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Single-Center Retrospective Evaluation of Inhaled Corticosteroid Use for Chronic Obstructive Pulmonary Disease Exacerbation Patients Receiving Systemic Corticosteroids

Taylor Steuber, PharmD, BCPS,[*] and Dane Shiltz, PharmD, BCPS[†]

ABSTRACT

Purpose: To determine the frequency of inappropriate inhaled corticosteroid (ICS) therapy when it is prescribed concurrently with systemic corticosteroids; to identify cost-savings potential in the setting of chronic obstructive pulmonary disease (COPD) exacerbations.

Methods: Patients admitted to 1 of 8 hospital locations utilizing an integrated electronic health record within the health system for COPD exacerbations treated with systemic corticosteroids (equivalent to at least 30 mg of oral prednisone) between July 1, 2013 and June 30, 2014 were included in a retrospective chart review. Endpoints assessed included number of ICS, with or without long-acting beta-2 agonists (LABA), respiratory medications potentially wasted due to overlap therapy with systemic corticosteroids, as well as overall cost attributed to drug product, administration products, and respiratory therapy labor cost from potentially inappropriate overlap therapy. Results were extrapolated based on the number of admissions within the specified time period. Length of stay data were also compared between the 2 groups (overlap therapy vs no overlap therapy) to determine whether overlap therapy results in a reduction of hospital stay.

Results: A total of 10,710 admissions were identified and 74 charts were randomly identified for review. Forty-six (62%) patients received at least one dose of overlapping ICS or ICS/LABA. One hundred forty-two nebulized budesonide vials were wasted along with 43 ICS or ICS/LABA inhalers. A total cost of $8,152.75 was attributed to drug product, administration products, and labor cost. Extrapolating to the 10,710 admissions identified, there would potentially be 20,551 wasted budesonide vials and 6,223 wasted ICS or ICS/LABA inhalers, resulting in an estimated annual cost savings of $1,180,090.03 for the health system. Additionally, length of stay was shorter in the group not receiving overlap therapy compared to the group receiving overlap therapy, but it was not statistically significant (6.8 ± 3.3 days vs 7.3 ± 4.8 days; $p = .54$).

Conclusion: Significant cost savings could be accomplished through intervention and appropriate utilization of ICS or ICS/LABA therapy in patients admitted for COPD exacerbations treated with systemic corticosteroids.

Key Words—COPD, cost analysis, corticosteroids, disease exacerbation

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Chronic obstructive pulmonary disease (COPD) is a chronic disease characterized by inflammation and thickened mucosal airways, weakened or destroyed alveolar walls, and excess mucus production, all which lead to airflow limitation with limited reversibility.[1] As of 2008, COPD remains the third leading

[*]Auburn University Harrison School of Pharmacy, Department of Pharmacy Practice, Huntsville, Alabama; [†]Ferris State University College of Pharmacy, Department of Pharmacy Practice, Grand Rapids, Michigan. At the time this research was conducted, Dr. Steuber and Dr. Shiltz were affiliated with Indiana University Health, Methodist Hospital, Department of Pharmacy, Indianapolis, Indiana. Corresponding author: Taylor Steuber, PharmD, BCPS, Assistant Clinical Professor, Auburn University Harrison School of Pharmacy, 301 Governors Drive, Huntsville, AL 35801; phone: 256-551-4538; fax: 256-551-4567; e-mail: tsteub13@gmail.com

cause of death in the United States.[1] Patients admitted to the hospital for acute exacerbations of COPD frequently require systemic corticosteroids, typically dosed at the equivalent of at least 30 to 40 mg of prednisone equivalents per day, with 40 mg per day for 5 days being the guideline recommended dosing regimen.[2,3] In this setting, systemic corticosteroids have been shown to improve lung function as well as reduce the risk of early relapse, treatment failures, and hospital length of stay.[4-7]

In the setting of chronic COPD management, inhaled corticosteroids (ICS), in combination with long acting beta-2 agonists (LABA), have demonstrated benefit by improving symptoms, lung function, and quality of life while reducing exacerbation frequency.[2] In acute exacerbations, nebulized budesonide is the only ICS that has demonstrated potential benefit by reducing the number of exacerbations at similar rates compared with oral prednisone; however, it is a more expensive alternative to systemic steroids and requires further investigation.[8-10] Furthermore, budesonide is not US Food and Drug Administration–approved for this indication.[11] To date, there are no studies supporting combined systemic and ICS routes during acute exacerbations, and their combined use increases the risk of adverse drug events and total health care costs.

