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Rational selection of inhalation devices in the treatment of chronic obstructive pulmonary disease by means of the System of Objectified Judgement Analysis (SOJA)

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ABSTRACT

Objectives The large number of available medicines and devices makes it almost impossible to have sufficient knowledge of each individual medicine and device, especially for general practitioners. This may lead to suboptimal treatment, more exacerbations, hospitalisations and higher treatment costs. Reducing the number of medicines and devices, based on rational criteria, allows physicians and pharmacists to build experience with a more limited set of medicines and to standardise the inhalation instructions.

Methods In this study inhalers are compared by means of the System of Objectified Judgement Analysis (SOJA) method. The following selection criteria were applied: uniformity in device, number of steps per inhalation, risk of errors, hygienic aspects, feedback mechanism, and risk of inhalation with an empty inhaler.

Results Substantial differences were seen in the overall scores, with the Ellipta device showing the highest score, followed by Diskus/Accuhaler, Genuair and Nexthaler. Several devices require more or less identical techniques, such Ellipta and Diskus/Accuhaler as well as Genuair and Novolizer. When patients use these devices in combination this increases their uniformity, because additional medicines become available for the devices: starting therapy with Diskus or Novolizer and follow-up with Ellipta or Genuair. The resistance of Respimat and Breezhaler is lower than that of other devices, which makes these devices suitable for patients who cannot generate sufficient inhalation flow.

Conclusions A substantial reduction of inhalers, combined with optimal and standardised instructions, should improve the care of patients with chronic obstructive pulmonary disease.

INTRODUCTION

Effective bronchodilatation is the cornerstone of pharmacological treatment of chronic obstructive pulmonary disease (COPD). Several different treatment options are available, such as long-acting β agonists (LABA), long-acting muscarinic antagonists (LAMA), combinations of both, combinations of LABA and inhaled corticosteroids (ICS), and triple combinations of LABA, LAMA and ICS. Each treatment option is used in different stages of COPD. Besides these pharmacological options, different inhalation forms, such as metered dose inhalers (MDIs), dry powder inhalers (DPIs) and soft mist inhalers are available.

The large number of available medicines and devices makes it almost impossible to have sufficient knowledge of each individual medicine and device, especially for general practitioners.[1 2] Patient compliance in COPD is multifactorial, including understanding of the disease by the patient, physician–pharmacist–patient interactions, and personal factors of the patients, including incorrect inhalation techniques. A poor inhalation technique may lead to suboptimal treatment, more exacerbations, hospitalisations and higher treatment costs.[3 4]

Reducing the number of medicines and devices, based on rational criteria, allows physicians and pharmacists to build experience with a more limited set of medicines and to standardise the inhalation instructions.

In a previous article,[5] we have shown that there are no major differences between medicines within various drug classes of inhaled medication in COPD. The conclusion was that the properties of inhalers could well determine the choice of inhaled medication in COPD. It should be kept in mind that substantial differences in clinical efficacy and/or safety of the drugs within a class may exist in individual patients.

METHODS

Research question

The authors of the present article were members of the expert group (working party) of the Dutch Lung Association. The aim of this Working Party (consisting of pulmonologists, general practitioners, researchers, and hospital and community pharmacists) was to provide criteria for the selection of inhalation devices for the maintenance treatment of COPD in the Netherlands. The first draft of the article was prepared by authors RJ and JK and extensively discussed with authors EM and RD. Finally, the article was discussed with the working party in two sessions, resulting in the addition of the criterion "risk of inhalation with an empty inhaler" and minor adjustments in the methodology of scoring for the selection criteria.

Inclusion and exclusion criteria

This analysis was performed to compare soft mist inhalers, dry powder inhalers (DPIs) and metered dose inhalers (MDIs).

Applied methodology

In this study inhalers were compared by means of the System of Objectified Judgement Analysis (SOJA) method.

