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Research Article

Early Switch from Intravenous to Oral Therapy in Hospitalized Patients in Neuroscience Center at KFMC: A Cost-minimization Approach

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Abstract

Most of the hospital admitted patients with severe diseases are usually started on intravenous (IV) medications, in particular, those who are released from operation room to intensive care units. Although IV to oral therapy conversion is not suitable for critical patients or those who are unable to absorb orally, there is still a good number of patients in each hospital, who are candidates for the switchover from IV to oral therapy.

Keywords: IV to Oral, Pharamcoeconomic, Switch, Hospitalized

Introduction

The main hindrance that restricts IV to oral conversion is the idea that oral medications do not reach the same bioavailability as that of IV medications and that the same item must be used both intravenously and orally. Although several drugs commonly used in hospitalized patients are equally bioavailable intravenously and orally, Patients usually are not shifted to the oral route when stable and able to tolerate oral intake. Earlier conversion from IV to oral therapy has many advantages including -but not conclusive- to less nursing time for medication administration, lower cost, and enhancement of patient's satisfaction and safety.

There is no defined protocol at KFMC for conversion from IV to oral therapy, and physicians are not always aware of the suitable time to implement this conversion. In our study, the question is whether a pharmacist-initiated intervention to encourage conversion would make a difference in decreasing unnecessary use of the intravenous forms of a group of targeted medications among National Neuroscience Institute (NNI) inpatients.

Many research efforts have focused on early 'switch' to oral therapy (PO) after an initial clinical response to empiric treatment has occurred.

Although Most of the studies connected to IV-PO conversion have been directed towards a certain antibiotic or specific medical cases like patients with respiratory tract infections, the principle idea behind these studies and ours is the same.

World Health Organization (WHO) stated that the improper use of medicines is a major problem worldwide. The overuse of IV items, when oral formulations would be more fitting, is one of the key reasons for the irrational use of medications [1].

Siegel published one of the earliest studies regarding this issue and suggested that "adult patients who are not severely ill can be successfully treated with an abbreviated (2-day) course of intravenous antibiotics and then switched to oral therapy" [2]. They found that longer courses of intravenous therapy associated with longer hospital stay and higher cost, with no improving in therapeutic outcome.

In a randomized clinical trial carried out by Solomkin and colleagues, they compared IV imipenem (IMI)/cilastatin followed by oral therapy with Ciprofloxacin plus Metronidazole (CIP/MTZ) to the use of IV imipenem (IMI)/cilastatin for Intraabdominal Infections. The randomization was either to: Ciprofloxacin + metronidazole IV (CIP/MTZ IV), throughout their treatment course, or,

Imipenem IV (IMI IV) throughout their treatment course, or, Ciprofloxacin + metronidazole IV with shift to oral CIP/MTZ when oral intake was resumed (CIP/MTZ IV/PO) [3]. The results demonstrated that Conversion to oral therapy with CIP/MTZ appeared to be as effective as a continued IV therapy in patients who are able to tolerate oral feeding [3].

In a retrospective study, Weingarten identified that at least 33% of hospitalized patients with pneumonia were 'low risk' and could be switched to an oral regimen and discharged on the 3rd hospital day [4].

Another study by Palanisamy and colleagues in south India was conducted in the general medicine division of a 450-bed-tertiary care center over a period of six months. The results showed that the average cost of antibiotics and the length of stay of patients could be reduced by an early switch over from parenteral to oral therapy [5].

Only few studies have been done to assess physician's knowledge, beliefs and acceptance of the switchover from IV to oral therapy. One of the published articles (cross-sectional) study was conducted to explore clinicians' basic knowledge, practice beliefs and acceptability of IV-to-oral antibiotic switching practice in a Hospital in Pinang. There was considerable variation in several practice beliefs among clinicians of various characteristics. The highest score in knowledge was given to specialists and consultants. However, they were less encouraged about integrating a guideline into practice [6].

Objective of the Study

Our objective is asses the amount of annual savings of direct medication cost in case of early switch over from IV to PO. This could be a start to initiate a well-established switch over program.

Methods

Study design

Prospective cohort study design.

Study sitting and order entry

The site for this intervention was the National Neuroscience Institute (NNI) at King Fahad Medical City (KFMC). The medication entry in the wards is manual, where the physician reviews the patient case every morning during a multidisciplinary rounds including clinical pharmacist. In case of a new order, the physician will write it manually in the order sheet with a copy to be sent to the pharmacy for processing.

Participants: (Inclusion and exclusion criteria)

The study has been conducted over 6 months starting on February 2018 till July 2018.

All adult patients admitted in NNI who were able to eat their regular or modified diet, or receiving enteral nutrition (by oral, gastric or nasogastric tube), or receiving other scheduled oral medications were included. For patients who receive antibiotics, they were included if signs and symptoms of infection have been resolved or improving (WBC improving, normal temperature). Inclusion criteria also included: an available appropriate oral dosage form of the prescribed drug, and the targeted oral medications that the patient will be taking must have comparable absorption and bioavailability to that of the parenteral forms.

