the clinical rounds [38-41].

In addition, technology-based interventions have been proposed, such as computerized physician order entry and bar codes [42-44]. Nevertheless, although technology-based interventions have the potential to reduce MEs prevalence, their implementation is not simple and implies new risks if it is not carried out adequately [45]. Moreover, they require a considerable investment of economic resources that many institutions in our region are not able to bear.

Different Latin-American studies have addressed the effect of individual interventions on specific stages of the medication management process [11-16]. However, there is no published information on the evaluation of a bundle of preventive measures, applied by a multidisciplinary team to all the stages of medication use.

The present study is the first of its kind to demonstrate that a formal and structured PIP was associated with a significant reduction of prevalence of patients with at least 1 ME in an ICU. Our results provided evidence of a reduction in the most critical stages of the medication use procedure, such as prescription and administration.

Among the strengths of the study is the evaluation of all stages in the medication use procedure. In fact, this study differs from others that have focused mainly on the prescription and administration stages [28,29,46,47]. A relevant aspect to be taken into consideration is that not only parenteral dosage forms were included, as reported in some studies [4,28], but also enteral forms, thus allowing the identification of the MEs related to such drugs. The random design for patient selection and schedules of the study, the reporting method used, based on an external and independent pharmacist, and the programmed supervision of data collected provided more reliability and internal validity to the results achieved. In addition, the assessment of the impact of the PIP was not carried out immediately after its implementation, as is usually reported, but was intentionally delayed. The results of the present work could reflect a change in the culture of safety of the health care team; however, there were no data to confirm this association. Finally, the nature of the intervention, not technology-based, could make the results reproducible at other institutions within Latin America or developing countries in general.

However, the present work has several limitations. The study was conducted in only 1 center, a feature that might attenuate external validity. Nevertheless, the number of patients included was enough to detect statistical differences, and multicenter international studies have reported similar results to ours [7].

The design (before-after) is not as robust as a randomized control trials. The case matching of patient was not done, and potential confounding factors would affect the ME occurrence. However, the nurse:patient ratio and APACHE II were similar, and no other interventions related to medication processes and safety were implemented beyond PIP during the study period. In addition, control and postintervention assessment were performed during the same 3 months of the calendar year, to control bias due to possible seasonal variations.

Medical errors immediately informed to staff could change or improve their behavior related to medication procedures. In addition, medications administered through continuous infusion were not evaluated, thus excluding drugs commonly used in ICUs. These biases may have generated an underestimation of ME occurrence. Nevertheless, the latter only highlights the importance of the issue.

The observations carried out during this study only occurred during the daytime, working hours and recorded by pharmacists; therefore, they did not include information regarding medication management processes that take place during night shifts, weekends, or by multidisciplinary collection.

The present study does not include reports of the frequency, the capacity of being intercepted, or the seriousness of adverse events. Therefore, it was not possible to calculate clinical and economical outcomes of MEs detected. However, we believe these improvements would likely translate to a benefit to the patients and health care system.

Finally, because bundle interventions were implemented, the identification of the relative contribution of each individual intervention was not possible. However, as reported other authors [37,48,49], we believe that a pharmacist in the ICU was critical to the results obtained. The presence of a pharmacist spending time with residents and nursing staff allowed more comprehensive application of the PIP and proactive participation on each intervention implemented.

5. Conclusion

The implementation of a formal and structured PIP by a multidisciplinary team was associated with a significantly reduction of the prevalence of patients with ME in an adult medical-surgical ICU.

Acknowledgments

We thank Thomas Einarson, PhD, for his critical appraisal of the manuscript and the staff of ICU at Hospital

Clínico Universidad de Chile, for their excellent attitude and willingness to improve healthcare safety and quality at our institution.