Despite the initiation of systemic corticosteroid therapy in the inpatient setting, ICS or ICS/LABA treatment regimens are often initiated or continued concomitantly despite a lack of evidence to support this practice. Given the order volume of combination use, increased drug cost with combination therapy (primarily attributed to ICS), potential for increased adverse drug events, and the increased time spent by respiratory therapy administering inhaled products, potentially inappropriate use can increase pharmacy drug cost and respiratory therapy labor cost. We did not set out to measure the effect of treatment, but rather to identify the estimated total costs associated with a practice that is not supported by evidence and has the potential to put patients at risk of increased adverse events. The objective of this medication use evaluation was to determine the frequency of inappropriate ICS therapy when prescribed concurrently with systemic corticosteroids and to identify cost-savings potential in the setting of acute exacerbation of COPD.

METHODS

Patients and Setting

An electronic medical record database was used to identify hospital inpatients with acute COPD exacerbation (ICD-9-CM code 491.21) who received orders for systemic steroids (prednisone, methylprednisolone, dexamethasone, prednisolone, hydrocortisone, and/or cortisone) from July 1, 2013 through June 30, 2014. Data were collected by a retrospective chart review. Patients were included in the analysis if they received at least one dose of systemic corticosteroids in the specified search query from 1 of 8 hospital locations utilizing an integrated electronic health record within the health system. The institution is a comprehensive academic health care system partnered with a school of medicine and includes urban and rural locations across the state. However, at the time of the analysis, only 8 locations had implemented the electronic health record and were therefore the only locations included. No additional exclusion criteria were identified. A total of 70 patient admissions and charts were initially planned for review based on The Joint Commission sampling guidelines that are utilized by the institution to conduct medication use evaluations. According to these guidelines, a recommended sample for a population greater than 500 patients is approximately 70 charts. Given the academic time constraints of the residency year, this was the number of charts planned for review. Charts to include in the review were identified utilizing a random number generator. To obtain adequate representation of ICS use across the health system, stratified sampling was used so the distribution of charts reviewed per location was based on the percentage of total admissions per hospital. For example, 10% of the total COPD admissions identified during the specified study period were from one hospital. Therefore, 7 charts (10% of 70) from that location were included in the review. The number of charts reviewed per location was rounded up to the nearest whole number for a total of 74 charts reviewed. Results were then extrapolated to the number of admissions identified.

Endpoints and Measurements

This medication use evaluation was conducted primarily to identify potential cost savings. The endpoints assessed included number of nebulized budesonide vials and ICS and ICS/LABA metered dose inhalers (MDI) or dry powder inhalers (DPI) used during potentially inappropriate overlap therapy with systemic corticosteroids (defined as oral prednisone equivalent ≥30 mg per day with at least 1 dose of ICS or ICS/LABA administered during ongoing systemic therapy). At the time of the study, the guideline-based treatment recommendation was a dose of 30 to 40 mg of prednisolone equivalents per day for 10 to 14 days.[12] Therefore, a dose cut-off of greater than or equal to 30 mg of prednisone

per day was used to identify potential inappropriate overlap therapy. Individual medication administration records were inspected to determine whether the medication was actually administered. With the electronic health record, we were able to determine if a dose was given or if it was not given, with a reason why. If the medication was ordered but not administered, it was not included in the endpoint. Additionally, if patients received systemic corticosteroid doses of less than or equal to 20 mg of oral prednisone per day for at least 48 hours, their MDI or DPI was not counted as potentially unnecessary overlap unless they had received the full contents of an inhaler when their systemic corticosteroid was above the specified threshold (≥30 mg of oral prednisone per day). Furthermore, overall cost attributed to drug product, administration products, and respiratory therapy labor cost from overlap therapy with ICS and systemic corticosteroids was assessed and extrapolated based on the number of admissions within the specified time period in the health system. Drug product cost differed among sites that were disproportionate share hospitals (sites serving a significantly disproportionate number of low-income or uninsured patients) or non-disproportionate share hospitals (**Table 1**), and respiratory therapy labor cost was calculated based on price per medication administration. Data for endpoints were extrapolated to the sample population identified that met inclusion (n = 10,710) from the random sample reviewed (n = 74). Finally, length of stay was compared between groups (overlap therapy vs no overlap therapy) to determine if overlap therapy was potentially beneficial. Statistical analysis was performed by means of a t test in IBM SPSS version 23 (IBM, Inc., Armonk, NY), with a p value of less than .05 indicating statistical significance.

