Review Article

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Inhaler Competence in Nepalese Patients with Asthma and Chronic Obstructive Pulmunory Disease: A Systematic Review

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ABSTRACT

Background: Incorrect use of inhalers in patients with asthma and chronic obstructive pulmonary disease is prevalent internationally. This review aims to determine the prevalence and associated factors of incorrect inhaler use and effectiveness of intervention to improve the correct use among Nepalese patients with asthma and chronic obstructive pulmonary disease.

Methods: The protocol was registered in PROSPERO. Systematic literature search was performed in PubMed, Embase, CINAHL,and Google Scholar using predefined search terms. Studies in patients with asthma or chronic obstructive pulmonary disease, reporting at least one overall or critical error, using dry powder inhalers and pressurized metered dose inhalers were included. The quality of included studies was assessed using the National Heart, Lung, and Blood Quality Assessment Tools. A descriptive narrative synthesis was undertaken.

Results: Twelve studies were eligible for analysis. At least one overall and critical step of the inhaler technique was performed incorrectly by the large number of patients, ranging from 64-100% and 9-100%, respectively. The incorrect use was associated with factors related to patients, inhalers, and health care professionals. The interventions included a combination of verbal instruction, physical demonstration, and/or face-to-face training on correct inhaler use. Following the intervention, an improvement of 23-37% in the overall inhaler technique and 7-42% in the critical steps was achieved.

Conclusions: Existing literature suggests that Nepalese patients with asthma and chronic obstructive pulmonary disease have high overall and critical error rates in the use of dry powder inhalers and pressurized metered dose inhalers. A well-designed educational intervention is necessary to improve the correct use of inhalers in this population.

Keywords: Asthma; COPD; Dry powder inhalers; Metered-dose inhalers; Nepal

INTRODUCTION

Inhaled drug therapy using dry powder inhalers (DPIs) and pressurized metered-dose inhalers (pMDIs) are commonly used to treat and manage patients with bronchial asthma and chronic obstructive pulmonary disease (COPD).[1,2] The evidence suggest that most patients fail to use such inhaler devices correctly, with error in critical steps.[3] Incorrect use of inhaler devices may consequently result poor health outcomes, including increased risk of the emergency visits and hospitalizations.[1,4] To improve and promote the correct use of inhalers, it becomes imperative to identify the inhaler competency of patients with asthma and COPD, and introduce effective intervention.[5] This review aims to identify the prevalence and factors associated with

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incorrect inhaler use in Nepalese patients with asthma and COPD. This review also examines effectiveness of various interventions used to improve inhaler use in these patients.

METHODS

Protocol registration

The protocol was registered in PROSPERO[6] and review was conducted in adherence with Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA).[7]

Inclusion and exclusion criteria

Studies on patients with asthma or COPD, reporting at least one overall or critical error, using dry powder inhalers (DPIs) and pressurized metered dose inhalers (pMDIs) were included. Studies that did not report on the proportion of patients with incorrect inhaler technique (not applying to other outcome measures) or on newly diagnosed patients with asthma and COPD were excluded. Case reports, case series, conference abstracts, those without full texts, not conducted in Nepal and in languages other than English were also excluded.

Comparator/control

All the interventional studies included in this study were pre-post design without control. So, the comparator was pre-interventional data. This was not applicable in cross-sectional studies.

Outcome measures

The primary outcomes of interest were as follows:

- Proportion of patients performing at least one step of inhaler technique incorrectly. The detailed steps of the inhalers technique are presented in supplementary file S1.
- Proportion of patients performing at least one critical step of inhaler technique incorrectly. Some of the steps of the inhaler technique are essential to adequately deliver medication to the lungs. Failure to correctly perform or missing any of these steps could cause insufficient or no delivery of medication to the lungs, which consequently causes therapeutic failure. These steps were defined as critical steps in this study. The detailed of the critical steps of inhalers technique are presented in supplementary file S1.
- Most common incorrect steps of inhaler technique.
- Risk factors associated with incorrect inhaler technique.

The secondary outcome of interest were as follows:

- Types of interventions used for improving inhaler techniques.
- Effectiveness of interventions-proportion of improvement in overall inhaler technique and critical steps.
- Reason for failure of intervention.

Search strategy

The literature search was conducted in PubMed, Embase, CINAHL, and Google Scholar from the inception of the database to November 2020. Keywords and controlled vocabulary related to inhalers, asthma or/and COPD and Nepal were used to identify the relevant studies publish English language. The forward and backward citation of all the relevant articles also performed to identify the eligible studies. The detailed search strategy is presented in the supplementary file S2.