Appendix E1. Definitions, types and subtypes of medication errors assessed in 278 study patients

| Medication error | Study definition | Subtypes |
|------------------|---|---|
| Prescription | Any error or omission occurring during the writing/placing of the medical order, regardless of the quality of the selection of the prescribed medication. | <ul style="list-style-type: none"> –Wrong dose –Wrong frequency –Wrong route –Missing data (order not complete) |
| Transcription | Any omission or difference between the prescription and the data documented on the nursing procedure cards. | <ul style="list-style-type: none"> –Omission –Transcription different to prescribed data |
| Dispensing | Any omission or difference between the data requested on the medical order and the product dispensed from the pharmacy. | <ul style="list-style-type: none"> –Deteriorated medication (expired, wrong preservation, wrong labeling) –Medication different from prescribed product. –Omission –Wrong dosage form –Wrong dose |
| Preparation | Any difference between data indicated in the scientific literature and/or the manufacturer versus the procedures carried out by the ICU staff. | <ul style="list-style-type: none"> –Wrong preparation (wrong dilution, diluent, or fractioning) –Wrong manipulation (contamination) |
| Administration | Any omission or difference between the indications on the order and the product administered to the patient. | <ul style="list-style-type: none"> –Wrong time^a –Missed administration –Wrong dose –Wrong route –Medication different to medication prescribed –Different patient –Wrong rate |

^a Wrong time: related medication error was registered when the medication was administered with more than 30 minutes anticipation or delay with regard to time schedule for administration.

Appendix E2. Bundle components of preventive interventions program to reduce medication errors in ICU

1. Incorporation of a clinical pharmacist into the ICU, responsible for the following activities:
 - To evaluate drugs, dose, route, dosage form, and dosing intervals.
 - To monitor efficacy and drug safety
 - To provide pharmacokinetics monitoring and consultation
 - To participate in the development and implementation of drug related policy, procedure, and guidelines
 - To determine a specific schedule to fill the medical prescriptions.
 - To check medical indications and prescriptions for potential corrections.
 - To determine a specific schedule to send medical prescriptions to pharmacy.
 - To cross-checking of nurses list with the planning of medications.
 - To check medications dispensed by the pharmacy before they are sent to the ICU.
 - To determine a specific schedule for the delivery of medical prescriptions to the pharmacy and the reception of medicaments at the ICU.
 - To establish a record of the administration of prescriptions including the identification of the responsible person.
 - To participate actively during daily clinical rounds.
 - To participate on quality improvement activities.
2. Standardization of medication use:
 - Development of a standard operating procedure (SOP) for the preparation of medications administered by nasogastric tube.
 - Development of a SOP for the administration of medications by nasogastric tube.
 - Development of a SOP for the preparation of medications administered by intravascular device.
 - Development of a SOP for the administration of medications by intravascular device.
 - Reorganization of the administration of medications, reducing drugs concurrently, if possible.
3. Training and motivation:
 - Conference regarding medication errors and security culture in the ICU.
 - Conference regarding the importance of the adequate filling of medical prescriptions at the ICU.
 - Workshop about preparation and administration of medications by nasogastric tube.
 - Workshop about preparation and administration of medications by intravascular device.
 - Conference and workshop about the implementation and importance of the medications errors reporting system.

- Motivational conferences showing the achievements of the ICU in other areas of safety and quality.
4. Medication errors reporting system:
- Periodical checking of reporting files to promote the continuous improvement of the medications utilization system.