RESULTS

A total of 10,710 admissions for acute COPD exacerbation that met inclusion criteria were identified during the specified study period. Seventy-four charts were reviewed and results were extrapolated to the sample population. Forty-eight of 74 (65%) had orders placed for overlapping ICS or ICS/LABA, although only 46 (62%) of the 48 patients actually received one or more doses of overlapping therapy. Of these 46 patients who received overlapping therapy, 38 (83%) patients used an ICS or ICS/LABA therapy at home. Respiratory therapy administered all ICS and ICS/LABA therapies. The ICS and ICS/LABA order details are summarized in **Table 2**.

There were 236 total days of overlap therapy (average, 3.2 days; range, 0-16 days); during those days, a total of 398 overlapping ICS or ICS/LABA doses with systemic steroids were administered (average, 5.4 doses per encounter; range, 0-30 doses). In total, 142 budesonide vials along with 43 DPI/HFA inhalers were potentially inappropriate overlap therapy. Extrapolation was done by multiplying data from 74 charts by a factor of 144.73 (10,710/74). After extrapolation, there were an estimated 57,602 overlapping ICS plus ICS/LABA doses. In addition, a total of 20,551 budesonide vials and 6,223 DPI/HFA inhalers were calculated.

Table 1. Pharmacy medication cost

Medication	Cost (dollars per vial/inhaler)	
	DSH site	Non-DSH site
Budesonide 0.5mg nebulized solution	6.52	6.52
Fluticasone-Salmeterol diskus 100/50mcg	102.18	102.18
Fluticasone-Salmeterol diskus 250/50mcg	102.18	102.18
Fluticasone-Salmeterol diskus 500/50mcg	113.41	166.14
Fluticasone-Salmeterol HFA 45/21mcg	102.18	143.09
Fluticasone-Salmeterol HFA 115/21mcg	102.18	143.09
Fluticasone-Salmeterol HFA 230/21mcg	113.43	212.21
Fluticasone diskus 250mcg	104.96	104.96

Note: DSH = disproportionate share hospital; Non-DSH = non-disproportionate share hospital.

Table 2. Inhaled corticosteroid (ICS) orders

ICS medication	No. of orders
None	26
Budesonide 0.5mg nebulized solution	12
Fluticasone-Salmeterol diskus 100/50mcg	1
Fluticasone-Salmeterol diskus 250/50mcg	27
Fluticasone-Salmeterol diskus 500/50mcg	8
Fluticasone-Salmeterol HFA 45/21mcg	2
Fluticasone-Salmeterol HFA 115/21mcg	2
Fluticasone-Salmeterol HFA 230/21mcg	1
Fluticasone diskus 250mcg	1
Total	**74**

Total cost of associated therapy was calculated from the sum of pharmacy medication cost incurred by the hospital, respiratory therapy labor cost, and respiratory therapy equipment cost (breath-actuated nebulizer [BAN] for nebulized budesonide and Optichamber for delivery of HFA products). Respiratory therapy administered all of the doses of ICS or ICS/LABA during the specified study period. The respiratory therapy labor cost for administration of one dose of any ICS or ICS/LABA product was $6.90 per treatment. The associated respiratory therapy equipment cost for the BAN and Optichamber were $5.47 and $4.80, respectively.

In the 74 charts reviewed, the cost of wasted drug product was $5,359.31, respiratory therapy labor cost was $2,704.80, and respiratory therapy equipment cost was $89.64, totaling $8,152.75. Extrapolating to the 10,710 admissions identified, there was an estimated 20,551 wasted budesonide vials and 6,223 wasted DPI/HFA inhalers, resulting in an inappropriate annual expenditure and estimated potential cost savings for the pharmacy department of $775,651.49. When factoring in respiratory therapy labor and equipment cost, there was a total annual savings potential of $1,180,090.03 (**Table 3**). Additionally, length of stay was shorter in the group not receiving overlap therapy compared to the group receiving overlap therapy, but it was not statistically significant (6.8 ± 3.3 days vs 7.3 ± 4.8 days; $p = .54$), indicating no significant benefit of overlap therapy in the study population identified.