Data extraction and synthesis

Two authors independently performed the title and abstract screening, along with the assessment of full text against the pre-specified inclusion/exclusion criteria using Endnote. The reasons for the exclusion of studies at full-text screening were recorded. Any disagreement was resolved with a consensus among authors. A pre-specified data extraction template was used to extract all the relevant data from eligible studies. Two authors performed the data extraction independently and disagreement was resolved through consensus.

Considerable heterogeneity existed between the included studies in terms of disease diagnosis, study design, inhaler devices use, checklist and method used for assessment of correct inhaler technique and thus a descriptive narrative synthesis was undertaken rather than a meta-analysis.

Quality assessment

Three authors independently assessed the quality of included studies. Quality assessment of cross-sectional studies was conducted using the National Heart, Lung, and Blood Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies[8] while the quality of pre/post studies with no control was assessed by using the National Heart, Lung, and Blood Quality Assessment Tool for Before-After (Pre-Post) Studies with No Control

Group.[9] Each article was rated as good, fair and poor after the assessment. Any disagreement was resolved through consensus among authors.

RESULTS

Search results

A total of 392 articles were identified from four databases (n=388) and back referencing of the primary source (n=4). After the removal of duplicates, the titles and abstracts of 369 studies were screened, this led to the assessment of 20 full texts. Twelve studies were included in the final synthesis of results (Figure 1).

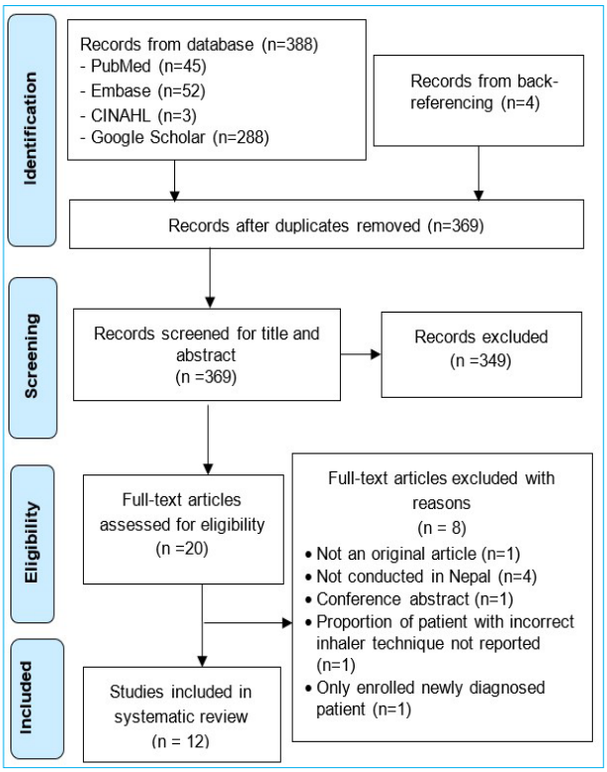

Figure 1. PRISMA flow diagram.

Study characteristics

Study sites: The studies were conducted in the major cities of Nepal, including Pokhara (n=4),[10-13] Kathmandu (n=3),[14-16] Dhulikhel (n=3)[17-19] and Bharatpur (n=2).[20,21]

Participants and setting: The identified studies involved an overall 1322 patients using inhalers who were aged five years and above. All the studies were conducted in hospitals, either in the inpatient setting (n=3),[13,16,18] outpatient setting (n=5)[10,15,19-21] or both settings (n=4).[11,12,14,17] Of the 12 studies, six were on those with COPD only (n=6)[11,15-18, 21] and the remaining six were on asthma and/or COPD (n=6).[10,12-14,19,20] Females were predominant in all reported studies (n=10) (Table 1).[10,11,13-17,19-21]

Study design: There were eight studies with a pre-post design without control[10,12,14,15,18-21] and four with a cross-sectional design (Table 1).[11,13,16,17]

Inhaler devices: Of the 12 studies, eight were on DPI,[11-13,17-19] two were on pMDI,[10,15] and two studies included both DPI and pMDI.[14,16] Rotahaler® device was included in all DPI studies,[11-14,16-21] with one study also included Revolizer® device (Table 1).[14]

Quality assessment

One study was rated as "good,"[11] ten studies were rated as "fair,"[10,13-21] and one study was rated as "poor" quality.[12] A detailed description of the quality assessment is presented in the supplementary file S3.