The SOJA method is a model for rational drug selection. The relevant selection criteria for inhalers are defined and judged by a panel of experts and each selection criterion is given a relative weight. The more important a selection criterion is considered, the higher the relative weight that is given to that criterion. The ideal properties for devices are determined and each device is scored as a percentage of the score of the ideal device for all selection criteria. The devices with the highest total score are most suitable for formulary inclusion.[6]

Selection criteria

The following selection criteria were applied:

- Criterion: relative weight
- Uniformity in device: 250
- Numbers of steps per inhalation: 250
- Risk of (critical) errors: 200
- Hygienic aspects: 20
- Feedback mechanism: 180
- Risk of inhalation with an empty inhaler: 100
- Total score: 1000

The following devices were included in the analysis:

- Aerolizer
- Autohaler
- Axahaler
- Breezhaler
- Cyclohaler
- Diskus/Accuhaler
- Easyhaler
- Ellipta
- Elpenhaler
- Fospiro
- Genuair
- Handihaler
- MDI solution
- MDI suspension
- Nexthaler
- Novolizer
- Redihaler
- Respimat
- Spiromax
- Turbuhaler
- Zonda

Uniformity of device

This was judged as follows:

It is an advantage when patients can make use of the same inhaler during all steps in the treatment of COPD. This allows the patient to use the same inhaler when medicines are added or changed during the course of the disease. The scoring of the weighting was based on discussions within the working party. A relatively low weight was therefore given to the addition of an ICS or to triple therapy, because these are necessary in a limited number of patients.

Obviously any method of scoring is more or less arbitrary. There may also be debate over which weight is given to each sub-criterion.

The scoring is described in table 1.

Table 1 Uniformity per device, methodology

Treatment steps for COPD per device plus score	Score (%)
1 SABA or SAMA or combination	SABA or SAMA 15%, both +3%, combination +2%
2 LABA or LAMA	LAMA 25%, LABA 23%, both (separate) 30% (fixed combination is scored below)
3 Combination of LABA/LAMA	Fixed combination 25%
4 Combination of ICS/LABA	Fixed combination 10%, separate 5%
5 Combination of ICS/LABA/LAMA	Fixed combination 15%, separate 5%

COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroid; LABA, long-acting β agonist; LAMA, long-acting muscarinic antagonist; SABA, short-acting β agonist; SAMA, short-acting muscarinic antagonist.

Number of steps per inhalation

The lower the number of steps per inhalation, the more convenient for the patient; therefore the easier the instruction and the lower the risk of errors.

The device with the smallest number of steps was awarded 100%, whereas the device with the largest number of steps did not score. The scores for the other devices were obtained by linear intrapolation.

Risk of (critical) errors

Factors were considered as critical if there was a substantial risk of a significant decrease of drug delivery with incorrect use. The methodology of scoring was extensively discussed in the working party. The estimation of the risk of incorrect use was based on both clinical studies[3 4 7–10] as well as observations during training and education of patients by authors JK and EM.

The scoring is described in table 2.

Hygienic aspects

Re-use of a device or space chamber could result in poor hygienic conditions. Also it is important that a device is easy to clean.

Feedback mechanism

Feedback mechanisms give information to the patient whether or not the device has produced a dose.

This was scored as follows:

1 feedback 60%
2 feedbacks 90%
3 or more feedbacks 100%

Risk of inhalation with an empty inhaler

There is a risk that a patient will keep using an empty inhaler.

For users of strips or capsules it is obvious that these are empty and the risk of inhalation with an empty inhaler is low.

A counter is a useful tool in reducing the risk of inhalation with an empty inhaler, but it does not provide a guarantee. When the inhaler blocks, this makes it impossible to continue use of the inhaler.

This was scored as follows:

Capsule or strip: score
Counter and blockade after last dose: 100%
Extra large dose counter: 90%
Counter or indicator: 80%
No counter: 0%

RESULTS

Uniformity of device

The score is presented in table 3.

Table 2 Risk of critical errors, methodology

	Incidence	Risk	Deduction critical	Deduction non-critical
Estimated error rate	<2%	Very low	2%	1%
	>2–5%	Low	3%	1%
	>5–<15%	Moderate	10%	2%
	15–35%	High	25%	3%
	>35%	Very high	35%	5%

Number of steps per inhalation

The number of steps per inhalation are presented below. There are huge differences in the number of actions needed to inhale.

The Ellipta inhaler showed the smallest number of steps and scored 100%. Various devices needed 14 steps per inhalation.

A specification of the steps per inhalation is provided in online supplementary file S1.

3 steps Ellipta 100%
4 steps Nexthaler, Redihaler, Spiromax 91%
5 steps Autohaler, Diskus, Turbuhaler 82%
6 steps Forspiro, Genuair 73%
7 steps Easyhaler, Novolizer 64%
8 steps MDI solution 55%
9 steps Respimat 46%
12 steps MDI suspension 19%
13 steps Elpenhaler 10%
14 steps Aerolizer, Axahaler, Breezhaler, 0%
Cyclohaler, Handihaler, Zonda

Risk of (critical) errors

The results are presented below.

