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Original Article

Evaluation of the techniques and steps of intranasal corticosteroid sprays administration

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Conflict of Interest
The authors have no financial conflicts of interest.

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ABSTRACT

Background: Intranasal corticosteroid (INCS) is one of the most effective treatments for allergic rhinitis (AR). To achieve optimum efficiency while avoiding adverse effects (AEs), patients must comply with and follow the drug administration instructions.
Objective: To evaluate INCS administration techniques and steps and the association between inaccurate drug administration and AEs.
Methods: A descriptive cross-sectional study was performed in patients diagnosed with AR who had used an INCS for more than 1 month at the HRH Princess Maha Chakri Sirindhorn Medical Center, Nakhon Nayok, Thailand between September 2020 and August 2021. Patient information was collected, evaluate the accuracy of the application techniques and the steps they followed for INCS administration and the occurrence of any associated AEs.
Results: In total, 150 subjects diagnosed with AR met the criteria. Only 6 patients (4%) correctly performed all 12 steps of INCS administration, while 44 patients (29.33%) correctly performed the 5 recommended essential steps. AEs were found in 23 patients (15.33%), with not pointing the tip slightly outward away from the septum significantly associated with a 3.6 times higher risk of AEs in patients (odds ratio, 3.6; 95% confidence interval, 1.3–9.4; $p = 0.012$).
Conclusion: Investigations into INCS use in patients with AR revealed that only 4% of patients correctly performed all the administration techniques and steps, while 30% of patients at least followed the 5 recommended essential steps perfectly. Not pointing the tip slightly outward away from the septum was found to result in the most AEs.

Trial Registration: Thai Clinical Trials Registry: TCTR-20210718003

Keywords: Nasal spray; Administration; Intranasal corticosteroid; Allergic rhinitis

INTRODUCTION

Allergic rhinitis (AR) is a very common condition [1, 2], with a prevalence of up to 40% worldwide [3], and 42% in Thailand according to Bunnag's study [4]. Intranasal corticosteroids (INCS) are one of the highest potency medications to control AR [5]. INCS can directly modulate the pathophysiology of AR due to their potent anti-inflammatory effects [6], which prevent disease manifestation by inhibiting inflammatory cells and pro-inflammatory signals [7]. INCS have been shown to be beneficial for AR and chronic rhinosinusitis (CRS) [8, 9].

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INCS are generally regarded as safe drugs [10]. When taken in the prescribed dosages, no systemic bioactivity was reported in adults [11]. However, local nasal effects (epistaxis, nasal irritation), and headache may generally occur as adverse effects (AEs) [10, 12]. Most INCS are administered in the form of a spray. An accurate administration technique and the need to follow multiple steps in the INCS administration are important. The use of improper INCS administration techniques and not following all the recommended administration steps may be correlated with reduced pharmacological efficacy, AEs, and lower treatment adherence [13].

Instructions for the patient regarding the correct administration and recommended steps they should follow are usually provided by their healthcare provider or in an information leaflet. However, a recent study reported that most patients use INCS improperly [14].

To evaluate the accuracy of patients performing the recommended 12 steps required for INCS administration, especially the 5 recommended essential steps, and the relationship between inaccurate drug administration and the occurrence of AEs.

MATERIALS AND METHODS

Study design and population

A descriptive cross-sectional study was performed involving all AR patients who received INCS treatment at the Rhinology Clinic, Department of Otolaryngology, HRH Princess Maha Chakri Sirindhorn Medical Center (MSMC), Nakhon Nayok, Thailand between 1 September 2020 and 31 August 2021. The study inclusion criteria were: (1) patients aged 18 to 60 years old, (2) AR was diagnosed by an otolaryngologist, and (3) a duration of INCS usage of more than 1 month. The exclusion criteria were: (1) allergy to INCS, (2) contraindication to INCS usage, i.e., glaucoma, pulmonary tuberculosis, fungal sinusitis, (3) pregnancy, and (4) administration of another intranasal medication. The termination criteria were: (1) the presence of serious AEs from INCS usage, and (2) the subject made a withdrawal request from the study. The Human Ethics Committee of Srinakharinwirot University approved the study (SWUEC-050/2563E). Informed consent was obtained from all study participants.

