Rational Selection of valved holding chambers in the treatment of COPD or Asthma by means of the system of objectified judgement analysis

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Abstract

Valved inhalation chambers are important instruments to increase the available dose of pressurized metered dose inhalers, in this study inhalation chambers are 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 inhalation chambers are defined and judged by a panel of experts and each selection criterion is given a relative weight. The following inhalation chambers were included: Aerochamber, Inspirachamber, Optichamber, Volumatic and Vortex. Selection criteria were: Transparancy, Feedback system in case of too forceful inhalation, Antistatic properties, Dose delivery, Availability of mouth masks, Easy to carry, Suitability for children and inclusion in Summaries of Product Characteristics of metered dose inhalers.

Aerochamber showed by far the highest score. If performed well on all selection criteria. Vortex and Optichamber also performed well. Volumatic showed the lowest score.

Keywords: Asthma; COPD; Valved Holding; Aerochamber

Introduction

Inhalation therapy is the cornerstone of the drug treatment of patients with asthma and chronic obstructive lung disease (COPD). There are four main groups of dosage forms: metered dose inhalers (PDMIs), dry powder inhalers (DPI), soft mist inhalers and nebulizers. In line with (inter) national guidelines, PDMIs are usually prescribed in combination with an inhalation chamber in order to optimize lung deposition, to facilitate use and reduce the chance of local side effects, especially for inhaled corticosteroids. About 600,000 patients in the Netherlands use an inhalation chamber (data on file Benu pharmacies).

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 and asthma is multi factorial, including understanding of the disease by the patient, physician-pharmacist-patient interactions, incorrect inhalation techniques and personal factors by the patient. A poor inhalation technique may lead to sub optimal treatment, more exacerbations, hospitalizations 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 standardize the inhalation instructions.

This study aims to develop a set of rational and transparent selection criteria for inhalation chambers.

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 chambers for the maintenance treatment of COPD in the Netherlands. The first draft of the article was prepared by authors JK, PH and RJ and extensively discussed with author RD.

Inclusion and exclusion criteria

This analysis was performed to compare inhalation chambers, in combination with PMDIs.

Applied methodology

In this study inhalation chambers are compared by means of the SOJA method

The System of Objectified Judgement Analysis (SOJA) method is a model for rational drug selection. The relevant selection criteria for inhalation chambers 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 [5].

Selection criteria

The following selection criteria were applied.

table a

Criterion	Relative weight
Transparancy	50
Feedback system in case of too forceful inhalation	50
Antistatic properties	300
Dose delivery	300
Availability of mouth masks	50
Easy to carry	100
Suitability for children	50
Included in SPC's of pMDIs	100
Total score	1000

The following devices were included in the analysis.

table b

Aerochamber
Inspirachamber
Optichamber
Volumatic
Vortex

The Spacechamber was not included in the set of valved holding chambers, because it is no longer available in the Netherlands.
The Able Chamber was also not included, because this is not available in the Netherlands.

Selection criteria

Transparency

- Transparency of the spacer is an advantage. The patient then experiences more feedback in the sense that the spray and the valve are visible from the PMDI. If the spray is not visible, the care recipient might press the PMDI a second time if in doubt.
- Furthermore, the user notices more quickly that the spacer chamber is dirty and has to be cleaned.
- The more transparent, the better. An inhalation chamber which is completely transparent scores 100%, whereas a chamber, which is not at all transparent does not score for this criterion.
- Inhalation chambers, which are not fully transparent score in between 0% and 100%.

Feedback system

- Feedback when inhaling too strongly is nice because it can prevent deposition in the throat. It is therefore and advantage when the patient receives feedback in case of inhaling too strongly.
- Some inhalation chambers have a feedback system in the form of a whistle signal. This must be interpreted correctly because the whistle signal is audible if you inhale too forcefully.
- In addition, the whistle signal depends on the type of chamber and the internal resistance of the pMDI.
- Internal resistance of the chamber plays a role in this.

Antistatic properties

The antistatic properties have the advantage that significantly less aerosol particles are lost to the spacer wall. This means that the available dose for the patient is considerably less if the spacer does not have antistatic properties.

Methods

The spacer must be cleaned in a mild detergent solution weekly and either rinsed with water depending of the antistatic properties (drip and dry method) or cleaned in a mild detergent solution without rinsed water (drip and rinsed method). Only the antistatic spacers can be rinsed with water. In case of non-antistatic spacers, it is advised to clean without rinsing water.

Dose delivery

- Unfortunately, no clinical studies are available regarding the effects of the devices on clinically relevant criteria, such as exacerbations, hospitalizations or mortality.
- The only studies that are available deal with the effects on dose delivery of bronchodilators and inhaled corticosteroids.
- This was scored as follows: the inhalation chambers with the lowest delivery did not score, whereas the one with the highest delivery was assigned 100%. The scores for the other devices were obtained by linear intrapolation.