The error rate cannot be specified directly from a large scale comparative study including all available devices. Several studies identifying the (critical) error rate of the available devices were taken into consideration.[3 4 7–10]

A specification of the potential critical errors is provided in online supplementary file S2.

95%: Ellipta, Nexthaler. Spiromax
93% Genuair, Novolizer,
91% Diskus, Forspiro, Turbuhaler
95% Redihaler
81% Handihaler
80% Zonda
79% Aerolizer, Axahaler, Breezhaler, Cyclohaler
75% Autohaler
60% Respimat
58% Easyhaler
43% Elpenhaler
37% MDI solution
19% MDI suspension

Hygienic aspects

The hygienic aspects were scored as follows:

Most devices scored 100%: change inhaler each time, and easy to clean. This was the case for Autohaler, Axahaler, Breezhaler, Clickhaler, Diskus, Easyhaler, Ellipta, Forspiro, Genuair, Nexthaler, Redihaler, Respimat, Spiromax, Turbuhaler and Zonda.

Cyclohaler, Handihaler and Novolizer have to replaced actively and score 50%.

Elpenhaler is difficult to clean, because the inhaler contains the strips and also scores 50%.

MDIs have to be actively replaced and are difficult to clean and do not score.

Table 3 Uniformity per device, results

	Step 1 SABA or SAMA or combination	Step 2 LABA or LAMA	Step 3 Combination of LABA/LAMA	Step 4 Combination of ICS/LABA	Step 5 Combination of ICS/ LABA/LAMA	Total score
Aerolizer	0	23	0	0	0	23
Autohaler	15	0	0	0	0	15
Axahaler	0	0	0	10	0	10
Breezhaler	0	30	25	0	0	55
Cyclohaler	18	23	0	5	0	46
Diskus	15	23	0	10	0	48
Easyhaler	0	23	0	10	0	33
Ellipta	0	25	25	10	15	75
Elpenhaler	0	0	0	10	0	10
Forspiro	0	0	0	10	0	10
Genuair	0	25	25	0	0	50
Handihaler	0	25	0	0	0	25
MDI solution	17	23	25	10	15	90
MDI suspension	15	23	0	10	0	48
Nexthaler	0	0	0	10	0	10
Novolizer	15	23	0	5	0	43
Redihaler	15	0	0	0	0	15
Respimat	0	30	25	0	0	55
Spiromax	0	0	0	10	0	10
Turbuhaler	15	23	0	10	0	48
Zonda	0	25	0	0	0	25

ICS, inhaled corticosteroid; LABA, long-acting β agonist; LAMA, long-acting muscarinic antagonist; MDI, metered dose inhaler; SABA, short-acting β agonist; SAMA, short-acting muscarinic antagonist.

Table 4 Feedback mechanisms, results

Device	Empty capsule	Rattling of the capsule	Empty strip	Click	Visual	Counter	Taste (lactose)	Spray	Total feedback mechanisms	Score	Lactose (mg)
Aerolizer	1	1					1		3	100%	25
Autohaler				1					1	60%	
Axahaler	1	1					1		3	100%	24.4
Breezhaler	1	1					1		3	100%	23.6
Cyclohaler	1	1					1		3	100%	25
Diskus						1	1		2	90%	12.5
Easyhaler						1			1	60%	3.8
Ellipta						1	1		2	90%	25
Elpenhaler			1				1		2	90%	24.6
Fospiro			1			1	1		3	100%	11.95
Genuair				1	1	1	1		4	100%	12
Handihaler	1	1							2	90%	5.5
MDI solution						1		1	2	90%	
MDI suspension						1		1	2	90%	
Nexthaler				1		1			2	90%	9.9
Novolizer				1	1	1	1		4	100%	10.7
Redihaler									0	0%	
Respimat				1		1				90%	
Spiromax						1			1	60%	5
Turbuhaler						1			1	60%	0.73
Zonda	1	1					1		3	100%	18

Not every MDI device has a counter and a spray is not a guarantee that it contains medication. We have given MDIs the "benefit of the doubt".
MDI, metered dose inhaler.

Feedback mechanisms

The score is presented in table 4.

Risk of inhalation with an empty device

The results are presented below:

All capsule or strip devices were awarded 100%: Aerolizer, Axahaler, Breezhaler, Cyclohaler, Elpenhaler, Handihaler and Zonda.