Study process

The patients' demographic information and treatment history were obtained, sex, age, education background, history of diagnosis of AR, CRS without nasal polyps (CRSsNP), CRS with nasal polyps (CRSwNP), and history of intranasal medication usage.

The patients were asked to demonstrate the techniques they used and the steps they followed for INCS self-administration, with all the participants evaluated by the same physician (SR). The assessment was done by observation techniques covering the 12 recommended step for INCS administration, comprising: (1) shake the spray in the vertical plane, (2) remove the dust cap, (3) blow the nose, (4) hold the bottle with the opposite hand from the nostril to be sprayed, (5) hold the bottle pointing up and replace the hand on the pusher, (6) put the tip of the nozzle into the nostril and close the other side, (7) slightly tilt the head forward, (8) point the tip slightly outwards, away from the septum, (9) squirt the spray in to the nose while breathing in, (10) breathe out through the mouth, (11) wipe the nozzle with a tissue or handkerchief, and (12) replace the cap. If the physician considered that the assessment was inadequate or that the patient had a poor administration technique or missed out steps, he gave the patient accurate instructions about the correct techniques and all the steps to follow

for proper INCS administration. The physician also took the patient's history and performed a physical examination to check for AEs, including epistaxis, nasal irritation, cough, pharyngeal irritation, and headache.

Sample size calculation and statistical analysis

The required sample size for the study was determined based on the one sample test of proportion formula [15]. A previous study reported that the prevalence of patients who carried out all the recommended essential steps was 11% [14]. We estimated we required a sample size of 130 patients to provide 90% power to detect a difference of 10% at a two-sided alpha of 0.05.

Descriptive statistics were used to analyze the basic data and categorical data were reported in the form of numbers and percentages. Continuous data were reported using the mean and standard deviation. Rates were calculated to estimate the percentage of patients who completed the steps correctly as well as the percentage who completed all the recommended essential steps. The association between incorrectly performing the recommended essential steps and the occurrence of AEs was performed by chi-square tests and was reported in terms of the relative risk and odds ratio (95% confidence interval [CI]). Stata ver. 14.0 (StataCorp LLC, College Station, TX, USA) was used in the analysis. A *p* value of less than 0.05 was considered statistically significant.

RESULTS

In total, 228 patients diagnosed with AR who received INCS treatment at the Rhinology Clinic of MSMC between 1 September 2020 and 31 August 2021 were initially considered for the study, of whom 78 were then excluded from the analysis, comprising 38 patients for not meeting the inclusion criteria, 32 patients who declined to participate, and 8 patients who were pregnant (**Fig. 1**). This left 150 patients who were included in the study, comprising 89 females (59.33%) and 61 males (40.67%), Their mean age was 38.71 ± 12.08 years old. The participants' demographic data, sex, education background, history of diagnosis of AR, CRSsNP, CRSwNP, and history of intranasal medication usage, are shown in **Table 1**.

Among the 150 patients included in the study analysis, only 6 patients (4%) correctly performed all 12 steps for INCS administration. Dust cap removal was the step that was most correctly done, with all patients doing this correctly (100%). On the other hand, the most

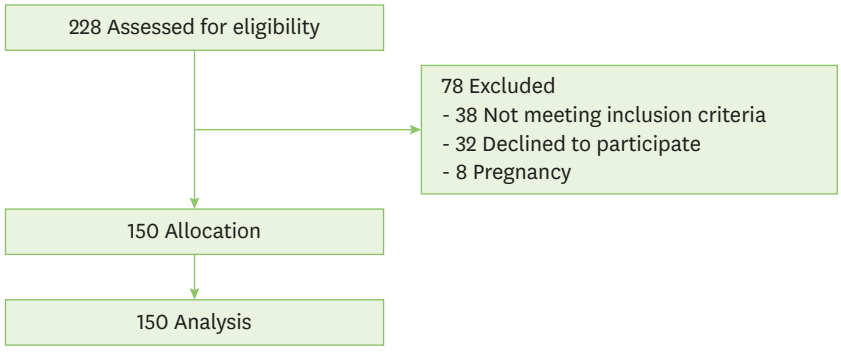

Fig. 1. Participant flowchart: CONSORT (consolidated standards for reporting of trials) diagram.

