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Effect of critical care pharmacist's intervention on medication errors: A systematic review and meta-analysis of observational studies

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ABSTRACT

Pharmacists are integral members of the multidisciplinary team for critically ill patients. Multiple nonrandomized controlled studies have evaluated the outcomes of pharmacist interventions in the intensive care unit (ICU). This systematic review focuses on controlled clinical trials evaluating the effect of pharmacist intervention on medication errors (MEs) in ICU settings. Two independent reviewers searched Medline, Embase, and Cochrane databases. The inclusion criteria were nonrandomized controlled studies that evaluated the effect of pharmacist services vs no intervention on ME rates in ICU settings. Four studies were included in the meta-analysis. Results suggest that pharmacist intervention has no significant contribution to reducing general MEs, although pharmacist intervention may significantly reduce preventable adverse drug events and prescribing errors. This meta-analysis highlights the need for high-quality studies to examine the effect of the critical care pharmacist.

1. Background

Over the past 3 decades, the role of the critical care pharmacist has expanded in the intensive care unit (ICU) from traditional dispensing responsibilities to active members of multidisciplinary teams [1]. Pharmacists play an important daily role in ICU patient care by assisting physicians and other health care providers with pharmacotherapy decision making and monitoring, ultimately improving medication safety [2].

Medication errors (MEs) and adverse drug events (ADEs) occur at high rates in the ICU [3] due to the (1) severity of disease of this population, (2) multiple medications administered, (3) high-risk nature of the medications, and (4) high frequency of changes in pharmacotherapy regimens [1,3-6]. Pharmacists are considered to be effective in reducing MEs and ADEs by reducing the causes of these events through pharmacotherapy decision making and monitoring support [2,4]. Numerous studies have assessed the effect of ICU pharmacists' intervention in reducing MEs [6-15]. However, these data are limited by the ability to collect data without impeding care; thus, few of these studies are randomized controlled trials [1] or are cohort studies that have an ICU without a pharmacist as a control site [10,15]. Conversely, most of these studies are preintervention/postintervention designs [6-14], which are more realistic to conduct in the ICU setting.

It is, therefore, challenging to quantitatively evaluate the effect of ICU pharmacist interventions on MEs. Pooling data from available studies to perform a meta-analysis will help to better determine the true effect and magnitude of the interventions. Based on our literature review, no such meta-analysis exists. Therefore, we aimed to conduct a systematic review and meta-analysis of the literature to assess the effect of the ICU pharmacist intervention on MEs.

2. Methods

2.1. Scope

A systematic review of published works following the methods specified in the Cochrane Handbook for Reviews on Interventions [16] and the Meta-analysis of Observational Studies in Epidemiology guidelines was conducted (Supplementary material 1) [17].

2.2. Searching

Studies were identified by electronically searching the MEDLINE and EMBASE databases and the Cochrane Database until August 2014. The following keywords were used in combination for the following medical subject headings and text words: “critical care,” “intensive care unit,”

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"pharmacist," "pharmaceutical care," "pharmacy service," "medication error," and "adverse drug event." The search strategy (Supplementary material 2) was adjusted to fit the requirements specified in each database. Manual searches were also completed by scanning reference lists in relevant published articles and conference proceedings of major ICU journals. The literature search was conducted by 2 independent reviewers (RL and TW).

2.3. Inclusion criteria and definitions

Studies were included if they met the following inclusion criteria: (1) nonrandomized controlled trials: controlled before-and-after study (CBA), historical control study (HCS), and cohort studies; (2) compared an intervention delivered by ICU pharmacists (ie, intervention phase) with the delivery of no comparable service (ie, control phase); (3) the pharmacist interventions and the effect on MEs (including prescribing errors) and preventable ADEs had to be identified and clearly reported; (4) full-text publications were available in the English language. The participants for all comparative studies that we included in this analysis were pharmacists who work and deliver pharmaceutical care in the ICU and not those solely involved in drug dispensing.

An *ME* was defined as "any preventable event that may cause or lead to inappropriate medication use or patient harm" [18]. Medication errors could occur at any stage of the medication management process, including prescription, transcription, preparation, and administration. *Adverse drug events* were defined as an injury resulting from administration of a drug, although the event may not be caused solely by the drug itself but rather may relate to the circumstances surrounding use of drug [19]. *Serious MEs* were defined as MEs resulting in an ADE. A *preventable ADE* was defined as an injury caused by an error in the use of a medication that was deemed to be avoidable [12]. A *prescribing error* was defined as any prescribing issue that may have caused or led to inappropriate medication use or patient harm [20]. Two authors (TW and RL) independently read identified abstracts to identify studies that met inclusion criteria. Disagreements were resolved by discussion of the articles by at least 2 of the authors of the analysis.