A combination of counter and blockade is applicable to Genuair and Respimat: these devices score 100% as well.

A large counter is available for Ellipta: this device scores 90%.

The following devices have a counter and score 80%: Diskus, Easyhaler, Forspiro, MDIs, Nexthaler, Novolizer, Spiromax, and Turbuhaler.

No counter is applicable for Autohaler and Redihaler: these devices do not score.

It should be noted that not every MDI device has a counter and a spray is not a guarantee that it contains medication. We have given MDIs the "benefit of the doubt".

SCORE

The SOJA score is presented in table 5.

DISCUSSION

Applied methodology

This was done by means of the SOJA method, which is a well-established rational and transparent way of selecting medicines (or in this case inhalation devices) within a therapeutic class from a formulary perspective.

In the SOJA method, selection criteria for a given group of drugs (or in this case devices) are prospectively defined and the extent to which each individual device fulfils the requirements for each criterion is studied. Each criterion is given a relative weight (ie, the more important a given selection criterion is considered to be, the higher is the relative weight given to that criterion). Both the relative scores for each drug for each selection criterion and the relative weight of each criterion are determined by a panel of experts in this field. The properties of all drugs are compared with the hypothetical "ideal" device from that group, which is assigned the full relative weight for each criterion. This device will be available in all treatment options of COPD, very easy to use, no errors possible, easy to clean, provides optimal feedback that the drug was correctly inhaled, and is not associated with the risk of using an empty inhaler.

In the published SOJA scores, 1000 points are divided over the criteria that are considered to be relevant for a particular group of drugs. In the interactive programme, the scores for each drug have been determined by a group of experts and the user is free to assign his own relative weight to each criterion using any scale he wishes. The programme then computes the ranking scores for the drugs in the group.

Outcome

Substantial differences were seen in the overall scores, with the Ellipta device showing the highest score, followed by Diskus/Accuhaler, Genuair and Nexthaler. Several devices require more or less identical techniques, such Ellipta and Diskus/Accuhaler as well as Genuair and Novolizer. When patients use these devices in combination this increases their uniformity, because additional medicines become available for the devices: starting therapy with Diskus or Novolizer and follow-up with Ellipta or Genuair.

The resistance of Respimat and Breezhaler is lower than that of other devices, which makes these devices also suitable for patients who cannot generate sufficient inhalation flow.

Table 5 SOJA score for inhalation devices in COPD treatment

Device	Uniformity	Steps	Critical errors	Hygiene	Feedback	Risk of empty inhaler	Score
Weight	250	250	200	20	180	100	1000
Aerolizer	58	0	158	20	180	100	516
Autohaler	38	205	150	20	108	0	521
Axahaler	25	0	158	20	180	100	483
Breezhaler	138	0	158	20	180	100	596
Cyclohaler	115	0	158	10	180	100	563
Diskus	120	205	182	20	162	80	769
Easyhaler	83	160	116	20	108	80	567
Ellipta	188	250	190	20	162	80	890
Elpenhaler	25	25	86	10	162	100	408
Fospiro	25	183	182	20	180	80	670
Genuair	125	183	186	20	180	100	794
Handihaler	63	0	162	10	162	100	497
MDI solution	225	138	74	0	162	80	679
MDI suspension	120	48	38	0	162	80	448
Nexthaler	25	228	190	20	162	80	705
Novolizer	108	160	186	10	180	80	724
Redihaler	38	228	170	20	0	0	456
Respimat	138	115	120	20	162	100	655
Spiromax	25	228	190	20	108	80	651
Turbuhaler	120	205	182	20	108	80	715
Zonda	63	0	160	20	180	100	523

COPD, chronic obstructive pulmonary disease; MDI, metered dose inhaler; SOJA, System of Objectified Judgement Analysis.

Strength and limitations of the methodology

It should be taken into consideration that this analysis is limited to the devices. In clinical practice, patient-related factors play an important role, such as inhalation flow, hand-eye coordination and personal preferences of the patient.