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Table 1. Participants' characteristics

Characteristic	Number (%)
Sex	
Male	61 (40.67)
Female	89 (59.33)
Education	
Grade 1–6	23 (15.33)
Grade 7–12	62 (41.33)
Bachelor's degree	50 (33.33)
Above bachelor's degree	15 (10.00)
Diagnosis	
AR	94 (62.67)
AR with CRSsNP	33 (22.00)
AR with CRSwNP	23 (15.33)
Intranasal corticosteroid	
Budesonide	32 (21.33)
Mometasone furoate	36 (24.00)
Fluticasone furoate	82 (54.67)

AR, allergic rhinitis; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps.

Table 2. Assessed steps for the administration of intranasal corticosteroid sprays

Steps	Carried out, n (%)
1. Shake the spray in the vertical plane*	124 (82.66)
2. Remove the dust cap	150 (100)
3. Blow the nose*	115 (76.67)
4. Hold the bottle with the opposite hand from the nostril to be sprayed	42 (28)
5. Hold the bottle pointing up and replace hand on the pusher	144 (96)
6. Put the tip of the nozzle into the nostril and close the other side	66 (44)
7. Hold head in a neutral upright position, or slightly tilt the head forward	138 (92)
8. Point the tip slightly outwards, away from the septum*	85 (56.67)
9. Squirt the spray in the nose while breathing in*	138 (92)
10. Breathe out through the mouth*	107 (71.33)
11. Wipe the nozzle with a tissue or handkerchief	90 (60)
12. Replace the cap	144 (96)

*Recommended essential steps.

incorrectly performed step was holding the bottle with the opposite hand from the nostril to be sprayed, which only 28% of patients did correctly (**Table 2**).

Among the 12 steps in the spray usage, there are 5 recommended essential steps that must be performed for correct INCS administration: (1) shake the spray in the vertical plane, (2) blow the nose, (3) point the tip slightly outwards, away from the septum, (4) squirt the spray in the nose while breathing in, and (5) breathe out through the mouth. Only 44 patients (29.33%) performed these recommended essential steps correctly. The step that most patients could perform correctly was the step that required the patient to squirt the spray in the nose while breathing in (92%), while the step that was most commonly performed incorrectly by patients was the step that required the patient to point the tip slightly outwards, away from the septum, with that performed correctly by only 56.67% of patients (**Table 2**).

Overall, 23 patients (15.33%) had AEs from INCS usage (epistaxis and nasal irritation). In analyzing these with the recommended essential steps, the step requiring the patient to "point the tip slightly outwards, away from the septum" was found to be statistically significantly related with the occurrence of AEs, with a 3.6 times higher risk (odds ratio, 3.6; 95% CI, 1.3–9.4; $p = 0.012$) (**Table 3**). Additionally, no other AEs were found to be associated with use of the medication in this study.

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Table 3. Association between incorrectly performing the recommended essential steps and the occurrence of adverse effects (AEs)

Essential steps	No AEs, n (%)	AEs, n (%)	OR (95% CI)	*p* value
1. Shake the spray in the vertical plane			1.88 (0.66–5.37)	0.367
Yes	107 (71.33)	17 (11.33)		
No	20 (13.33)	6 (4)		
2. Blow the nose			1.19 (0.43–3.30)	0.943
Yes	98 (65.33)	17 (11.33)		
No	29 (19.33)	6 (4)		
3. Point the tip slightly outwards, away from the septum			3.63 (1.39–9.477)	0.012*
Yes	78 (52)	7 (4.67)		
No	49 (32.67)	16 (10.67)		
4. Squirt the spray in the nose while breathing in			1.96 (0.49–7.89)	0.583
Yes	118 (78.66)	20 (13.33)		
No	9 (6)	3 (2)		
5. Breathe out through the mouth			1.75 (0.69–4.43)	0.341
Yes	93 (62)	14 (9.33)		
No	34 (22.67)	9 (6)		

OR, odds ratio; CI, confidence interval.
*$p < 0.05$, statistically significant difference.

DISCUSSION

INCS treatment is the most effective treatments for AR [5]. To maximize its efficacy, all medications must be used with proper techniques together with following all the recommended administration steps. However, there is no standard guideline for INCS use in Thailand. Consequently, the researcher gathered and adapted 12 techniques and steps used for INCS administration in previous studies [5, 16-18], as well as a Dutch protocol [19], and from leafletless usage. Further, there are some differences in using the methods, as shown in **Table 4**. The 5 recommended essential steps were determined in reference to previous studies [14, 16-19].