References

- [1] Rothschild JM, Landrigan CP, Cronin JW, et al. The Critical Care Safety Study: the incidence and nature of adverse events and serious medical errors in intensive care. *Crit Care Med* 2005;33:1694-700.
- [2] Lesar T, Briceland I, Stein D. Factors related to errors in medication prescribing. *JAMA* 1997;277:312-3.
- [3] Camiré E, Moyen E, Stelfox HT. Medication errors in critical care: risk factors, prevention and disclosure. *CMAJ* 2009;180:936-43.
- [4] Herout P, Erstad B. Medication errors involving continuously infused medications in a surgical intensive care unit. *Crit Care Med* 2004;32:428-32.
- [5] Cullen D, Sweitzer B, Bates D, et al. Preventable adverse drug events in hospitalized patients: a comparative study of intensive care and general care units. *Crit Care Med* 1997;25:1289-97.
- [6] Ridley S, Booth S, Thompson C. Intensive Care Society's Working Group on Adverse Incident. Prescription errors in UK critical care units. *Anaesthesia* 2004;59:1193-200.
- [7] Valentin A, Capuzzo M, Guidet B, et al. Errors in administration of parenteral drugs in intensive care units: multinational prospective study. *BMJ* 2009;338:b814.
- [8] Kane-Gill S, Weber R. Principles and practices of medication safety in the ICU. *Crit Care Clin* 2006;22:273-90.
- [9] Kohn IT. The Institute of Medicine report on medical error: overview and implications for pharmacy. *Am J Health Syst Pharm* 2001;58:63-6.
- [10] van den Bemt PM, Egberts TC, de Jong-van den Berg LT, Brouwers JR. Drug-related problems in hospitalised patients. *Drug Saf* 2000;22:321-33.
- [11] Costa LA, Loureiro S, de Oliveira MGG. Errores de medicación de dos hospitales de Brasil. *Farm Hosp* 2006;30:235-9.
- [12] Graciano M, Borges M, Dean B, et al. Concomitant prescribing and dispensing errors at Brazilian hospital: descriptive study. *Clinics* 2011;66:1691-7.
- [13] de Bartoli Cassiani S, Silvia Monzani A, Bauer de Camargo Silva A, et al. Identificación y análisis de los errores de medicación en seis hospitales brasileños. *Cienc Enferm* 2010;XVI:85-95.
- [14] Lavalle-Villalobos A, Payro-Cheng T, Martínez-Cervantes K, et al. El error médico en la prescripción de medicamentos y el impacto de una intervención educativa. *Bol Med Hosp Infant Mex* 2007;64:83-90.
- [15] Gutierrez S, Mogni A, Berón A, et al. Errores de medicación en niños hospitalizados. *Arch Pediatr Urug* 2011;82:133-40.
- [16] Salamano M, Palchik V, Botta C, et al. Patient safety: use of quality management to prevent medication errors in the hospital medication use cycle. *Rev Calif Asist* 2012. <http://dx.doi.org/10.1016/j.cali.2012.05.004>.
- [17] Breeding J, et al. Medication Error Minimization Scheme (MEMS) in an adult tertiary Intensive Care Unit (ICU) 2009–2011. *Aust Crit Care* 2012. <http://dx.doi.org/10.1016/j.aucc.2012.07.003>.
- [18] Flynn EA, Baker KN, Pepper DW, et al. Comparison of methods for detecting medication errors in 36 hospitals and skilled-nursing facilities. *Am J Health Syst Pharm* 2002;59:436-46.
- [19] Ferner RE, Aronson JK. Clarification of terminology in Medication Errors: definitions and classification. *Drug Saf* 2006;29:1011-22.
- [20] Leape LL. Preventing adverse drug events. *Am J Health Syst Pharm* 1995;52:379-82.
- [21] National Coordinating Council for Medication Error Reporting and Prevention. NCCMERP Index for categorizing medication errors; 2001. <http://www.nccmerp.org/pdf/taxo2001-07-31.pdf>. Accessed January 2009.
- [22] Barker KN, McConnell WE. The problem of detecting medication errors in hospitals. *Am J Hosp Pharm* 1962;19:360-9.
- [23] Kopp BJ, Erstad BL, Allen ME, et al. Medication errors and adverse drug events in an intensive care unit: direct observation approach for detection. *Crit Care Med* 2006;34:415-25.
- [24] Brod M, Tesler LE, Christensen TL. Qualitative research and content validity: developing best practices based on science and experience. *Qual Life Res* 2009;18:1263-78.
- [25] ATC classification index. Structure and Principles. WHO Collaborating Centre for Drug Statistics Methodology; 2001. http://www.whocc.no/atc/structure_and_principles. Accessed on September 2012.
- [26] Hussain E, Kao E. Medication safety and transfusion errors in the ICU and beyond. *Crit Care Clin* 2005;21:91-110.
- [27] Jirón M. Pharmacy-Nursing shared vision for safe medication use in hospitals: Executive Session Survey. *Am J Health Syst Pharm* 2003;60:1046-52.
- [28] van den Bemt PM, Fijin R, van der Voort PH, et al. Frequency and determinants of drug administration errors in the intensive care unit. *Crit Care Med* 2002;30:846-50.
- [29] Calabrese A, Erstad B, Brandl K, et al. Medication administration errors in adult patients in the ICU. *Intensive Care Med* 2001;27:1592-8.
- [30] Moyen E, Camiré E, Stelfox HT. Clinical review: medication errors in critical care. *Crit Care* 2008;12:208.
- [31] Kiekkas P, Karga M, Lemonidou C, et al. Medication errors in critically ill adults: a review of direct observation evidence. *Am J Crit Care* 2011;20:36-44.
- [32] Curtis JR, Cook DJ, Wall RJ, et al. Intensive care unit quality improvement: a "how-to" guide for the interdisciplinary team. *Crit Care Med* 2006;34:211-8.
- [33] Kim MM, Barnato AE, Angus DC, et al. The effect of multidisciplinary care teams on intensive care unit mortality. *Ann Intern Med* 2010;170:369-76.
- [34] Netzer G, Liu X, Shanholtz C, Harris A, et al. Decreased mortality resulting from a multicomponent intervention in a tertiary care medical intensive care unit. *Crit Care Med* 2011;39:284-93.
- [35] Rhodes A, Moreno RP, Azoulay E, et al. Prospectively defined to improve the safety and quality of care for critically ill patients: a report from the Task Force on Safety and Quality of the European Society of Intensive Care Medicine (ESICM). *Intensive Care Med* 2012;38:598-605.
- [36] Bertsche T, Mayer I, Stahl R, et al. Prevention of intravenous drug incompatibilities in an intensive care unit. *Am J Health Syst Pharm* 2008;65:1834-40.
- [37] Grindrod K, Patel P, Martin J. What interventions should pharmacists employ to impact health practitioners' prescribing practices? *Ann Pharmacother* 2006;40:1546-57.
- [38] Kane SL, Weber RJ, Dasta JF. The impact of critical care pharmacists on enhancing patient outcomes. *Intensive Care Med* 2003;29:691-8.
- [39] Kopp BJ, Erstad BL, Duby JJ. Cost implications of and potential adverse events prevented by interventions of a critical care pharmacist. *Am J Health Syst Pharm* 2007;64:483-7.
- [40] MacLaren R, Bond CA, Marin SJ, Fike D. Clinical and economic outcomes of involving pharmacists in the direct care of critically ill patients with infections. *Crit Care Med* 2008;36:3185-9.
- [41] Klopotoska J, Kuiper R, van Kan H, et al. On-ward participation of a hospital pharmacist in a Dutch intensive care unit reduces prescribing errors and related patient harm: an intervention study. *Crit Care* 2010;14:R174.
- [42] Colpaert K, Claus B, Somers A, et al. Impact of computerized physician order entry on medications prescription errors in the