All patients with low level of consciousness (unable to swallow) and patients with (Nothing per oral) NPO orders before surgery were excluded. Other reasons for exclusion included: patients with nausea and vomiting, patients with seizure who are at risk of aspiration in case of oral intake, and patients who are on IV antibiotics for active infection.

Recruitments

NNI has 6 units, each has 10-18 beds. There are two clinical pharmacists covering only three units with 28-bed capacity. We identified five target medications that are commonly used in NNI inpatient setting with almost identical oral and intravenous bioavailability. All patients exposed to one or more of these targeted medications during study period were included in the study if they fit the inclusion criteria (Table 1).

Data collection and outcome measures

The data is collected by the clinical pharmacist covering the area. He/she should identify patients who receive IV medications, recognize the need for IV medication in those patients and check for the indication. If the patient is eligible for conversion, the pharmacist will inform the physician about this group of patients who are not yet converted to oral within the appropriate time. Documentation is kept within the patient file as well as in an excel sheet for completion and follow up of the base-line data. The outcome will be measured based on the cost saved estimated annually.

Drug	Oral bioavailability	Comments	Price of IV/unit In SAR	Price of Oral/unit In SAR
Ranitidine[1]	50% [7]	In other references The bioavailability of ranitidine ranges from 39 to 88% [8,9]	1.04	0.1
Dexamethazone	86.1% [10]	----------	2.05	0.88
Levetiracetam	100% [11,12]	Levetiracetam immediate-release tablets and oral solution are bioequivale nt in rate and extent of absorption [13]	90	4.1/tab 210/ syrup bottle
Omeprazole[2]	30% to 40% [14]	The low degree of bioavailability is primarily due to pre-systemic metabolism [15]	2.63	0.072
Pantoprazole[2]	77% [16]	Oral compared to IV dosing; unchanged during multiple dosing (chronic use) [17]	1.9	0.33
Hydrocortisone	96% [18]	The bioavailability of hydrocortisone is dose-dependent; bioavailability is less with higher doses [19]	4.65	0.34

Table 1: Targeted medications bioavailability, oral and intravenous prices.

Notes: [1]Ranitidine intravenous dose is 50mg every 8 hours. When we convert it to oral the dose is 150 mg every 12 hours. With 50% bioavailability the dose become equivalent.

[2]IV Omeprazole is converted to oral equivalent dose according to reference or Pantoprazole for better bioavailability.

The number of medication items switched to oral based on clinical pharmacist recommendations will be collected and accordingly the amount of money saved (direct medication cost) will be calculated in Saudi Riyal.

Sample size and statistical calculation:

A biostatistician is consulted to calculate the sample size.

Study parameters

Alpha = 0.050 (Type I error), Power = 0.95 (1 - Type II error), Difference = 2.3

Mean price per patient Omeprazole IV group = 2.63

Mean price per patient Omeprazole oral drug = 0.072

Common standard deviation = 1.0

Estimated sample sizes:

N = 70

At least 7 patients in each treated group.

Statistical analysis procedure

Data was reported as mean (SD) or median (25^{th} and 75^{th} percentiles) for continuous variables, respectively and counts (percentage) for categorical variables. Difference between oral and IV medication cost and were compared using Mann-Whitney U test. All data entry and statistical analyses were performed using SPSS 22.0 software (SPSS Inc., Chicago, IL, USA) package; two-tailed a p-value of 0.05 was considered significant.

Results

Patient's characteristics

This program has been in place for 6 months from January through June 2018.

We had more female participants 27 (60.0%) compared to males. The age range among the females was 15 to 79 years with the mean age of 43 ± 18.4, whereas the age among males ranged

from 15 to 81 years with the mean age of 44.8 ± 16.8 years. The difference in age across gender was not significant, suggesting that the selected sample was age and sex matching.

Gender	Frequency (%)	min -- max	Mean ± SD	p value
Female	27 (60.0)	15 -- 79	43 ± 18.4	0.739
Male	18 (40.0)	15 -- 81	44.8 ± 16.8	
Total	45 (100.0)	15 -- 81	43.7 ± 17.6	

Table 2: Age and gender distribution of the study sample.

During this period, 71 recommendations were made. Of these recommendations, 60 were accepted and implemented, resulting in a cost savings of 10,652 SAR (P=0.001). When annualized, the expected savings were adding up to 21,304 SAR.

Of these recommendations, Omeprazole and Pantoprazole (Proton pump inhibitors) were the commonest items for intervention with 24 recommendations (34%). Of these 24, 18 were accepted and only 6 were rejected. Levetiracetam (anti-epileptic drug) came second with 20 (28%) recommendations, which were all accepted except one. For Dexamethasone (corticosteroid), 18 (25.4%) recommendations were made and 15 were accepted. Only one recommendation was rejected for Ranitidine (H2-blocker) out of a total of 8 (11.2%) recommendations. Hydrocortisone (corticosteroid) was the drug involved in one (1.4%) recommendation for switch and that was implemented.