Availability of mouth masks

Some categories of patients may benefit from a mask instead of a mouthpiece, such as babies and patients with dementia. There are no comparative data to the best of our knowledge. Ranking will depend on the setting of the patients (young children, elderly patients in a nursing home).

Easy to carry

- It is important that an inhalation chamber has a limited size, in order to make it easy to carry. The lower the volume, the better.
- The chamber with the lowest volume received 100% and the chamber with the highest volume did not score.

Suitability for children

It is important that a chamber is approved for use in children. This was scored as such.

Included in SPC's of PMDIs

The European Medicines Agency (EMA) recommends that with each PMDI data are shown on the in vitro outcomes with at least one specific spacer. On the basis of this data an inhalation chamber is recommended in the Summary of Product Characteristics (SPC) of the PMDI. In case of substitution of a spacer solid equivalence data must be shown by the producer of dose delivery and particle size distribution. Also the Medicines Evaluation Board (CBG) takes the position (found in the SPC of various generic PMDIs) that spacers cannot be interchanged because "changing spacers may result in changes in dose delivery to the lungs.

It is therefore an advantage when an inhalation chamber has been tested in a wide range of PMDIs. This was scored as follows

Included in the SPC of

SABA:	15%
SAMA:	15%
SABA/SAMA:	10%
LABA:	10%
LAMA:	10%
LABA/LAMA:	10%
LABA/ICS:	10%
ICS:	10%
Triple:	10%

Results

Transparency

The properties of the inhalation chambers are summarized below.

table c

	Fully transparant	Semi transparant	Non transparant	Score
Aerochamber	Yes			100%
Inspirachamber		Yes		75%
Optichamber	Yes			100%
Volumatic	Yes			100%
Vortex			Yes	0%

Feedback system

The properties of the inhalation chambers are summarized below.

table d

	Whistle (80%)	Visible flow indicator for the healthcare provider (20%)	Score
Aerochamber	Yes	Yes	100%
Inspirachamber	Yes	Yes*	85%
Optichamber	Yes	Yes	100%
Volumatic	No	No	0%
Vortex	No	No	0%

The visual flow indicator shows the inspiration and expiration flow of the patient during the inhalation which is very helpful to instruct the patient in a proper way. One manufacturer* build the flow indicator only in the mouth mask and this is still useful to check if the mouth mask is placed correctly but gives no flow indicator information without this mouth mask. Mouth masks are used in a minority of patients.

Antistatic properties

The antistatic properties of the valved holding chambers are quite different. This is because there are spacers available that do bear the label that they are anti-static, but the degree of the anti-static character differs considerably. In addition, there are also spacers on the market that do not have these anti-static properties.

table e

	Not antistatic	Limited antistatic	Antistatic	Score
Aerochamber			x	100%
Inspirachamber		x		50%
Optichamber			x	100%
Volumatic	x			0%
Vortex			x	100%

Cleaning procedure

The desired cleaning procedure depends on the antistatic properties of the respective chambers. If the chamber is not or only slightly antistatic, it should be cleaned in a soap solution, not rinsed and then allowed to air dry. The dried soap solution provides the antistatic character. This does not only apply to weekly cleaning but also to the first use [6]. When the spacer is antistatic, it can be rinsed during the weekly cleaning and special pre-treatment before first use is not necessary.

Results

Dose delivery

The study of Hagedoorn., et al. [6] was used for comparison of the inhalation chambers. Delivered doses of salbutamol (Ventolin) and beclomethasone (Qvar) from different antistatic valved holding chambers after rinsing or drip-drying. The highest delivery was found for beclomethasone drip dried for the Vortex (67%). This was assigned a score of 100%. The lowest delivery was seen for the salbutamol drip dried for the Optichamber (13%). This did not score. The scores were calculated as follows.

table f

	Salbutamol rinsed	Salbutamol drip dried	Beclomethasone rinsed	Beclomethasone drip dried
Aerochamber	35% (32-37)	33% (32-36)	61% (54-67)	58% (50-62)
Inspirachamber	13% (13-14)	27% (15-36)	31% (21-40)	64% (53-70)
Optichamber	22% (17-26)	19% (16-20)	52% (41-56)	49% (42-56)
Volumatic	NA	NA	NA	NA
Vortex	30% (26-35)	32% (26-38)	58% (47-70)	67% (56-75)

table g

	Salbutamol rinsed	Salbutamol drip dried	Beclomethasone rinsed	Beclomethasone drip dried	Mean	Score after intrapolation
Aerochamber	41%	37%	89%	83%	63%	100%
Inspirachamber	0%	26%	33%	93%	38%	60%
Optichamber	15%	9%	72%	67%	41%	65%
Volumatic	0%	0%	0%	0%	0%	0%
Vortex	31%	33%	83%	100%	62%	98%

Availability of mouth masks

table h

	Masks	Score
Aerochamber	Baby / Children 1 - 4 / Children > 5 / Adults small / Adults normal / Adult large	100%
Inspirachamber	Soother / Inspiramask	100%
Optichamber	Adults / Children	100%
Volumatic		0%
Vortex	0 - 2 years / 2 - 4 years / > 4 years / Adults	100%