The evaluation of criteria in the SOJA method is highly standardised in order to promote unbiased judgement of drugs from various pharmacotherapeutic categories based on clinically relevant criteria. There will always be room for debate whether or not the correct scoring system was used for each criterion and judgement may be arbitrary for most, if not all, criteria. This is the case with any method used to quantify properties of drugs. The SOJA method is intended as a tool for rational drug decision making, forcing clinicians and pharmacists to include all relevant aspects of a certain group of drugs, thereby preventing formulary decisions being based on only one or two criteria. Besides this, possible "hidden criteria" are excluded from the decision making process. The outcome of this study should be seen as the basis for discussions within formulary committees and not as an absolute truth.

Obviously, the score depends on the relative weight that is assigned to each individual selection criterion. Therefore an interactive programme is available, which makes it easy for local and regional formulary committees to assign personal weights to each selection criterion by individual members. If a physician or pharmacist considers individual criteria as totally irrelevant, this criterion may be assigned 0 points, thereby ignoring this criterion.

There is some overlap between two of the criteria that we applied: number of steps per inhalation and the error rate. The more steps, the more likely that (critical) errors occur. This can be "compensated" for by means of adjusting the assigned weight to these criteria.

Acquisition cost was not taken into account, because this varies with time. In practice acquisition cost is of course an important selection criterion, especially because there are very limited differences between the medicines from a clinical perspective. Exclusion of this criterion also makes this comparison more internationally applicable.

The criterion internal resistance was not included, because this is one of the patient-related factors, which cannot be expressed in a "generic matrix". Patient-related factors should also be taken into consideration. This is expressed in figure 1. The present matrix only applies to those patients who can inhale in a conscious manner, are able to inhale, exhale and hold their breath for sufficient time, and are able to generate enough inhalation flow to overcome the internal resistance of the device. When this is not the case, other choices should be made.

The main outcome of this matrix may be that major steps can be made in reducing the number of different devices, thereby

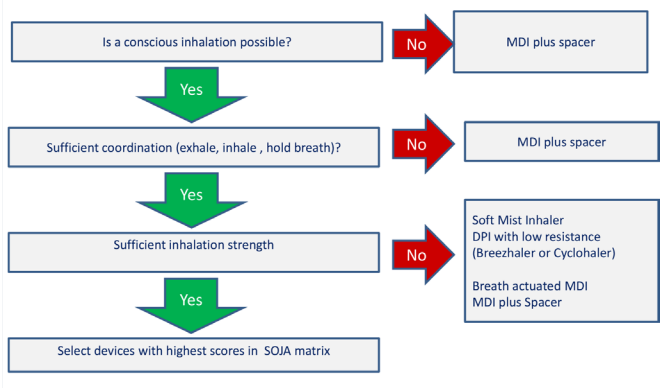

Figure 1 Flowchart for device selection based on the SOJA matrix. DPI, dry powder inhaler; MDI, metered dose inhaler; SOJA, System of Objectified Judgement Analysis.

allowing standardised and optimal patient information, which can be the same provided by all caregivers.

The set of selection criteria was determined by the panel of experts in the Dutch working party after extensive discussions. Several potential selection criteria were not used for the following reasons.

Patient preference

The results of these studies are highly dependent on study design. Most studies (if not all) show a preference for the device from the sponsor of the study. Besides this, no studies are available comparing all devices.

Ease of use

The same limitations apply as described under patient preference. We have used a concrete criterion, such as the number of steps per inhalation.

Effects of humidity and temperature

Although this may well be a relevant selection criterion, there are little or no data for most devices, which makes it impossible to judge their properties.

Environmentally friendly

This criterion may be important from a society perspective, but there is very little, if any, published information on the devices.

CONCLUSIONS

Large differences are observed in the scores of the devices. It seems logical to limit the number of different devices that are used in the treatment of COPD through regional or local formulary decisions. This results in a smaller number of different devices used by individual patients, which will likely result in better treatment results through fewer inhalation errors. Also, reducing the number of different devices prescribed by physicians and dispensed by pharmacists will make it easier to standardise inhalation instructions, which may even improve treatment outcomes further.

Key messages

What is already known on this subject

- Many inhalation devices are available for the treatment of chronic obstructive pulmonary disease.
- The use of these inhalers is far from optimal.

What this study adds

- Rational selection of inhalation devices for formulary purposes.
- Standardisation of instruction of patients is easier to organise with fewer devices.

Collaborators Lung Alliance Netherlands working party on COPD devices.

Contributors The first manuscript was set up by RJ and JK. The manuscript was debated extensively with EM and RD. JK, EM and RD discussed their experiences with the various inhalers. The resulting article was discussed in the LAN working party and the final manuscript was agreed by all four authors.

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