Discussion

Clinical pharmacist inclusion as one of multidisciplinary health care provider team has a brilliant impact on patients' outcome and health care organization. The role of clinical pharmacist is wide and includes reviewing patients' medication and choosing the most appropriate medication with suitable dose, frequency and route of administration and other interactions during patients' round. Using oral medication instead of parenteral dosage forms have less complication due to medication preparation, administration and monitoring, which increase the work load on pharmacists and nurses. Over that, parenteral medication will increase both direct and indirect organizational cost due to extended duration of hospitalization.

NNI at KFMC includes 6 units with around 100 beds. There are two clinical pharmacists only covering two units, including 28 beds.

The aim of this study was to show the potential of clinical pharmacist in implementing early IV-oral switch program in a number of wards inside KFMC premises. We have found that careful assessment of medication route use in relation to patient's situation can lead to the reduction of the cost of medication use among hospitalized patients without compromising outcomes. In our study 84.5% of the targeted medications were actually converted to the oral form by the physician.

The early conversion from IV to oral form has been discussed in many studies. The majority were focusing on antibiotics. One of the earliest studies done in 1999 at Brigham and Women's hospital in Boston, in which an automated list of potential conversion suggestions was raised to the pharmacists, who then suggested IV-oral conversion through phone calls to the attending physician. As a result, 30% of the recommendation raised to the doctor were applied. They found that high rate of rejection was mainly in patients who are in critical ward settings, patients who were undertaking chemotherapy and patients on their first or second day post-surgery. In their conclusion they suggested that more complex rules should be applied to identify possible conversion with higher specificity [20].

Ehrenkranz and colleagues used the same idea of our project but with the nurse being leading the suggestion for oral conversion and they were targeting antibiotics. Their results showed a reduction in use of antibiotics and hospital stay without affecting outcomes [21].

Stirling [22] and coworkers were able to prove the same in their study with the help of clinical pharmacist intervention to reduce the use of IV Ofloxacin.

The selection of medications in our study was based on the frequently prescribed medications. We have targeted five medications (Omeprazole, Pantoprazole, Ranitidine, Dexamethasone, Levetiracetam). Hydrocortisone was included once although it was not one of the targeted items.

The bioavailability of these items is quite good, Levetiracetam has the best bioavailability (100%). Hydrocortisone has 96% bioavailability. Dexamethasone has 86% bioavailability, but in most cases the doctors plan to start tapering dose down after few days on IV therapy. Ranitidine has only 50% bioavailability but the dose in oral is three times the dose in IV which compensate for the dif-

ference. For Proton Pump inhibitors used for stress ulcer prophylaxis, the bioavailability for omeprazole is low 40%. When we shift it to oral we should be following the recommended dose according to literature, which is 40mg once daily. In some cases, we shifted to pantoprazole, which has better bioavailability 77% (Table 1).

In this Study, Physicians' response to conversation and verbal recommendation varied according to each medication. For example, there were 20 recommendations for converting Levetiracetam to oral form (28%) and 19 of them were approved. Knowing that the medication is expensive in IV form has been possibly a motivating factor for early conversion by the physician. Also dexamethasone had high acceptance rate for conversion with 15 out of 18 recommendations. Most of physicians recommended to start tapering the dosage also. In regard to other medications, physicians were willing to start shifting to oral route in most of the cases. Overall, the rejection rate was quite low with 11 (15.5%) of recommendations being rejected, in which 7 were due to the patient's related level of consciousness and the remaining for unclear reasons.

Limitations to our study were: Only five drugs were evaluated due to their high bioavailability and it was impossible to evaluate all possible drugs because the project was carried out in limited number of wards. Second, because the project was covered by clinical pharmacist, there was many gabs in between due to holidays and personal vacations. Which lead to interruption in collecting data process which would not be the same in case of automated intervention system.

Conclusion

By automating the intervention, we will be able to address many clinical areas targeting different medication classes (infectious disease, gastroenterology, and cardiology) and reach many more patients while using much less person-time than the current situation. Also by incorporating it in the medication renewal process it could reach the physicians before the medication is even prescribed. Third, the data available about the control period (without interventions) is hypothetical. In this way, we calculated the price of the medication in IV form assuming that the intervention was not applied, which is not reflecting as a real control arm of the study.

Recommendations

Active interventions are necessary to stimulate the switch from IV to PO administration of bioavailable drugs and to continuously educate the medical staff in hospitals about drugs with high bioavailability. With a future before-after study, actual savings can be measured. Also automation of the conversion alert would help in spreading the protocol to cover all areas of inpatient setting resulting in more annual savings.

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