Easy to carry

table i

	Volume	Score
Aerochamber	149 ml	98%
Inspirachamber	161 ml	97%
Optichamber	140 ml	100%
Volumatic	750 ml	0%
Vortex	194 ml	91%

Suitability for children

table j

	Baby	Child	Adults	Score
Aerochamber	x	x	x	100%
Inspirachamber	x	x	x	100%
Optichamber	x	x	x	100%
Volumatic	x	x	x	100%
Vortex	x	x	x	100%

Obviously, this criterion is only relevant for asthma and not for COPD treatment.

Results

Included in SPC's of PMDIs

There are considerable differences between the inhalation chambers regarding the clinical documentation in the SPCs.

table h

	Aerochamber	Inspirachamber	Optichamber	Volumatic	Vortex
SABA	Salbutamol			Ventolin	Salbutamol
SAMA	Ipratropium				
LABA	Salmeterol			Salmeterol	
LAMA					
LABA/LAMA					
LABA/ICS	Airflusal Flutiscasone/salmeterol Flutiform Foster Seretide Symbicort			Airflusal Flutiscasone/salmeterol Seretide	
ICS	Alvesco			Flixotide	
Triple	Trimbow				
Score	80%	0%	0%	45%	15%

Score

The SOJA score for inhalation chambers in COPD and asthma treatment is presented below.

table I

	Aerochamber	Inspirachamber	Optichamber	Volumatic	Vortex	Weight
Transparency	50	38	50	50	0	50
Feedback system	50	43	50	0	0	50
Antistatic properties	300	150	300	0	300	300
Dose delivery	300	180	195	0	294	300
Mouth mask	50	50	50	0	50	50
Easy to carry	98	97	100	0	91	100
Suitability for children	50	50	50	50	50	50
Included in SPCs of PMDIs	80	0	0	45	15	100
Score	978	608	795	145	800	1000

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 chambers) 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 fulfills the requirement for each criterion is studied. Each criterion is given a relative weight (i.e., 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 to the hypothetical 'ideal ' device from that group, which is assigned the full relative weight for each criterion. The ideal inhalation chamber will have to score 100% on all selection criteria.

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 program, 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 program then computes the ranking scores for the drugs in the group.

Outcome

Substantial differences were seen in the overall scores, Aerochamber showed the highest score, followed by Vortex and Optichamber. Volumatic showed by far the lowest score.

Strength and limitations of the methodology

In most cases SOJA scores are derived from a large number (between 50 and 400) of references, including double-blind comparative studies, systematic reviews and meta-analyses. In this case no clinical studies are available regarding the effects of valved inhalation chambers on clinically relevant endpoints, such as exacerbations and hospitalizations, let alone comparative studies between two or more inhalation chambers on these endpoints. That is the reason why so few references were included in this article.

It should be taken into consideration that this analysis is limited to the inhalation chambers. In clinical practice, patient related factors play an important role, such as personal preferences of the patient.

The evaluation of criteria in the SOJA method is highly standardized in order to promote unbiased judgment of drugs from various pharmacotherapy 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 judgment may be arbitrary for most, if not all, criteria. This is the case with any method used to quantify properties of drugs or devices. 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. 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 program 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. This could be the case for the criterion availability of mouth masks, which are relevant for a small minority of patients (such babies and patients with dementia).

It offers advantages for the healthcare provider when an inhalation chamber can be autoclaved. This makes it possible to re-use the inhalation chamber during lung function tests. This criterion was not included in our set of criteria, because these are aimed at patients and not at healthcare providers.

In the most unfavorable case, therefore a factor 4 difference between the "best and worst" combination of PMDI and inhalation chamber, which should be relevant, but the clinical impact was not investigated. The major differences between the spacers are largely in the degree of their anti-static character, despite the fact that they are all labeled as anti-static. This was scored under the criterion dose delivery

To the best of our knowledge, there are no comparative studies comparing VHCs to each other on clinical endpoints like dyspnea scores and exacerbations.

The main outcome of this matrix may be that major steps can be made in reducing the number of different inhalation chambers, thereby allowing standardized 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.

Discussion

Several potential selection criteria were not used in this analysis

Acquisition cost

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.

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.

Environmentally friendly

This criterion may be important from a society perspective, but there is very little, if any, published information on the inhalation chambers.
The disposable spacers are not included in these scores because they are rarely or not prescribed and there is also insufficient data available to include them for the SOJA method.

Conclusions

Large differences are observed in the scores of the inhalation chambers. Aerochamber showed by far the highest score, followed by Vortex and Optichamber. Volumatic showed by far the lowest score. 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 inhalation chambers 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 further improve treatment outcomes.

Several authors recommended not to switch easily between valved inhalation chambers, because of differences in dose delivery [7-9].

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