The present study showed that few patients accurately performed all the techniques and followed all the recommended steps for INCS drug administration, which concorded with the study of Rollema, who reported that only 6% of volunteers were able to properly complete all the steps [14]. It was also found that 30% of the patients followed the recommended essential steps in this study, which was a higher percentage than that reported by Rollema (11%) [14], which could be because the patients in this study received instructions from a healthcare professional, whereas in prior studies, participants took their instructions from a drug

Table 4. Directional steps from prior studies and as outlined in patient information leaflets

Steps	Rollema et al. [17]	Dutch Protocol [19]	Bridgeman [5]	Benninger et al. [16]	Lee et al. [18]	BUD	MF	FF
1. Shake the spray in the vertical plane*	✓	✓			✓	✓	✓	✓
2. Remove the dust cap	✓	✓				✓	✓	✓
3 Blow the nose*	✓	✓	✓	✓	✓	✓	✓	✓
4. Hold the bottle with the opposite hand from the nostril to be sprayed	✓	✓		✓			✓	
5. Hold the bottle pointing up and replace hand on the pusher	✓	✓	✓			✓	✓	✓
6. Put the tip of the nozzle into the nostril and close the other side	✓	✓	✓					
7. Hold head in a neutral upright position, or slightly tilt the head forward	✓	✓	✓	✓			✓	✓
8. Point the tip slightly outwards, away from the septum*	✓	✓	✓	✓	✓			✓
9. Squirt the spray in the nose while breathing in*	✓	✓	✓	✓	✓		✓	✓
10. Breathe out through the mouth*	✓	✓	✓		✓			✓
11. Wipe the nozzle with a tissue or handkerchief	✓	✓	✓			✓		✓
12. Replace the cap	✓	✓	✓			✓	✓	✓

BUD, budesonide; MF, mometasone furoate; FF, fluticasone furoate.
*Recommended essential steps. ✓The steps are evident in studies or information leaflets.

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information leaflet. However, the following of the recommended essential steps in this study was still at a very low rate. This may not be surprising as even studies involving healthcare personnel showed that only 3% of them followed all the recommended essential steps [19].

Epistaxis and nasal irritation were identified as AEs in this study, in line with the data from a prior meta-analysis that showed that patients were at greater risk of epistaxis when using INCS than a placebo [10]. This study showed that not pointing the tip slightly outward away from nasal septum had a 3.6 times higher risk of causing epistaxis and nasal irritation than normal, which was in accordance with the study of Benninger, who reported that pointing the tip slightly inward could increase the risk of epistaxis more than the outward method [16]. As a result, this step should receive more attention. For other AEs, a prior study reported that more cases of headache could be found [20], but none of the patients with this symptom were found in the present study, and from the meta-analysis, it was found that there was no statistically significant difference in the INCS group's incidence of headache when compared with the placebo group, which is consistent with other studies that found headache to be a common AE but not statistically significant [10].

For INCS efficacy, in addition to the precision of performing all the techniques and following all the steps in INCS administration, the INCS efficacy was significantly influenced by patient compliance with the treatment and its proper administration, emphasizing that patient education and compliance monitoring are essential components of successful therapy [21].

The strength of this study is its assessment of the accuracy of INCS usage by the SR, which minimizes interpersonal variation in the assessment, which would otherwise make the results less accurate. In addition to investigating the accuracy of INCS use, the relationship between AEs and INCS usage was also studied. Nonetheless, there are still several limitations related to the study's descriptive nature. Furthermore, this study was conducted at a single center, thus limiting the generalizability of the study's findings.

In a subsequent study, the researcher intends to conduct a prospective study to determine the relationship between incorrect INCS usage and the outcomes of treatment following proper INCS usage to emphasize the greater effectiveness from the correct use of INCS.

In conclusion, the study of the use of INCS in patients with AR revealed that only 4% of patients performed all the administration techniques properly and followed all the steps correctly while 30% of patients at least followed the 5 recommended essential steps perfectly. Not pointing the tip slightly outward away from the septum was found to be related with a higher risk of epistaxis and nasal irritation, so physicians should continuously evaluate patients' INCS usage and educate patients in the proper techniques and full steps required for effective INCS usage to reduce the risk of AEs occurring.

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