2.4. Measure of treatment effect

As most studies evaluating ICU pharmacist intervention did not compare outcomes to a control site (ie, nonpharmacist ICU), we extracted outcome data only from the study unit (intervention unit). We reported results for baseline (preintervention) and end-of-study (postintervention) periods. In all cases, we reported a more favorable outcome in the intervention group as a positive finding (ie, changes from baseline are in the intended direction) and vice versa as a negative finding. We used the number of events and the monitored patient-days to perform the meta-analysis because "patient-days" could be considered as the sample size (denominator) and "no. of medication error" could be considered as "no. of events" (numerator). Using patient-days allowed investigators to synthesize and evaluate the risk of MEs regardless of the different lengths of preintervention/postintervention phases and size of ICUs among the included studies.

2.5. Level of evidence and quality assessment

For HCSs (ie, no control group at a different site), we used the Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group to assess the quality [21]. For CBA studies (ie, has a control group at a different site), we used the same method rather than the method recommended by the Cochrane Effective Practice and Organization of Care Review Group [22] because preintervention and postintervention data were only extracted for the intervention sites of included studies.

2.6. Statistical analysis

A meta-analysis was conducted using ReviewManager (Revman Version 5.2, Copenhagen, Denmark). Random-effects model was used for the primary analyses because we expected clinical heterogeneity between trials (owing to different ICU settings and different intervention regimens) [23]. Results of the meta-analysis were expressed as odds ratios (ORs) for dichotomous outcomes, both with 95% confidence intervals and with I^2 and P values as markers of intertrial heterogeneity. I^2 values of 25%, 50%, and 75% were considered as low, moderate, and high, respectively [24]. The meta-analysis was repeated using a fixed-effects model to test the robustness of the results after attributing less weight to small trials. Results of the fixed-effects model were reported only if they differed from random-effects models.

We did a post hoc analysis by omitting 1 study at a time to assess whether the pooled estimates were excessively influenced by any single study. We performed subgroup analysis to examine different types of MEs based on severity (ie, general MEs or preventable ADE) to explore the heterogeneity. Publication bias was examined by Egger test if more than 10 studies were included in the analysis of the primary outcomes [25,26]. Meta-regression was performed to investigate the characteristics of different studies if more than 10 studies were included [27].

3. Results

The electronic search identified 741 potentially relevant articles. After initial screening and full-text review, 8 articles were identified (Fig. 1), including 4 studies reporting monitored patient-days [6,11–13] and 4 studies that did not [7-10]. The 8 included publications contained 3 CBA studies [10-12] and 5 HCSs [6-9,13] (Tables 1 and 2).

3.1. Evidence from studies reporting monitored patient-days

The basic characteristics, pharmacist intervention, and ascertainment of outcomes of included studies are summarized in Table 1 [6,11-13]. Study patients were from different types of ICUs (2 medical, 1 pediatric,

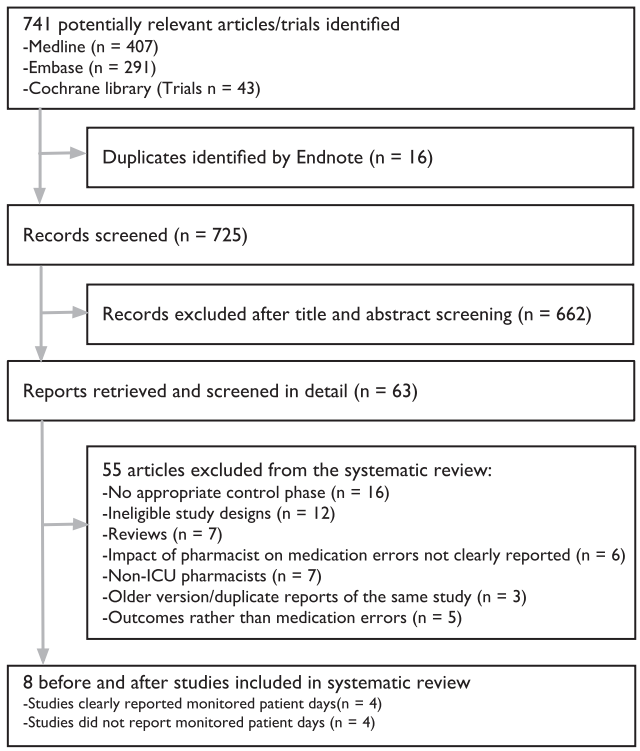

Fig. 1. Flow chart of article selection.