- intensive care unit: a controlled cross-sectional trial. *Crit Care* 2006; 10:R21-9.
- [43] Wolfstadt JI, Gurwitz JH, Field TS, et al. The effect computerized physician order entry with clinical decision support on the rates of adverse drug events: a systematic review. *J Gen Intern Med* 2008;23:451-8.
- [44] Poon EG, Keohane CA, Yoon CS, et al. Effect of bar-code technology on the safety of medication administration. *N Engl J Med* 2010;362: 1698-707.
- [45] Institute of Medicine. Report: health IT and patient safety: building safer systems for better care. The National Academies. Available at: www.iom.edu. Accessed 9 November, 2011.
- [46] Tissot E, Cornette C, Demoly P, et al. Medication errors at the administration stage in an intensive care unit. *Intensive Care Med* 1999;25:353-9.
- [47] Martinez-Anton A, Sanchez JI, Casanueva L. Impact of an intervention to reduce prescribing errors in a pediatric intensive care unit. *Intensive Care Med* 2012;38:1532-8.
- [48] Schneider PJ. Opportunities for pharmacy. *Am J Health Syst Pharm* 2007;64(Suppl. 9):S10-6.
- [49] Leape LL, Cullen DJ, Clapp MD, et al. Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. *JAMA* 1999;282:267-70.