Inhaler competence

Overall inhaler competence

At least one error was experienced by 64-100% of patients,[10-21] with higher errors in pMDIs users (90-100%)[10,14-16] compared to DPIs users (64-96%) (Table 2).[11-14,16-21] The most common errors while using DPIs (Rotahaler® and Revolizer®) included no exhalation before inhalation, no breath holding, and no forceful and deep inhalation.[11,12,14,16-19] No breath holding, no exhalation before inhalation, and no continuous slow and deep inhalation were the most common errors on using pMDIs.[15,16]

Competence on critical steps

Approximately 9-96% of patients using DPIs made at least one critical error, with most studies reporting <30% of patients making at least one critical error.[11-14,16-21] The proportion of patients making critical error using pMDIs was 29-100%, with three out of four studies reporting >94% of patients making at least one critical error (Table 2).[10,14-16]

Associated factors for incorrect use

Studies reported that characteristics related to patient, inhaler and health care professional (HCP) were associated with increased risk of incorrect use of inhaler devices by the patients (Table 2).

Table 1. Characteristics of studies included in the review

Author (year)	Study design	Setting	Sample size	Participants characteristics	Inhaler type	Overall quality
Baral(2019) [11]	Cross-sectional	Inpatients and outpatients	204	67.2 years*; 46.1% male; COPD	DPI	Good
Maya(2018)[13]	Cross-sectional	Inpatients	101	68.5 years*; 46.5% male; 12.9% asthma, 87.1% COPD	DPI	Fair
Pun(2015)[16]	Cross-sectional	Inpatients	100	68 years*; 44% male; COPD	22% pMDI, 78% DPI	Fair
Sapkota(2016)[17]	Cross-sectional	Inpatient and Outpatient	100	63.4 years*; 41% male; COPD	DPI	Fair
Bista(2006)[10]	Pre-post	Outpatients	9	16-70 years; 44.4% male; 33.% asthma; 66.7% COPD	pMDI	Fair
Graham(2001)[15]	Pre-post	Outpatient	33	40-60 years; 39.4% male; COPD	pMDI	Fair
Khan(2016)[12]	Pre-post	Inpatient and Outpatient	50	All ages; asthma and COPD	DPI	Poor
Manandhar(2016)[14]	Pre-post	Inpatients and outpatients	160	≥ 5 years -100 years; 36.9% male; 85% asthma, 15% COPD	13.1% pMDI, 86.9% DPI	Fair
Poudel (2017)[20]	Pre-post	Outpatient	174	64 years†; 44.8% male; asthma and COPD	DPI	Fair
Poudel(2017)[21]	Pre-post	Outpatient	30	66 years; 30% male; COPD	DPI	Fair
Shrestha(2013)[18]	Pre-post	Inpatient	54	≥45 years ; COPD	DPI	Fair
Shrestha(2019)[19]	Pre-post	Outpatient	307	>18 years ; 45% male; 20.8% asthma, 69.1% COPD, 10.1% ACOS	DPI	Fair

*Mean age of the patients. † Median age of the patients. ACOS= Asthma-COPD overlap syndrome; COPD= Chronic obstructive pulmonary disease; DPI= Dry powder inhaler; pMDI= pressurized metered dose inhaler.

Table 2. Prevalence and factors associated with incorrect inhaler technique

Dry powder inhaler - rotahaler

Author (Year)	Assessment method	Checklist	No. of checklist steps	% of patient with ≥1 error	% of patient with ≥1 critical error	Associated factors for incorrect use
Baral (2019)[11]	Physical demonstration	Dutch Asthma Foundation	13	96.1	22.5	older age (>60 years), illiterate patient, living in rural area, and lack of practical demonstration of technique to the patient
Khan (2016)[12]	Physical demonstration	Self-developed	8	96	96	NR
Manandhar (2016)[14]	Physical demonstration	Self-developed	10	71.27	8.5*	Illiterate patient, female gender, and lack of practical demonstration of technique to the patient
Maya (2018)[13]	Physical demonstration	Dutch Asthma Foundation	11	70.30	10*	Older age (>60 years)
Poudel (2017)[20]	Physical demonstration	GINA	8	94.2	12.6	Older age, formally uneducated patient, lack of previous instruction to the patient, and nurses as an inhaler technique instructor
Poudel (2017)[21]	Physical demonstration	GINA	8	66.7	13.34	NR
Pun (2015)[16]	Interview	Dutch Asthma Foundation	11	90.9	42*	Younger age (<50 years), patient with ≥ secondary level of education, agriculture as primary occupation, and longer duration of rotahaler use (>5 years)