DISCUSSION

Our analysis identified a cost-savings potential in the setting of COPD exacerbation. The management of this patient population includes administration of short-acting bronchodilators and systemic corticosteroids, with or without antibiotics.[2] At the present time, administration of systemic corticosteroids in combination with ICS or ICS/LABA has not directly been evaluated. However, our retrospective analysis suggests that patients are frequently prescribed overlapping therapy (65%), potentially increasing the risk of adverse drug events without any substantiated benefit beyond systemic corticosteroid therapy alone. While most patients received overlap therapy in clinical trials validating the use of systemic corticosteroids, the rationale of their use remains a question and has yet to be systematically evaluated.[4,5]

We attempted to provide some insight into this matter by evaluating length of stay data between groups. Our analysis indicated no difference in length of stay between the group receiving systemic corticosteroids alone and the group receiving ICS or ICS/LABA concomitantly with systemic corticosteroids. This information may be limited as some patients may have only received one dose of overlapping therapy, whereas others may have received overlapping therapy for the entire course of systemic corticosteroids. Although this is a drawback of a retrospective review, it is overall reflective of current clinical practice and prescribing patterns. Additionally, patients were not stratified based on disease severity

Table 3. Annual cost-savings estimates table (extrapolated to 10,710 admissions in one year)

Cost category	Cost in 74 charts (dollars)	Extrapolation factor	Extrapolated savings potential
ICS medication	5,359.31	(10,710/74)	775,651.49
Respiratory therapy labor cost	2,704.80	(10,710/74)	391,464.97
Respiratory therapy equipment cost	89.64	(10,710/74)	12,973.57
Total savings potential			**$1,180,090.03**

Note: ICS = inhaled corticosteroid.

or comorbid conditions. There is currently no guideline-based treatment recommendation for patients admitted with acute COPD exacerbations stratified based on disease severity or comorbid conditions. The benefit of overlap therapy needs to be elucidated in future studies. Until that information is available, we believe best practice would be to limit potentially inappropriate overlap therapy, which puts patients at increased risk of adverse drug events, regardless of these confounding factors.

ICS use is associated with an increased risk of local adverse effects, including oral candidiasis. A study conducted by Van Boven and colleagues assessed the risk of oral candidiasis and ICS use based on pharmacy claims data.[13] The authors observed that there were approximately twice as many prescriptions filled to treat oral candidiasis after ICS initiation, with an overall incidence of 1.4% after ICS initiation. The investigators identified additional predictive factors for oral candidiasis, including higher daily doses of ICS and concomitant oral corticosteroids.[13] While our study did not evaluate the incidence of oral candidiasis, the study by Van Boven and colleagues highlights the finding that patients who receive overlapping ICS and systemic corticosteroids are at a higher risk of developing oral candidiasis combined with additional costs to treat this largely preventable consequence. Since the benefit of overlapping ICS and systemic corticosteroids has not been evaluated, best practice remains to reduce inappropriate utilization, thus reducing the potential for side effects such as oral candidiasis. ICS use has also been correlated with systemic adverse effects; however, these adverse events develop over the course of time and are not applicable to an acute COPD exacerbation setting.[14,15]

Of the ICS or ICS/LABA ordered, fluticasone-salmeterol 250/50 mcg and nebulized budesonide 0.5 mg were the most commonly utilized strengths. Additionally, 38 out of 46 (83%) of patients who received at least one dose of inappropriate overlap therapy were on ICS or ICS/LABA therapy at home, indicating that most patients are potentially prescribed overlapping therapy as a continuation of home medications. Our institution does not currently have practices in place to alert prescribers if they are ordering overlap systemic and inhaled steroids during the medication reconciliation process. This limitation is a future direction of our institution and is currently being addressed in order to alert prescribers to potentially prevent initial dispensing of overlap therapy since guidelines do not specifically support this practice.

CONCLUSION

Factoring in medication cost, administration products, and respiratory therapy labor cost and extrapolating to the total admissions identified, a potential annual cost savings of $1,180,090.03 was calculated without an increase in hospital length of stay, indicating a need for intervention and education to decrease the use of overlap therapy. This could generate a substantial cost savings and potentially limit adverse drug events in patients admitted for COPD exacerbations treated with systemic corticosteroids. Additional studies are needed to assess the benefit of concomitant ICS and systemic corticosteroids to truly identify the potential for cost savings.

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