Sapkota (2016)[17]	Physical demonstration	WHO Checklist	8	67	25*	Older age (> 60 years), household activities as primary occupation, and lack of training on inhalers technique to the patient and nurses as an inhaler technique instructor
Shrestha (2013)[18]	Physical demonstration	Self-developed	8	98.1	81.5*	Lack of previous or proper instruction to the patient
Shrestha (2019)[19]	Physical demonstration	Self-developed	7	88.6	51.1*	Older age (>60yrs), low education level (<5th grade), and high level of disease severity (FEV 1 <50%)
Dry powder inhaler - Revoliser®						
Manandhar (2016)[14]	Physical demonstration	Self-developed	10	64.45	11.1*	Illiterate patient, female gender, and lack of practical demonstration of technique to the patient
Pressurized metered dose inhaler						
Bista (2006)[10]	Interview	National Asthma, Education and Prevention Program	10	100	100	NR
Graham (2001)[15]	Physical demonstration	Self-developed	7	100	100	NR
Manandhar (2016)[14]	Physical demonstration	Self-developed	10	90.47	28.6*	Female sex, illiterate patient, and lack of practical demonstration of technique to the patient
Pun (2015)[16]	Interview	Dutch Asthma Foundation	8	90.9	94*	Shorter duration of pressurized metered dose inhaler use (<10 years)

*% based on single critical steps. FEV= Forced expiratory volume; NR= not reported; WHO= World Health Organization

Patient-related factors:

Age: Patients in older age groups (>60 years) were more likely to make errors compared with younger counterparts (<60 years, n=5).[11,13,17,19,20]

Education: Illiterate or lower level of education (<5th grade) was likely to be associated with high rate of errors (n=4).[11,14,19,20]

Occupation: Patients with agriculture (n=1)[16] or household activities (n=1)[17] as a primary occupation were likely to be associated with high rate of errors.

Gender: Females were more prone to making an errors (n=1).[14]

Residential areas: Patients living in rural areas were likely to be associated with high rate of errors (n=1).[11]

Disease severity: Patients with more severe disease had poor inhaler technique (n=1).[19]

Inhaler-related factors:

Prior instruction on inhaler technique: The possibilities of incorrect inhaler technique was greater in those who had not received prior instruction compared to those who had received prior instruction (n=2).[18,20]

Prior practical demonstration or training on correct inhaler technique: Lack of practical demonstration of correct inhaler technique or training to the patients were likely to be associated with high errors frequency rate as compared to those who had received practical demonstration and training (n=4).[11,14,17,18]

Duration of inhalers use: Longer duration of DPI (rotahaler) use might be linked with higher errors rate (n=1).[16]

Health care professional-related factors:

Instruction provider: Patients instructed or trained by nurses were likely to be associated with high errors rate as compared to pharmacist and physician (n=2).[17,20]

Types of Intervention

Six groups of intervention were performed in eight studies.[10,12,14,15,18-21] The most commonly used intervention was combination of verbal instruction, physical demonstration and face-to-face training on the correct use of inhalers.[15,18-21] All interventions were delivered to individual patients and most of the interventions were provided by pharmacists or trained final year pharmacy students,[10,12,14,18-20,21] whereas two studies had physicians delivering the interventions.[15,19] With one exception of a study providing intervention for three sessions,[21] all the other interventions were contained entirely within a single session.[10,12,14,15,18-20] One study reported an average intervention time of 15 minutes, which provided a combination of verbal instruction, video, physical demonstration, and face-to-face training.[18] The follow-up time ranged from immediately after post-intervention to 1 month.[10,12,14,15,18-21]

Effectiveness of intervention

Overall, the form of the intervention did not have a significant effect on the improvement of inhaler technique over baseline, with studies reporting improvements of 23-37%.[10,12,18-21] There was a 7-42% improvement in critical steps performance.[10,12,18-21] However, the effectiveness of interventions declined over time following the intervention. One of the interventions used combination of verbal instruction, physical demonstration and face-to-face training, followed by telephonic reminder of correct inhaler technique on weekly basis for two weeks.[21] This intervention shows better improvement in overall inhaler technique (36.7%) than the improvement achieved by combination of verbal instruction, physical demonstration and face-to-face training.

Reasons for failure of intervention

Overall, the reasons for the failure of intervention were less explored. Two studies reported a partial loss of effect of the intervention over time.[12,18] Another study reported the intervention to be less effective for older adults, patients with a longer duration of therapy, and female patients;[20] however, the intervention was provided for a single session only.

Table 3. Intervention characteristics, effectiveness and the factors associated with the failure of the intervention.

Dry powder inhaler - rotahaler

Author (year)	Types of intervention	Deliverer	Delivery	Follow-up period	% of improvement in overall inhaler technique	% of improvement in critical steps	Reasons for failure of intervention
Manandhar (2016)[14]	Combination of verbal instruction, video, physical demonstration, and leaflet	Trained final year pharmacy undergraduate student	Individual	Immediately	2.10*	NR	NR
Khan (2016)[12]	Combination of verbal instruction and physical demonstration	Pharmacist	Individual	Immediately and 1 month	24.25 and 23.5	17.34 and 16.67	Longer time since intervention
Poudel (2017)[20]	Combination of verbal instruction, physical demonstration, and face- to- face training	Pharmacist	Individual	2 weeks	26.86	6.54	Old age, longer duration of therapy, and being a female
Poudel (2017)[21]	Combination of verbal instruction, physical demonstration, face-to-face training, and telephonic reminder	Pharmacist	Individual	4 weeks	36.66	15	NR
Shrestha (2013)[18]	Combination of verbal instruction, video, physical demonstration, and face-to-face training	Pharmacist	Individual	Immediately and 2 weeks	NR and 33.57	NR and 41.97	Longer time since intervention

Shrestha (2019)[19]	Combination of verbal instruction, physical demonstration, and face-to-face training	Physician	Individual	1 month	22.54	14.6	NR
Dry powder inhaler - Revoliser®							
Manandhar (2016)[14]	Combination of verbal instruction, video, physical demonstration, and leaflet	Trained final year bachelor's pharmacy student	Individual	Immediately	2.22*	NR	NR
Pressurized metered dose inhaler							
Bista (2006)[10]	Educational intervention	Pharmacist	Individual	Immediately	35.35	35.55	NR
Graham (2001)[15]	Combination of verbal instruction, physical demonstration and face-to-face training	Physician	Individual	1 month	1.4*	NR	NR
Manandhar (2016)[14]	Combination of verbal instruction, video, physical demonstration, and leaflet	Trained final year bachelor's pharmacy student	Individual	Immediately	2.67*	NR	NR

*Average improvement in the inhaler technique score; NR= not reported

DISCUSSION

Nepal has faced a substantial burden of chronic respiratory diseases, the most common being COPD and bronchial asthma. COPD is the most prevalent non-communicable disease in Nepal, with an estimated pool prevalence of 22.7%,[22] while the prevalence of severe asthma was estimated to be 7%.[23] The burden of asthma and COPD continues to grow in Nepal. The prevalence of COPD doubled in 2016 compared to 1990, and about 16,302 people were estimated to have died from COPD in Nepal in 2016.[24] The high mortality and morbidity from chronic respiratory diseases exert a high economic burden on individuals and the health care system.[25] Given such an increased burden of chronic respiratory diseases, it is crucial that patients are appropriately treated and educated on all the aspects of these diseases and treatment, which affect the patient outcomes. However, existing literature indicated that Nepalese patients with asthma and COPD had a high rates of overall error (64-100%) and critical error (9-100%) while using DPIs and pMDI. Our finding is almost similar to a previous systematic review that included studies exclusive of Nepal.[3] The reasons for the high prevalence of incorrect use of inhalers in Nepal might be multifactorial. Lack of prioritization of pharmaceutical care services in hospitals,[26,27] inadequate regulatory compliance and professional competency of community pharmacies,[28] inadequate competency of HCPs in using inhalers,[29] and low health literacy of patients[30,31]might be largely contribuing for the incorrect use of inhalers.

It should be noted that the frequently made errors by Nepalese patients with asthma and/or COPD are common to both the DPIs (Rotahaler® and Revolizer®) and pMDIs -failure to exhale before inhalation, failure to hold breath after inhalation and failure to execute forceful or slow continued and deep inhalation. Previous reviews also reported frequent errors in these steps among patients and HCPs while using DPIs and pMDIs.[3,32,33] This essentially suggest that focus should be given on these steps while providing training and educating on the correct use of inhalers as well as assessing the inhaler technique.

Previous review suggested that patients (e.g., older age), disease (e.g., high disease severity) and "inhaler related factors(e.g., lack of prior training on inhaler technique) were the predictors of incorrect inhaler technique.[3] Studies included in the current review also reported that similar factors related to patient and inhaler were associated with the increased risk of incorrect inhaler use. But, none of the studies had a randomized controlled trial design and had performed regression analyses to

identify the predictors for incorrect inhaler technique; hence, indicating the possible existence of confounders. Studies included in this review have reported that older (>60 years)[11,13,17,19,20] and illiterate patients[11,14,19,20] are likely to be associated with high device error rates. The previous review from the international context also suggests a negative correlation between advancing age and correct technique across pMDI and varying DPI devices when examined collectively.[34] We have not identified specific disease-related factors for incorrect inhaler technique, but one of the included studies in the present review indicates that patients with severe diseases may have poor inhaler technique.[19] Higher frequency of errors has also been reported in clinically severe patients with COPD than those with asthma.[3] Studies included in this review suggested that the lack of prior instruction is associated with high frequency of error.[18,20] Also, there was a higher chance of errors in patients not receiving practical demonstration and/or training on correct use inhaler.[11,14,17,18]

In this review, HCP-related factors were likely to be associated with incorrect inhaler technique of patients. Patients trained by pharmacists and physicians were found to demonstrate a better inhaler technique compared to those receiving training from nurses.[17,20] This might be due to poor knowledge and practice of Nepalese nurses on the obstructive airway disease and inhaler technique.[35-37] In addition to nurses, a significant number of all HCPs have been found to lack knowledge on the correct inhaler technique in Nepal[29] and internationally.[33] This highlights the importance of providing education to HCPs regarding the correct use of inhalers available in the market, which could be beneficial in improving their inhaler technique.[38] In addition, regular ongoing training should be provided to ensure that they retain these skills.

We found that the interventions aimed at improving the inhaler technique were effective in improving the overall inhaler technique and also the critical steps, at least in the short term. However, most of the interventions were provided for a single session and the long-term impact on the correct inhaler technique was not evaluated. A previous review also reported that interventions effectively improve patients' inhalers technique.[5] Our review also suggested that Nepalese patients were benefited from interventions, irrespective of the inhaler and the intervention types. This bears important consequences for health-economic decisions in clinical practice, as less time-consuming intervention can be selected without sacrificing effectiveness. However, face-to-face training rather than physical demonstration appears to be useful for correct inhaler use.[39,40] It has also been reported that patients who receive an additional inhalation instructions after the initial instruction have better inhaler technique than those who received a single inhalation instruction at the time of prescription.[41] All the interventions performed in the studies included in the current review focused on the inhaler technique but not on the proper management of inhaler devices, diseases, triggering factors, self-management skills and health beliefs. Hence, future intervention needs to focus on these factors in addition to the correct inhaler technique.

Reasons for the failure of intervention are less explored in the Nepalese context. One of the studies included in this review suggested that single session intervention was less effective in older adults, patients with longer duration of therapy, and female patients.[20] Two of the included studies also indicated that intervention effectiveness decreases with time.[12,17] However, none of the studies performed multivariate analysis and therefore, the influence of multiple factors was not taken into account. Regression analysis in a previous review showed that a poor initial technique, the number of steps of the inhaler technique, outpatient setting and short follow-up time were the major predictors for the success of the intervention.[5] However, intervention effect waned over time and was less effective in children.

The number of publications focusing on correct inhaler technique is relatively low from Nepal. While it is possible to draw qualitative conclusions from across the studies, the lack of consistency in device errors makes meta-analysis impossible. There were several potential sources of heterogeneity between included studies such as study design, inhaler devices studied and checklist used for assessment of correct use of inhaler devices. Hence, caution is warranted while interpreting the findings. Patients were observed using their regular inhaler, with a major focus on Rotahaler® device and pMDI. Hence, the current finding may not be applicable for other inhaler devices in Nepal such as Instahaler® and Easyhaler® and Synchrobreathe® (breath actuated inhaler).

CONCLUSIONS

Existing literature suggests that Nepalese patients commit high rates of overall and critical errors when using inhalers. Several factors related to patients, inhalers and HCPs are associated with incorrect inhaler technique of patients. Interventions aimed at improving inhaler technique in Nepal had an almost identical level of effectiveness and the reasons for the failure

of intervention remain to be explored. Well-designed educational interventions in patients with asthma and COPD are essential to improve the correct use of inhalers and patient outcomes in days to come.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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